

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Prime Medicine, Inc.
(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of incorporation or
organization)

2836
(Primary Standard Industrial Classification Code Number)

84-3097762
(I.R.S. Employer Identification No.)

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(617) 564-0013
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Securities Exchange Act of 1934.

Large Accelerated filer	<input type="radio"/>	Accelerated filer	<input type="radio"/>
Non-accelerated filer	<input checked="" type="radio"/>	Smaller reporting company	<input checked="" type="radio"/>
		Emerging growth company	<input checked="" type="radio"/>

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant files a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act, or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the Securities and Exchange Commission declares our registration statement effective. This preliminary prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated _____, 2022

Preliminary prospectus



Common stock

This is an initial public offering of shares of common stock by Prime Medicine, Inc. We are offering _____ shares of common stock. We expect that the initial public offering price will be between \$ _____ and \$ _____ per share.

Prior to this offering, there has been no public market for our shares. We have applied to list our common stock on The Nasdaq Global Market under the symbol “PRME.”

We are an “emerging growth company” and a “smaller reporting company” under the federal securities laws and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and for future filings.

	Per share	Total
Initial public offering price	\$ _____	\$ _____
Underwriting discounts and commissions ⁽¹⁾	\$ _____	\$ _____
Proceeds, before expenses, to Prime Medicine, Inc.	\$ _____	\$ _____

(1) See “Underwriting” beginning on page [251](#) of this prospectus for additional information regarding underwriting compensation.

We have granted the underwriters an option for a period of 30 days to purchase an additional _____ shares of our common stock from us at the initial public offering price, less underwriting discounts and commissions.

Investing in our common stock involves a high degree of risk. Before buying any shares, you should read carefully the discussion of the material risks of investing in our common stock under the heading “Risk Factors” starting on page [16](#) of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities, or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock to the purchasers on or about _____, 2022.

J.P. Morgan

Goldman Sachs & Co. LLC

Morgan Stanley

Jefferies

_____, 2022

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We have not, and the underwriters have not, authorized anyone to provide any information or to make any representation other than those contained in this prospectus, any amendment or supplement to this prospectus or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares of common stock offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus, any amendment or supplement to this prospectus or any applicable free writing prospectus is current only as of its date, regardless of its time of delivery or any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside the United States: We have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside the United States.

Market data and certain other statistical information used throughout this prospectus are based on independent industry publications, governmental publications, reports by market research firms, or other independent sources that we believe to be reliable sources. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. We are responsible for all of the disclosure contained in this prospectus, and we believe that these sources are reliable; however, we have not independently verified the

information contained in such publications. While we are not aware of any misstatements regarding any third-party information presented in this prospectus, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties, and are subject to change based on various factors, including those discussed under the section entitled “Risk Factors” and elsewhere in this prospectus. Some data are also based on our good faith estimates.

We intend to apply for various trademarks that we use in connection with the operation of our business. This prospectus may also contain trademarks, service marks and trade names of third parties, which are the property of their respective owners. Our use or display of third parties’ trademarks, service marks, trade names or products in this prospectus is not intended to, and does not imply a relationship with, or endorsement or sponsorship by us. Solely for convenience, the trademarks, service marks and trade names referred to in this prospectus may appear without the TM or SM symbols, but the omission of such references is not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the right of the applicable owner of these trademarks, service marks and trade names.

Through and including _____, 2022 (25 days after the date of this prospectus), all dealers that buy, sell or trade our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the obligation of dealers to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

PROSPECTUS SUMMARY

This summary highlights information contained in greater detail elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our consolidated financial statements and the related notes thereto included elsewhere in this prospectus. You should also consider, among other things, the information set forth under the sections entitled “Risk Factors,” “Special Note Regarding Forward-Looking Statements,” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” in each case included elsewhere in this prospectus. Unless the context otherwise requires, we use the terms “Prime Medicine,” the “Company,” “we,” “us,” “our,” and similar designations in this prospectus to refer to Prime Medicine, Inc. and, where appropriate, our subsidiary.

Overview

We are a biotechnology company committed to delivering a new class of differentiated one-time curative genetic therapies, Prime Editors, to address the widest spectrum of diseases by deploying Prime Editing technology, which we believe is a versatile, precise, efficient and broad gene editing technology.

Genetic mutations implicated in disease are diverse and can range from errors of a single base, known as point mutations, to errors that extend beyond a single base, such as insertions, deletions, duplications, or combinations thereof. We believe the ability to alter the human genome at the foundational level may confer the greatest therapeutic impact on human disease.

Gene editing, including platforms such as Prime Editing, is a novel technology that is not yet clinically validated for human therapeutic use. Over the last decade, the field of genetic medicine has evolved tremendously, with groundbreaking advances in gene therapy, cell therapy, RNA therapy, and, more recently, gene editing. These technologies represent dramatic advancements for genetic therapies, but lack the versatility to precisely and efficiently correct the diverse range of mutations or DNA alterations implicated in disease.

Prime Medicine was co-founded by a world-renowned leader in the field of gene editing, David Liu, Ph.D. Dr. Liu was joined as co-founder by Andrew Anzalone, M.D., Ph.D., who conceived of and developed Prime Editing technology. Drawn by the promise of Prime Editing’s ability to transform the field of gene editing, we have assembled a diverse team that has grown to more than 80 people as of December 31, 2021. There are no current plans for Dr. Liu to be an officer or director of our company following this offering. He is expected to continue to provide consulting services to us pursuant to a consulting agreement, which has a current term that runs through September 2025 and accommodates a previous commitment with respect to Beam Therapeutics, Inc., which could result in or may create the appearance of a conflict of interest. He is also expected to retain his position and affiliation with the Broad Institute, Inc., Howard Hughes Medical Institute and Harvard University.

We believe our in-licensed and company-owned Prime Editing technology has transformative potential that could change the course of how disease is treated and overcome the challenges associated with current genetic therapies. We in-license our Prime Editing technology pursuant to a license agreement with the Broad Institute, Inc., or Broad Institute. The licenses are limited to the field of prevention or treatment of human disease, and most licenses granted to us under this license agreement are further limited to the prevention or treatment of human disease by editing (including modifying or converting) or targeting DNA *ex vivo*, *in vivo*, or through xeno-transplantation methods, which we refer to as the Prime Broad Field. For more information regarding the scope of our rights and obligations under this license agreement, see the section titled “Business—Our License and Collaboration Agreements—License rights under the Broad License Agreement.”

Our Prime Editing Platform

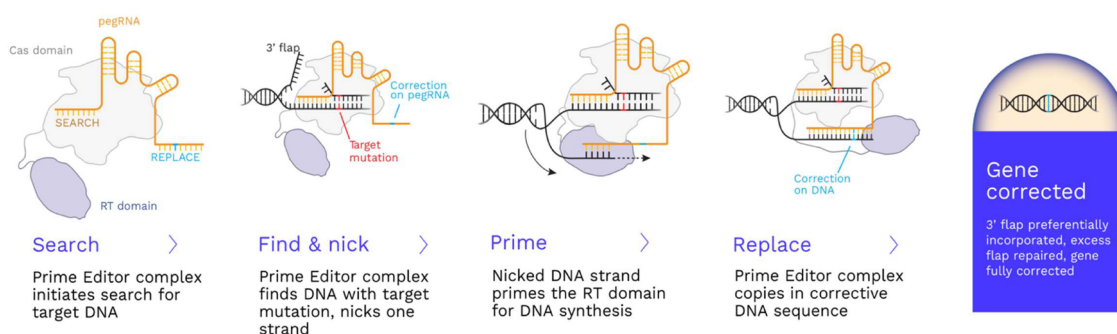
Prime Editing technology, as developed by Dr. Liu and Dr. Anzalone, has broad theoretical potential therapeutic applications. For example, Prime Editing technology has the ability to repair diverse mutations, including all types of point mutations, deletion mutations, insertion and duplication mutations and insertion-deletion mutations. Our analysis of more than 75,000 pathological, or disease-causing, mutations found in the National Center for Biotechnology Information ClinVar Database shows that those addressable by Prime Editing technology account for

approximately 90 percent of genetic variants associated with disease. As such, we believe Prime Editing technology has the theoretical potential for repairing approximately 90 percent of known disease-causing mutations across many organisms, organs and cell types. Because biotechnology companies can only initiate therapeutic programs for a subset of pathogenic mutations and the associated diseases, we have chosen to strategically focus on disease settings where we believe that Prime Editing technology could offer compelling advantages over both current standard-of-care and novel therapeutic modalities in development. Currently, at Prime Medicine, we are leveraging the breadth of our in-licensed Prime Editing technology to focus on our current portfolio of 18 therapeutic programs.

Prime Editors also have the ability to create permanent modifications at their natural genomic location, resulting in durable edits that are passed on to daughter cells, and retain their native physiological control. Our next generation gene editing technology is capable of a wide variety of precise, predictable and efficient genetic outcomes at the targeted sequence, while minimizing unwanted bystander edits and off-target edits and avoiding double-stranded DNA breaks. Our Prime Editors are designed to make only the right edit at the right position within a gene.

Our novel Prime Editors have two main components that act together to edit DNA: (i) a Prime Editor protein, comprising a fusion between a Cas protein and a reverse transcriptase enzyme, and (ii) a pegRNA, that targets the Prime Editor to a specific genomic location and provides a template for making the desired edit to the target DNA sequence. Prime Editing leverages the established DNA-targeting capabilities of CRISPR-Cas proteins modified to nick, but not cause double-stranded DNA breaks, and combines these with the DNA synthesis capabilities of reverse transcriptase enzymes, which have been engineered to efficiently and precisely copy a pegRNA-encoded edited sequence into target DNA.

Illustration of Editing Mechanism by Prime Editor – No Double-Stranded DNA Breaks



If nuclease gene editing approaches are “scissors” for the genome, and base editors are “pencils,” erasing and rewriting a subset of single letters in the gene, then Prime Editing is a “word processor,” searching for the correct location and replacing or repairing a wide variety of target DNA.

The Importance of Avoiding Double-Stranded DNA Breaks

- **Unlike first-generation nuclease-based technologies, Prime Editors do not generate double-stranded DNA breaks. Emerging literature supports that double-stranded DNA breaks result in many disadvantages, including:**
 - **Lack of editing precision at the target site, leading to many indels.**
 - **More likely to cause off-target edits elsewhere in the genome.**
 - **Can lead to large deletions, structural rearrangements, and chromosomal translocations.**
 - **Can activate p53, leading to apoptosis, and may select for somatic cells with p53 inactivation.**
 - **Can reduce cell viability in edited cells.**

We believe Prime Editing is a versatile, precise, efficient and broad gene editing technology with the following key advantages:



Versatility

Deep and highly differentiated toolbox of editing capabilities to enable a wide variety of therapeutic applications

- Applicability to a wide range of target mutations or alterations of DNA, including all twelve types of single base pair corrections, as well the ability to insert and delete DNA sequences.
- Direct correction of DNA with no requirement for delivery of the corrected DNA sequence in most applications of Prime Editing.
- Greater optionality with respect to editing site availability versus other approaches, due to a larger editing window.
- Programmable, which means that both the specified target location in the genome and the directed type of edit can be easily modified by replacing the Prime Editing guide RNA, or pegRNA, element of a Prime Editor.
- Multiple potential therapeutic applications, including but not limited to targeted gene correction, gene silencing or activation such as by altering the regulatory regions of genes, inserting or creating premature stop codons, or by modifying splicing sequences, hotspot region replacement, multiplex editing of several genes simultaneously, and wild-type variant modification to protect against or modify risk for a disease.
- Capable of inserting, deleting or inverting kilobase amounts of genomic DNA by combining Prime Editing with proprietary recombinase technology.

Ability to Correct All Twelve Potential Base Pair Mutations as well as to Address Sequence Insertions and Deletions

Point Mutation:
Convert any base pair into any other

Base Pair Changed

Deletion Mutation:
Extra base pairs can be removed

Extra Sequence Removed

Deletion Mutation:
Missing base pairs can be inserted

Missing Sequence Added

Precision

Highly specific and predictable gene editing

- Designed to specifically make only the directed type of Prime Edit at the desired target location.
- Avoidance of the potential negative impacts associated with double-stranded breaks, which results in minimal to potentially no unwanted on-target or off-target by-products and preservation of cell viability.
- Limited potential for bystander editing at the target site, a potential unwanted effect of base editing.

Efficiency

Durable gene edits with potential for superior therapeutic activity

- Single treatment resulting in permanent corrections of disease-causing mutations by restoring the targeted gene back to its wild-type sequence.
- Permanent, durable edits that persist in a cell and are passed along to daughter cells, creating potential for a life-long, "once and done" therapeutic outcome.
- Preservation of natural regulation and a normal number of copies of the gene in the cell by modification of genes in situ, or in their native genomic setting.
- Highly efficient, effecting therapeutically relevant levels of precise gene correction generally unachievable by nuclease-based methods.

Breadth

Ability to address a wide range of diseases in multiple tissue types

- Applicability in a wide range of human cells, including both dividing and non-dividing human cells, a wide range of organs and cell types, as well as in a wide variety of other organisms, including primary cells such as hepatocytes, hematopoietic stem cells and neurons.
- Potential ability to repair approximately 90% of all types of mutations known to cause genetically driven disease.
- Broad therapeutic potential, including rare, genetic diseases as well as severe, chronic, and acute diseases. Beyond correcting disease-causing mutations, potential for gene modification to edit in naturally occurring variations within genes known to protect against or modify risk for a disease.

Percentage Distribution of Pathological Genetic Variants Associated with Disease

Variant Type	Percentage
Transition Point Mutation	30.0%
Deletion	26.0%
Transversion Point Mutation	20.0%
Duplication	8.2%
Copy Number Loss	6.8%
Copy Number Gain	3.6%
Insertion	2.5%
Insertion and Deletion	2.0%
Other	0.9%

An important element of our capability is leveraging high-throughput screening and machine learning, coupled with automation of workflow, to build a data-driven model for designing optimized Prime Editing systems that can potentially accelerate our therapeutic candidate development and enhance efficiency. We have also optimized individual subcomponents of our Prime Editors to enhance their capability beyond first generation Prime Editing. Some notable developments include engineered pegRNAs and DNA mismatch repair modulation to further enhance efficiency of our Prime Editors where appropriate, and expanding the array of gene edits by incorporating recent innovations in Prime Editing, including dual-flap Prime Editing and targeted integration, deletion and inversion of gene-sized DNA.

We believe that we have built a leading position in Prime Editing by consolidating technology and intellectual property in the field, as well as by establishing extensive internal capabilities to deliver on the promise of this next generation gene editing technology.

Our Strategy

Our goal is to transform the lives of patients with debilitating diseases through the application of our ground-breaking Prime Editing platform and technology. Our key focus is on patients. We are committed to developing safe and efficient therapeutics using Prime Editing approaches to address high unmet need across a broad spectrum of diseases, from rare genetic diseases to severe, chronic and acute diseases, and ultimately to prevent disease before it occurs. Key components of our strategy are as follows:

- Deliver the broadest potential of Prime Editing in the service of patients.
- Deploy our technology to extend the application of one time curative therapeutics to areas that we believe were not addressable before.
- Advance our pipeline while simultaneously enhancing, validating and enabling our Prime Editing platform.
- Continue to push the frontier of innovation in gene editing by optimizing and expanding our Prime Editing technology and capabilities.
- Opportunistically evaluate synergistic and value-creating partnerships to maximize the broad potential of our platform.
- Lead with our culture of integrity, ethics, innovation and respect in everything we do.

Our Portfolio

To maximize the potential of our Prime Editing technology to provide one-time curative genetic therapies to the broadest set of diseases possible, we have purposefully built a diversified portfolio organized around four strategic indication categories, each set of indications chosen to deliver a different strategic goal:

- Immediate target indications: Deliberately chosen as potentially the fastest, most direct path to demonstrate technological success of Prime Editing in patients. We are initially focusing on diseases of the blood via *ex vivo* delivery to hematopoietic stem cells and on diseases of the liver, the eye and the ear.
- Differentiation target indications: Aimed to create therapeutics to address the underlying cause of severe genetic diseases with therapeutics that we believe could not have been created before, especially using other gene-editing approaches. These include repeat expansion diseases, or diseases where expansion of pathological DNA repeats results in serious disease.
- “Blue sky” indications: Intended to push new and innovative technological developments in Prime Editing and extend its application beyond rare genetic diseases and towards our goal of more broadly addressing human disease. These programs remain in the early stages of conception and will become an increasing focus over the next few years.

- “March up the chromosome” approaches: Represents opportunities to deliver upon our overarching vision to ultimately treat all patients with a disease and correct the full set of mutations in a particular gene. This category overlaps with other strategic indication categories, where most of our disclosed indications across other categories have a plan that can accommodate expansion opportunities to address additional mutations in that disease.

To unlock the full potential of our Prime Editing technology across a wide range of therapeutic applications, we are pursuing a comprehensive suite of clinically validated delivery modalities in parallel. For a given tissue type, we intend to use the delivery modality with the most compelling biodistribution. Our initial, immediate programs rely on three distinct delivery methodologies: (a) electroporation for efficient delivery to blood cells and immune cells *ex vivo*; (b) lipid nanoparticles, or LNPs, for non-viral *in vivo* delivery to the liver and potentially other organs in the future; and (c) AAV for viral delivery *in vivo* to the eye and ear.

We have constructed our portfolio of 18 therapeutic programs, including one partnered program, across our first two strategic indication categories in disease settings where the unique characteristics of Prime Editing could offer compelling advantages over current standard-of-care and novel therapeutic modalities in development. Our current portfolio includes the following 18 programs:

STRATEGIC CATEGORY	TARGET TISSUE	INDICATION	DELIVERY	DISCOVERY	IND-ENABLING	Phase 1	Phase 2	Phase 3	PARTNER
IMMEDIATE	BLOOD	Sickle Cell Disease	<i>ex vivo</i>						
		Chronic Granulomatous Disease	<i>ex vivo</i>						
		Fanconi Anemia	<i>ex vivo</i>						
	LIVER	Wilson's Disease	LNP						
		Glycogen Storage Disease 1b	LNP						
	EYE	Retinitis Pigmentosa/Rhodopsin	AAV						
		Retinitis Pigmentosa/Usher Syndrome	AAV						
	EAR	Usher's Syndrome Type 3	AAV						
		Non-Syndromic Hearing Loss – GJB2	AAV						
	DIFFERENTIATION: REPEAT EXPANSION DISEASES	NEURO-MUSCULAR	Friedreich's Ataxia	viral/non-viral					
Myotonic Dystrophy Type 1			viral/non-viral						
Amyotrophic Lateral Sclerosis			viral/non-viral						
Oculopharyngeal Muscular Dystrophy			LNP						
Fragile X Syndrome			viral/non-viral						
Huntington's Disease									
EYE	Fuchs' Endothelial Corneal Dystrophy	viral/non-viral							
DIFFERENTIATION: OTHER	MUSCLE	Duchenne Muscular Dystrophy	AAV						
	LUNG	Cystic Fibrosis	LNP						

• AAV = adeno-associated viral vectors; LNP = lipid nanoparticles

Key Achievements and Upcoming Milestones

We have established preclinical proof-of-concept *in vivo* with long term engraftment of *ex vivo* Prime Edited human CD34 cells in mice in our partnered sickle cell disease program, where we have precisely corrected the disease-causing mutation. This program is closely followed by Prime Editing for patients with chronic granulomatous disease where we have designed Prime Editors with high levels of correction of the disease-causing mutation in the cells that must be targeted. We have demonstrated Prime Editing of cells *in vitro* at predicted therapeutically relevant levels for all of our remaining named programs. We have designed proprietary high throughput methods to identify highly efficient Prime Editors and have advanced the reach and efficiency of the Prime Editing technology. We have incorporated new advances in Prime Editing technology enabling us to establish Prime Editors with greater than 77 percent precise removal of pathological expansion repeats in five different repeat expansion diseases.

We have not completed any *in vivo* studies to date. We expect to achieve preclinical proof-of-concept *in vivo*, which would include data from *in vivo* rodent studies in several programs in _____ and non-human primate studies in several programs in _____ through _____. If successful, this will allow us to initiate investigational new drug, or IND, enabling studies for several of our lead programs beginning in _____, leading to initial IND submissions beginning in _____. Since we are in early stages of product candidate development, we will provide

an update on our timelines in , with the potential to accelerate these programs. We also anticipate continuing to name additional programs as they advance over the next few years.

Selected Pipeline Programs

To highlight the breadth and diversity of our 18 programs, detailed below are selected example programs currently in development in unique target tissues. For a more detailed review of all of our pipeline programs, see the section entitled “Business.”

Indication	Target Tissue	Delivery
Chronic Granulomatous Disease	Blood	<i>ex vivo</i>
Wilson’s Disease	Liver	LNP
Retinitis Pigmentosa	Eye	AAV
Friedreich’s Ataxia	Neuromuscular	Viral / non-viral
Myotonic Dystrophy	Neuromuscular	Viral / non-viral

Chronic Granulomatous Disease – Correcting the NCF Gene via ex vivo Electroporation of Hematopoietic Stem Cells

Chronic granulomatous disease, or CGD, is a rare inherited hematologic disorder that results in a failure of immune defense against extracellular pathogens. In CGD patients, myeloid cells lack a functional NADPH oxidase, or NOX2, complex, which renders patients susceptible to prolonged and recurrent bacterial and fungal infections and inflammatory complications. CGD causative mutations occur in approximately one in 200,000 births in the United States, and most children are diagnosed within the first three years of life.

We are using Prime Editing in *in vitro* studies to precisely correct the ΔGT mutation in one copy of the *NCF1* gene to restore p47^{phox} protein expression and NOX2 activity. We have identified a series of Prime Editor complexes that demonstrate approximately 55 percent precise correction at the NCF gene in the target cells, or human primary HSCs. Following cloning of myeloid-differentiated clones after 14 days, clonal analysis showed that nearly 90 percent of clones had received at least one precise corrective edit to ΔGT. This greatly exceeds the approximately 15 percent precise editing target threshold that is predicted to provide a clinical benefit. We intend to demonstrate that we have restored NOX2 protein function in patient-derived myeloid cells as a result of Prime Editing.

Wilson’s Disease – Correcting the ATP7B Gene via LNP Delivery to the Liver

Wilson’s disease, or WD, is a devastating rare disease of the liver, with manifestations throughout the body, that is caused by copper accumulation. Most people are diagnosed with WD between ages five and 35 years. We estimate it affects at least 25,000, with some studies suggesting more than 50,000 patients in the United States and Europe annually. WD is caused by mutations in both genomic copies of the ATP7B gene, which encodes a copper transporter that removes excess copper. Two predominant mutations have been described in Wilson’s disease:

1. H1069Q, found in approximately 40 percent of all patients in the United States and 18 to 72 percent of all patients in Europe; and
2. R778L, frequently found in Asian patients and those of Asian ancestry, reported in 46 percent of Chinese, 38 percent of Korean, and 25 percent of Japanese Wilson’s disease patients.

Our initial approach to WD is to correct the prevalent mutations ATP7B H1069Q and R778L in hepatocytes of the liver at their genomic location. Correction of the gene in the liver should address all aspects of the disease, by normalizing the process in which the body removes copper in the liver. We have identified Prime Editors that

demonstrate precise correction of H1069Q ATP7B in 75 percent of cells in human hepatocyte lines and have observed similar results in primary human hepatocytes with the R778L mutation. This high level of precise editing in primary hepatocytes meets our threshold for predicted clinically relevant effects, and results in significant protection from copper toxicity in cell-based assays. We are currently conducting preclinical studies to confirm the ability to correct the human R778L sequence and the human H1069Q sequence in mouse models, using LNP technology.

Retinitis Pigmentosa Caused by Rhodopsin Mutations – Correcting the RHO gene via AAV Delivery to the Eye

Retinitis pigmentosa, or RP, is a subset of related inherited retinal diseases, or IRDs, where disease progression is characterized by loss of night vision in childhood or early adulthood, followed by loss of peripheral vision in adulthood characterized by constricting visual field, and eventual loss of central vision leading to blindness later in life. One of the most common IRDs is autosomal dominant RP, or adRP, caused by mutations in RHO which encodes the light sensitive Rhodopsin protein, or RhoP, expressed by rod photoreceptors of the retina. The disease is dominant, or manifests even with mutations to just one of the two gene copies in the genome. Approximately six to seven thousand patients have adRP in the United States caused by RHO mutations. We are initially focused on one predominant mutation, P23H; the P23H mutation is highly prevalent in the United States, causing disease in approximately 30 percent of all patients (approximately 2,000-2,500).

Our initial approach to adRP is to correct the RHO P23H mutation in rod photoreceptors of the retina at their natural genomic location. We believe a Prime Editor that corrects P23H will also correct rarer, nearby P23L and P23A mutations. Natural history studies suggest that correction of only 25 percent of rod photoreceptors would have an important clinical impact, because when 25 percent or more of rods are preserved, there is full preservation of cone photoreceptors that are critical to central vision. We have identified Prime Editors that demonstrate approximately 65 percent precise correction of the RHO P23H mutant locus. We are currently conducting preclinical studies to confirm that Prime Editing of P23H will correct healthy donor human retinal explants. We also plan to evaluate our approach in non-human primate studies where the Prime Editors will be delivered by subretinal injections to mimic the anticipated route of administration in the clinic.

Friedreich's Ataxia: Correcting Repeat Expansions in the FXN Gene

Friedreich's Ataxia, or FRDA, is a multisystem, autosomal recessive neurodegenerative disorder affecting the central and peripheral nervous systems as well as the heart and other organs. FRDA significantly reduces survival for patients, with the mean age of death being 39 years. FRDA is characterized by progressive ataxia, or lack of muscle control or coordination of voluntary movements, with mean age at onset of approximately five to 16 years. FRDA is caused by GAA-repeat nucleotide sequence expansions in intron 1 of the FXN gene encoding the frataxin protein, which plays important roles in mitochondria. The expanded repeats occur early in the gene, and cause disruptions in transcribing the FXN gene into RNA resulting in low levels of the frataxin protein. In the United States, it is estimated that around 4,000 individuals are affected by FRDA, while there are 15,000 to 94,000 patients globally.

Our Prime Editing technology enables us to precisely remove the expanded repeat sequences that cause FRDA. Our initial experiments are encouraging. Using the dual-flap technology with a Prime Editor targeted both upstream, or before the GAA pathological repeats, and downstream, or after the repeats, we have precisely removed the repeat sequence from intron 1 of the FXN gene to restore normal FXN regulation with more than 65 percent efficiency. In addition, in our models in donor- and patient-derived induced Pluripotent Stem Cells, or iPSCs, we measure the amount of frataxin expression in both FRDA patient cells, as well as cells derived from healthy donors. As expected, we demonstrated that patient cells have low levels of frataxin, and healthy donor cells have high levels of frataxin. When we Prime Edited the FRDA patient cells in this model, Prime Editors restored levels of frataxin towards that seen in healthy donor cells.

We have established preliminary methods to deliver Prime Editors to terminally differentiated cardiomyocytes and plan to establish editing and functional recovery of frataxin expression in this cell system. Then, to ultimately deliver Prime Editors to heart and other tissues, we expect initially to rely on the tropism of AAV capsids, each

optimized to deliver our Prime Editors to the central nervous system or heart. We are currently optimizing the AAVs for expression in neurons and glial cells as our first focus.

Myotonic Dystrophy – Correcting Repeat Expansions in the DMPK Gene

Myotonic Dystrophy type 1, or DM1, is a common autosomal dominant muscular dystrophy among people of European ancestry and is principally a muscle disease affecting skeletal and cardiac muscle but has multisystem manifestations. Patients often initially present with muscle weakness. DM1 is caused by expanded CTG repeats in the 3' UTR of one copy of the DMPK gene. When transcribed into RNA, the expanded repeat nucleotides in the case of DM1 sequester critical splicing factors, thereby preventing the correct function of many genes that regulate cell function. Recent newborn screening studies indicate that the true prevalence of DM1 is 1:2,100 (approximately 140,000 patients in the United States).

Our dual-flap Prime Editing technology enables the removal of the expanded repeat sequences that cause disease. Our goal in DM1 is to leverage our Prime Editing technology to precisely remove the repeat sequence from the UTR region of the DMPK gene, to restore DMPK regulation and expression of DMPK protein back to normal levels. The primary target tissues are cardiac and skeletal muscle, which we believe could have a transformative effect on patients; CNS is an important secondary target tissue. We have performed screens to identify pegRNA pairs that achieve highly efficient and precise removal of the expanded repeats and have demonstrated precise removal of pathological repeats from the DMPK gene. We have established precise removal of the smaller number of repeats in healthy cell lines with more than 80 percent efficiency. In patient derived stem cells, which contain approximately 1,600 pathological repeats, we have demonstrated precise removal of repeats with more than 20 percent efficiency, with our best Prime Editors achieving up to approximately 66 percent precise editing and removal of the pathological repeats.

We are developing patient-derived stem cell-derived models of disease. As a first step, we have generated patient-derived cardiomyocytes and patient fibroblasts in which to evaluate dual-flap Prime Editing. We have established preclinical methods to deliver Prime Editors to terminally differentiated cardiomyocytes and will establish editing and functional recovery in this cell system. In parallel, we will perform similar experiments in patient-derived skeletal muscle cells.

Risks Associated with Our Business

- We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.
- We will need substantial additional funding. If we are unable to raise capital when needed, we will be forced to delay, reduce, eliminate or prioritize among our research and product development programs or future commercialization efforts.
- Gene editing, including platforms such as Prime Editing, is a novel technology that is not yet clinically validated for human therapeutic use. The approach we are taking to discover and develop novel therapeutics is unproven and may never lead to marketable products. We may incur unexpected costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidates.
- Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. Because gene editing is novel and the regulatory landscape that will govern our potential product candidates is uncertain and may change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for our potential product candidates.
- We may enter into collaborations with collaborators and strategic partners such as Beam Therapeutics or other third parties for the research, development, delivery, manufacturing and commercialization of Prime Editing technology and certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to capitalize on the market potential of our Prime Editing platform or product candidates.

- If conflicts arise between us and our collaborators or strategic partners, these parties may act in a manner adverse to us and could limit our ability to implement our strategies.
- If we are unable to obtain and maintain patent and other intellectual property protection for any product candidates we develop and for our Prime Editing technology, or if the scope of the patent and other intellectual property protection obtained is not sufficiently broad, third parties could develop and commercialize products and technology similar or identical to ours and our ability to successfully commercialize any product candidates we may develop and our Prime Editing technology may be adversely affected.
- Our rights to develop and commercialize our Prime Editing platform technology and product candidates are subject, to the terms and conditions of licenses granted to us by others. If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business. With respect to our licenses from Broad Institute:
 - Our licenses are subject to Broad Institute’s inclusive innovation model, pursuant to which Broad Institute retains the right, in certain circumstances, to grant to third parties (other than specified competitors of ours) licenses under the licensed patent rights that would otherwise fall within the scope of the exclusive license granted to us.
 - All gene targets, which are any human genes to which a program is directed, are subject to Broad Institute’s march-in license, which means Broad Institute has the right to terminate our license to gene targets under certain conditions and could make one or more gene targets unavailable to us. However, once we initiate a program for a gene target, in accordance with the terms of such license agreement, Broad Institute loses the right to use its march-in license for such gene target, provided we continue to use commercially reasonable efforts to continue to progress such development. As such, we believe that Broad Institute cannot exercise its march-in license with respect to any of our current programs for gene targets because such programs have been initiated in accordance with the terms and requirements of such license agreement.
- The intellectual property landscape around the technologies we use or plan to use, including gene editing technology, is highly dynamic, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating their intellectual property rights, the outcome of which would be uncertain and may prevent, delay or otherwise interfere with our product discovery and development efforts.
- Our owned and in-licensed patent applications and other intellectual property may be subject to priority, inventorship or ownership disputes and similar proceedings. If we or our licensors are unsuccessful in any of these proceedings, we may be required to obtain licenses from third parties, which may not be available on commercially reasonable terms or at all, or to cease the development, manufacture and commercialization of one or more of our product candidates, which could have a material adverse impact on our business.
- The FDA, the EMA and the National Institutes of Health, or NIH, have demonstrated caution in their regulation of gene therapy treatments, and ethical and legal concerns about gene therapy and genetic testing may result in additional regulations or restrictions on the development and commercialization of any product candidates we may develop, which may be difficult to predict.
- Our future success depends on our ability to retain our President and Chief Executive Officer, our Co-Founder, our Chief Scientific Officer, our Chief Technical Officer and other key executives and to attract, retain and motivate qualified personnel.
- We expect to expand our research, development, delivery, manufacturing, commercialization, regulatory and future sales and marketing capabilities over time, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

- We have identified a material weakness in our internal control over financial reporting. If we fail to remediate this material weakness or identify additional material weaknesses in the future or otherwise fail to maintain effective internal control over financial reporting in the future, we may not be able to accurately report our financial condition or results of operations which may adversely affect investor confidence in us and, as a result, the value of our common stock.

Corporate Information

We were incorporated under the laws of the State of Delaware in September 2019 under the name Prime Medicine, Inc. Our principal executive offices are located at 21 Erie Street, Cambridge, MA 02139, and our telephone number is (617) 564-0013.

We have one subsidiary, Prime Medicine Massachusetts Securities Corp., formed in October 2020 under the laws of the Commonwealth of Massachusetts.

Our website address is <https://www.primemedicine.com>. The information contained in or accessible from our website is not incorporated into this prospectus, and you should not consider it part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

Implications of Being an Emerging Growth Company and a Smaller Reporting Company

We qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- being permitted to present only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced “Management’s discussion and analysis of financial condition and results of operations” disclosure in this prospectus;
- reduced disclosure about our executive compensation arrangements;
- not being required to hold advisory votes on executive compensation or to obtain stockholder approval of any golden parachute arrangements not previously approved;
- an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002; and
- an exemption from compliance with the requirements of the Public Company Accounting Oversight Board regarding the communication of critical audit matters in the auditor’s report on the financial statements.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of \$1.07 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of this offering; (iii) the date on which we have issued more than \$1.0 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, or the SEC. We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock. Additionally, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption and, therefore, while we are an emerging growth company we will not be subject to new or revised accounting standards at the same time that they become applicable to other public companies that are not emerging growth companies. As a result of this election, our financial statements may not be comparable to those of other public companies that comply with new or revised accounting pronouncements as of public company effective

dates. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies.

We are also a “smaller reporting company,” meaning that the market value of our shares held by nonaffiliates plus the proposed aggregate amount of gross proceeds to us as a result of this offering is less than \$700 million and our annual revenue was less than \$100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company after this offering if either (i) the market value of our shares held by non-affiliates is less than \$250 million or (ii) our annual revenue was less than \$100 million during the most recently completed fiscal year and the market value of our shares held by nonaffiliates is less than \$700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

THE OFFERING

Shares of common stock offered by us	shares.
Shares of our common stock to be outstanding after this offering	shares (or shares if the underwriters exercise their option to purchase additional shares in full).
Underwriters' option to purchase additional shares	We have granted the underwriters a 30-day option to purchase up to additional shares of our common stock at the initial public offering price, less underwriting discounts and commissions on the same terms as set forth in this prospectus.
Use of proceeds	We estimate that the net proceeds to us from the sale of shares of our common stock in this offering will be approximately \$ million, or \$ million if the underwriters exercise their option to purchase additional shares in full, assuming an initial public offering price of \$ per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds of this offering, together with our existing cash and cash equivalents and short-term investments, to: continue research and development of our immediate target indications and differentiation target indications; to develop our early-stage manufacturing processes and build out our dedicated chemistry facility; and for general corporate purposes. See "Use of Proceeds."
Proposed Nasdaq Global Market symbol	"PRME"
Risk factors	Investment in our common stock involves substantial risks. You should read this prospectus carefully, including the section entitled "Risk Factors" and the consolidated financial statements and the related notes to those statements included in this prospectus, before investing in our common stock.

The number of shares of our common stock outstanding after this offering is based on 265,613,476 shares (which includes 47,734,388 shares of unvested restricted common stock) of our common stock outstanding as of December 31, 2021, after giving effect to (i) the issuance of 3,424,422 shares of our common stock to Myeloid Therapeutics, Inc., or Myeloid, in January 2022 and (ii) the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 161,420,799 shares of our common stock upon the completion of this offering, and excludes:

- 9,335,220 shares of common stock issuable upon the exercise of stock options outstanding as of December 31, 2021, with a weighted-average exercise price of \$1.27 per share under our 2019 Stock Option and Grant Plan;
- 532,500 shares of common stock issuable upon the exercise of stock options granted after December 31, 2021, with a weighted-average exercise price of \$3.51 per share under our 2019 Stock Option and Grant Plan;
- 7,479,092 shares of common stock reserved for issuance under our 2019 Stock Option and Grant Plan as of December 31, 2021, which shares will cease to be available for issuance at the time our 2022 Stock Option and Incentive Plan becomes effective;

- _____ shares of common stock reserved for future issuance under our 2022 Stock Option and Incentive Plan, which will become effective upon the date immediately preceding the date on which the registration statement of which this prospectus is a part is declared effective; and
- _____ shares of common stock reserved for future issuance under our 2022 Employee Stock Purchase Plan, which will become effective upon the date immediately preceding the date on which the registration statement of which this prospectus is a part is declared effective.

Except as otherwise noted, all information in this prospectus:

- gives effect to a 1-for-_____ reverse stock split of our common stock effected on _____ ;
- assumes no exercise of the underwriters' option to purchase up to _____ additional shares of common stock in this offering;
- assumes no exercise of the outstanding options and restricted stock described above; and
- assumes the filing of our third amended and restated certificate of incorporation and the effectiveness of our amended and restated bylaws, which will occur upon the closing of this offering.

SUMMARY FINANCIAL DATA

You should read the following summary consolidated financial data together with our consolidated financial statements and the related notes appearing at the end of this prospectus and the “Management’s Discussion and Analysis of Financial Condition and Results of Operations” section of this prospectus. We have derived the consolidated statement of operations data for the period from September 13, 2019 (inception) to December 31, 2019, and the years ended December 31, 2020 and 2021 from our audited consolidated financial statements appearing at the end of this prospectus. Our historical results are not necessarily indicative of the results that may be expected in any future period.

	Period from September 13, 2019 (Inception) to December 31,		Year Ended December 31,			
	2019		2020	2021		
(in thousands, except share and per share data)						
Consolidated Statement of Operations Data:						
Related party collaboration revenue	\$	—	\$	5,210	\$	—
Operating expenses:						
Research and development ⁽¹⁾		920		2,980		70,550
General and administrative		1,252		3,162		13,924
Total operating expenses		2,172		6,142		84,474
Loss from operations		(2,172)		(932)		(84,474)
Other income (expense):						
Change in fair value of preferred stock tranche right liability		(353)		(10,904)		(74,319)
Change in fair value of anti-dilution obligation		—		(700)		(6,681)
Change in fair value of related party short-term investment		—		10,867		(391)
Other income, net ⁽²⁾		—		126		12
Total other expense, net		(353)		(611)		(81,379)
Net loss before income taxes		(2,525)		(1,543)		(165,853)
Provision for (benefit from) income taxes		4		1,867		(486)
Net loss		(2,529)		(3,410)		(165,367)
Accretion of preferred stock to redemption value		(265)		(1,645)		(1,468)
Cumulative dividend on preferred stock		—		—		(17,284)
Net loss attributable to common stockholders	\$	(2,794)	\$	(5,055)	\$	(184,119)
Net loss per share attributable to common stockholders, basic and diluted ⁽³⁾	\$	(0.60)	\$	(0.62)	\$	(4.57)
Weighted-average common shares outstanding, basic and diluted ⁽³⁾		4,622,576		8,206,374		40,332,091
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited) ⁽⁴⁾					\$	(0.82)
Pro forma weighted-average common shares outstanding, basic and diluted (unaudited) ⁽⁴⁾						201,752,890

(1) Includes related party amounts of \$0.1 million, \$0.2 million and \$42.2 million for the period from September 13, 2019 (inception) to December 31, 2019 and for the years ended December 31, 2020 and 2021, respectively. See Note 14 to our consolidated financial statements appearing at the end of this prospectus.

(2) Includes related party amounts of \$0.1 million for the year ended December 31, 2020. See Note 14 to our consolidated financial statements appearing at the end of this prospectus.

(3) See Note 13 to our consolidated financial statements included elsewhere in this prospectus for details on the calculation of basic and diluted net loss per share attributable to common stockholders.

(4) Pro forma basic and diluted net loss per share attributable to common stockholders has been prepared to give effect to adjustments to our capital structure arising in connection with the completion of this offering and is calculated by dividing the pro forma net loss attributable to common stockholders by the pro forma weighted-average common shares outstanding for the period. The unaudited pro forma net loss

attributable to common stockholders used in the calculation of unaudited pro forma basic and diluted net loss per share attributable to common stockholders adjusts net loss attributable to common stockholders to remove the accretion of preferred stock to redemption value and cumulative dividends on preferred stock for the year ended December 31, 2021 because the calculation gives effect to the automatic conversion of all shares of our preferred stock outstanding as of December 31, 2021 into shares of common stock as if such conversion had occurred on January 1, 2021. Pro forma weighted-average common shares outstanding is computed by adjusting the weighted-average common shares outstanding to give pro forma effect to the automatic conversion of all shares of our preferred stock outstanding as of December 31, 2021 into shares of common stock as if such conversion had occurred on January 1, 2021. For the year ended December 31, 2021, weighted-average common shares outstanding includes the impact of the 3,424,422 shares we were obligated to issue to Myeloid as of December 24, 2021, the date of the agreement. Pro forma basic and diluted net loss per share attributable to common stockholders does not include the effect of the shares expected to be sold in this offering.

	As of December 31, 2021	
	Actual	Pro Forma ⁽¹⁾
	Pro Forma As Adjusted ⁽²⁾	
	(in thousands)	
Consolidated Balance Sheet Data⁽¹⁾:		
Cash and cash equivalents	\$ 185,420	\$ 155,420
Working capital ⁽³⁾	212,596	224,616
Total assets	301,856	271,856
Related party forward contract liability	12,020	—
Total liabilities	62,296	20,276
Convertible preferred stock	395,800	—
Total stockholders' equity (deficit)	(156,240)	251,580

- (1) The pro forma balance sheet data gives effect to (i) the settlement of the consideration due to Myeloid in January 2022 consisting of a \$30.0 million payment and the issuance of 3,424,422 shares of common stock to settle our related party forward contract liability and (ii) the automatic conversion of all outstanding shares of our Series A and Series B convertible preferred stock into an aggregate of 161,420,799 shares of our common stock immediately prior to the completion of this offering. See Note 11 to our consolidated financial statements included elsewhere in this prospectus for details on the arrangement with Myeloid.
- (2) The pro forma as adjusted balance sheet data gives effect to (i) the pro forma adjustments set forth in footnote (1) above and (ii) the issuance and sale of _____ shares of our common stock in this offering at an assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each \$1.00 increase (decrease) in the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' equity (deficit) by \$ _____ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase (decrease) of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' equity (deficit) by \$ _____ million, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.
- (3) We define working capital as current assets less current liabilities.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this prospectus, including our consolidated financial statements and related notes appearing at the end of this prospectus, before deciding to invest in our common stock. If any of the events or developments described below were to occur, our business, prospects, operating results and financial condition could suffer materially, the trading price of our common stock could decline and you could lose all or part of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business.

Risks Related To Our Financial Position and Need for Additional Capital

We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was \$165.4 million for the year ended December 31, 2021, \$3.4 million for the year ended December 31, 2020 and \$2.5 million for the period from September 13, 2019 (date of inception) to December 31, 2019. As of December 31, 2021, we had an accumulated deficit of \$171.4 million. We have financed our operations primarily through private placements of our preferred stock. Substantially all of our losses have resulted from expenses incurred in connection with our research and development and from general and administrative costs associated with our operations. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

- continue our current research programs and preclinical development of any product candidates we identify;
- seek to identify additional research programs and product candidates;
- initiate preclinical studies and clinical trials for any product candidates we may identify;
- experience any delays or interruptions due to the ongoing COVID-19 pandemic, including delays in preclinical testing and clinical trials or interruptions in the supply chain for any future product candidates;
- further develop our in-licensed and company-owned gene editing platform, which we call our Prime Editing platform;
- maintain, expand, enforce, defend and protect our intellectual property portfolio and provide reimbursement of third-party expenses related to our patent portfolio;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- develop, maintain and enhance a sustainable, scalable, reproducible and transferable manufacturing process for the product candidates we may develop;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any therapies for which we may obtain marketing approval;
- hire additional research and development personnel;
- hire clinical and commercial personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development;
- acquire or in-license product candidates, intellectual property and technologies;

- establish and maintain collaborations;
- should we decide to do so, build and maintain a commercial-scale current Good Manufacturing Practices, or cGMP, manufacturing facility; and
- operate as a public company.

We have not initiated clinical development of any potential product candidate and expect that it will be many years, if ever, before we have a product candidate ready for commercialization. To become and remain profitable, we must develop and, either directly or through collaborators, eventually commercialize a therapy or therapies with market potential. This will require us to be successful in a range of challenging activities, including identifying product candidates, completing preclinical studies and clinical trials of product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those therapies for which we may obtain marketing approval and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability.

We have transitioned from research and development to early preclinical development for our most advanced potential product candidate. Because of the numerous risks and uncertainties associated with developing Prime Editing product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We will need substantial additional funding. If we are unable to raise capital when needed, we will be forced to delay, reduce, eliminate or prioritize among our research and product development programs or future commercialization efforts.

We expect our expenses to continue to increase in connection with our ongoing activities, particularly as we identify, continue the research and development of, initiate preclinical studies and clinical trials of, and seek marketing approval for, product candidates. Because we have limited financial and managerial resources, we have prioritized our research programs and lead optimization efforts in specific indications among many potential options. Specifically, our initial development programs target blood, liver, eye, and neuromuscular indications, amongst others. As a result of this prioritization, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater clinical or commercial potential and we may need to reprioritize our focus in the future. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable therapies.

In addition, if we obtain marketing approval for any product candidates we may develop, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of a collaborator. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and product development programs or future commercialization efforts.

As of December 31, 2021, our cash and cash equivalents and short-term investments were \$269.6 million. We estimate that the net proceeds of this offering will be approximately \$, assuming an initial public offering price of \$ per share, the midpoint of the price range set forth on the cover of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We expect that the net proceeds from this offering, together with our existing cash and cash equivalents and short-term investments will enable us to fund our operating expenses and capital expenditure requirements for at least the next . However, our operating plan may change as a result of factors currently unknown to us, and we may

need to seek funding sooner than planned. Our future capital requirements will depend on many factors, including those discussed in the risk factor entitled “We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.”

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize any product candidates we may develop. We cannot be certain that additional funding will be available on acceptable terms or at all. We have no committed source of additional capital and, if we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of any product candidates or other research and development initiatives. Our license and collaboration agreements and any future collaboration agreements may also be terminated if we are unable to meet the payment or other obligations under the agreements. We could be required to seek collaborators for potential product candidates earlier than we would otherwise plan or on terms that are less favorable than might otherwise be available. We could also be required to relinquish or license our rights to product candidates on unfavorable terms in certain markets where we otherwise would seek to pursue development or commercialization ourselves.

Raising additional capital may cause dilution to our stockholders, including purchasers of common stock in this offering, restrict our operations or require us to relinquish rights to our technologies or product candidates we may develop.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, declaring dividends and possibly other restrictions. In addition, if we raise funds through additional license and collaboration agreements, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our intellectual property, technologies, future revenue streams, research programs or product candidates we may develop, or we may have to grant licenses on terms that may not be favorable to us.

Our short operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are an early-stage company. We were founded in September 2019 and commenced operations in July 2020. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring and developing our platform and technology and identifying and beginning to advance preclinical testing of potential product candidates. All of our programs are still in the research or preclinical stage of development and their risk of failure is high. We have not yet demonstrated an ability to initiate or successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial-scale therapy, arrange for a third party to do so on our behalf or conduct sales and marketing activities necessary for successful commercialization. Typically, it takes about 10 to 15 years to develop a new therapy from the time it is discovered to when it is available for treating patients.

Our limited operating history, particularly in light of the rapidly evolving gene editing field, may make it difficult to evaluate our technology and industry and predict our future performance. Our very short history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by very early stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer.

In addition, as a new business, we may encounter other unforeseen expenses, difficulties, complications, delays, and other known and unknown factors. We will need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We have never generated revenue from product sales and may never become profitable.

Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with collaborative partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, product candidates we may identify for development. We do not anticipate generating revenues from product sales for many years, if ever. Our ability to generate future revenues from product sales depends heavily on our, or our collaborators', ability to successfully:

- identify product candidates and successfully complete research development of any product candidates we may identify;
- seek and obtain regulatory and marketing approvals for any product candidates for which we complete clinical trials;
- launch and commercialize any product candidates for which we may obtain regulatory and marketing approval by establishing a sales force, marketing and distribution infrastructure, or alternatively, collaborating with a commercialization partner;
- qualify for adequate coverage and reimbursement by government and third-party payors for any product candidates for which we may obtain regulatory and marketing approval;
- establish and maintain supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and the market demand for any product candidates for which we obtain regulatory and marketing approval;
- develop, maintain and enhance a sustainable, scalable, reproducible and transferable manufacturing process for the product candidates we may develop;
- address competing technological and market developments;
- negotiate favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations in such collaborations;
- receive market acceptance by physicians, patients, healthcare payors, and others in the medical community;
- maintain, protect, enforce, defend and expand our portfolio of intellectual property and other proprietary rights, including patents, trade secrets and know-how;
- defend against third party intellectual property claims of infringement, misappropriation or other violation; and
- attract, hire and retain qualified personnel.

Our expenses could increase beyond expectations if we are required by the U.S. Food and Drug Administration, or the FDA, the European Medicines Agency, or the EMA, or other regulatory authorities to perform clinical and other studies in addition to those that we currently anticipate. Even if one or more of the product candidates we may develop are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Additionally, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives. Even if we are able to generate revenues from the sale of any approved product candidates, we may not become profitable and may need to obtain additional funding to continue operations.

Our future ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

Since our inception, we have incurred losses and we may never achieve profitability. To the extent that we continue to generate taxable losses, under current law, our unused U.S. federal net operating losses, or NOLs, may be carried forward to offset a portion of future taxable income, if any. Additionally, we continue to generate business tax credits, including research and development tax credits, which generally may be carried forward to

offset a portion of future taxable income, if any, subject to expiration of such credit carryforwards. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an “ownership change,” generally defined as one or more shareholders or groups of shareholders who own at least 5 percent of the corporation’s equity increasing their equity ownership in the aggregate by more than 50 percentage points (by value) over a three-year period, the corporation’s ability to use its pre-change NOLs and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. Similar rules may apply under state tax laws. Our prior equity offerings and other changes in our stock ownership may have resulted in such ownership changes in the past. In addition, we may experience ownership changes in the future as a result of this offering or subsequent shifts in our stock ownership, some of which are outside of our control. As a result, if we earn net taxable income, our ability to use our pre-change NOLs or other pre-change tax attributes to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. Additional limitations on our ability to utilize our NOLs to offset future taxable income may arise as a result of our corporate structure whereby NOLs generated by our subsidiary may not be available to offset taxable income earned by our subsidiary. There is a risk that due to changes under the tax law, regulatory changes or other unforeseen reasons, our existing NOLs or business tax credits could expire or otherwise be unavailable to offset future income tax liabilities. At the state level, there may also be periods during which the use of NOLs or business tax credits is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For these reasons, we may not be able to realize a tax benefit from the use of our NOLs or tax credits, even if we attain profitability.

We face risks related to health epidemics, pandemics and other widespread outbreaks of contagious disease, including the ongoing COVID-19 pandemic, which could significantly disrupt our operations, impact our financial results or otherwise adversely impact our business.

Significant outbreaks of contagious diseases and other adverse public health developments could have a material impact on our business operations and operating results. For example, the spread of COVID-19 and identification of new variants of COVID-19 have affected segments of the global economy and our operations. As a result of the ongoing COVID-19 pandemic or similar public health crises that may arise, we may experience disruptions that could adversely impact our operations, research and development, and as we continue developing, any preclinical studies, clinical trials and manufacturing activities we may conduct, some of which may include:

- delays or disruptions in research programs, preclinical studies, clinical trials or investigational new drug, or IND-enabling studies that we or our collaborators may conduct;
- interruption or delays in the operations of the FDA, the EMA and comparable foreign regulatory agencies;
- interruption of, or delays in receiving and distributing, supplies of drug substance and drug product from our contract manufacturing organizations, or CMOs, to preclinical or clinical research sites or delays or disruptions in any preclinical studies or clinical trials performed by contract research organizations, or CROs;
- limitations imposed on our business operations by local, state or federal authorities to address a pandemic or similar public health crises, including if facilities and materials are commandeered under the Defense Production Act of 1950 or equivalent foreign legislation; and
- business disruptions caused by potential workplace, laboratory and office closures and an increased reliance on employees working from home, disruptions to or delays in ongoing laboratory experiments and operations, staffing shortages, travel limitations, and cybersecurity and data accessibility or security issues.

For example, our laboratory-based personnel have been unable to maximize use of our existing laboratory space due to restrictions on density of people and other aspects of our work have been limited by the need for our staff to isolate.

In addition, the trading prices for biopharmaceutical companies have been highly volatile as a result of the ongoing COVID-19 pandemic and we may face similar volatility in our stock price after we complete this public offering. We cannot predict the scope and severity of any economic recovery after the COVID-19 pandemic abates,

including following any additional “waves” or other intensifying of the pandemic. If we or any of the third parties with whom we engage were to experience additional shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively affected, which could have a material adverse impact on our business, financial condition, our results of operations and prospects. Furthermore, the COVID-19 pandemic could exacerbate the other risks described in this section. For additional information regarding the impact of the ongoing COVID-19 pandemic, see the section entitled “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Impact of COVID-19 on Our Operations.”

Risks Related To Discovery, Development and Commercialization

Gene editing, including platforms such as Prime Editing, is a novel technology that is not yet clinically validated for human therapeutic use. The approach we are taking to discover and develop novel therapeutics is unproven and may never lead to marketable products. We may incur unexpected costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidates.

We are focused on developing therapies utilizing gene editing technology, which is new and largely unproven. The Prime Editing technologies that we have licensed and that we are utilizing in our research programs have not yet been clinically tested, nor are we aware of any clinical trials for safety or efficacy having been completed by third parties using Prime Editing or similar technologies. The scientific evidence to support the feasibility of developing product candidates based on gene editing technologies is both preliminary and limited. Successful development of product candidates will require us to safely deliver a gene editor into target cells, optimize the efficiency and specificity of such product candidates and ensure the therapeutic selectivity of such product candidates. We may need to address other safety issues as well, and to demonstrate the full value of these products, we will need to achieve these goals with single administration and demonstrate a permanent correction. There can be no assurance that our Prime Editing platform will achieve these goals, lead to the development of genetic therapies or be successful in solving any or all of these issues.

Our future success is highly dependent on the successful development of gene editing technologies, cellular delivery methods and therapeutic applications of that technology. We may decide to alter or abandon our initial programs as new data become available and we gain experience in developing gene editing therapeutics. We cannot be sure that our technologies will yield satisfactory products that are safe and effective, scalable or profitable in our initial indications or any other indication we pursue. Adverse developments in the clinical development efforts of other gene editing technology companies could adversely affect our efforts or the perception of any product candidates we may develop by both investors and regulatory authorities.

Similarly, other gene therapy approaches may be determined to be more attractive than Prime Editing. Moreover, if we decide to develop gene editing technologies other than those involving Prime Editing, we cannot be certain we will be able to obtain rights to such technologies. Although both of our co-founders have entered into agreements with us pursuant to which they assign any inventions to us with respect to the services they perform for us, such assignment obligations are subject to certain limitations, and do not extend to their work in other fields or to the intellectual property arising from their employment with their respective academic and research institutions. To obtain intellectual property rights assigned by our co-founders to such institutions, we would need to enter into license agreements with such institutions, such as Broad Institute, Howard Hughes Medical Institute, or HHMI, and Harvard University, or Harvard, which may not be available on commercially reasonable terms or at all. Additionally, our consulting agreement with David Liu is subject to (i) the policies and regulations of certain institutions and (ii) certain agreements between such co-founder and certain third parties, including Beam Therapeutics, Inc. Any of these factors could reduce or eliminate our commercial opportunity and could have a material adverse effect on our business, financial condition, results of operations and prospects.

Development activities in the field of gene editing are currently subject to a number of risks, including risks related to the ownership and use of certain intellectual property rights that are subject to patent interference proceedings in the United States and opposition proceedings in Europe. For additional information regarding the risks that may apply to our and our licensors’ intellectual property rights, see the section entitled “—Risks Related To Our Intellectual Property” for more information.

Additionally, public perception and related media coverage relating to the adoption of new therapeutics or novel approaches to treatment, as well as ethical concerns related specifically to gene editing, may adversely influence the willingness of subjects to participate in clinical trials, or, if any therapeutic is approved, of physicians and patients to accept these novel and personalized treatments. Physicians, health care providers and third-party payors often are slow to adopt new products, technologies and treatment practices, particularly those that may also require additional upfront costs and training. Physicians may not be willing to undergo training to adopt these novel and potentially personalized therapies, may decide the particular therapy is too complex or potentially risky to adopt without appropriate training, and may choose not to administer the therapy. Furthermore, due to health conditions, genetic profile or other reasons, certain patients may not be candidates for the therapies. In addition, responses by federal and state agencies, Congressional committees and foreign governments to negative public perception, ethical concerns or financial considerations may result in new legislation, regulations or medical standards that could limit our ability to develop or commercialize any product candidates, obtain or maintain regulatory approval or otherwise achieve profitability. New government requirements may be established that could delay or prevent regulatory approval of any product candidates we may develop. It is impossible to predict whether legislative changes will be enacted, regulations, policies or guidance changed, or interpretations by agencies or courts changed, or what the impact of such changes, if any, may be. Based on these and other factors, health care providers and payors may decide that the benefits of these new therapies do not or will not outweigh their costs.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. Because gene editing is novel and the regulatory landscape that will govern our potential product candidates is uncertain and may change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for our potential product candidates.

The time required to obtain approval for any of our potential product candidates from the FDA, the EMA or other comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of regulatory authorities. For more information on the regulatory approval process, see “Business—Government Regulation.” Clinical trials may fail to demonstrate that our product candidates are safe for humans and effective for indicated uses. Even if initial clinical trials in any of our product candidates we may develop are successful, such product candidates may fail to show the desired safety and efficacy in later stages of clinical development despite having successfully advanced through preclinical studies and initial clinical trials. There is a high failure rate for drugs and biologics proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials even after achieving promising results in earlier stage clinical trials.

Because gene editing is novel, the regulatory requirements that will govern any novel gene editing product candidates we develop may continue to evolve. Within the broader genetic therapy field, a limited number of gene therapy products have received marketing authorization from the FDA and the EMA to date. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. Regulatory requirements governing gene therapy products and cell therapy products have changed frequently and may continue to change in the future. Moreover, there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of existing gene therapy products and cell therapy products. For example, in the United States, the FDA has established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees basic and clinical research conducted at the institution participating in the clinical trial. Although the FDA decides whether individual gene therapy protocols may proceed, the review process and determinations of other reviewing bodies, such as an IBC, can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation.

The same applies in the European Union. The EMA’s Committee for Advanced Therapies, or CAT, is responsible for assessing the quality, safety and efficacy of advanced-therapy medicinal products (i.e. gene therapy, somatic-cell therapy or tissue-engineered medicines). The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to the Committee

for Medicinal Products for Human Use, or CHMP, before CHMP adopts its opinion which is submitted to the European Commission for the final opinion on whether to grant a marketing authorization or not. In the European Union, the EMA publishes guidelines for the development and evaluation of gene therapy medicinal products to assist in preparing marketing authorization applications, however these are continually under review. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines.

Adverse developments in post-marketing experience or in clinical trials conducted by others of gene therapy products, cell therapy products or products developed through the application of gene editing technology may cause the FDA, the EMA and other regulatory bodies to revise the requirements for development or approval of our potential product candidates or limit the use of products utilizing gene editing technologies, either of which could materially harm our business. In addition, the clinical trial requirements of the FDA, the EMA and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates can be more expensive and take longer than for other, better known or more extensively studied pharmaceutical or other product candidates. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing gene editing technology in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays or other impediments to our research programs or the commercialization of resulting products.

The regulatory review committees and advisory groups described above and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions. As we advance our research programs and develop future product candidates, we will be required to consult with these regulatory and advisory groups and to comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of any product candidates we identify and develop.

Because we are developing product candidates in the field of genetic medicines in which there is little clinical experience, there is increased risk that the FDA, the EMA or other regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results and that these results may be difficult to analyze.

In order to proceed into clinical development of any product candidates we identify, we will need to submit INDs or clinical trial applications to regulatory authorities and obtain regulatory clearance to commence clinical development. Because the product candidates we identify are based on novel gene-editing technology, we may be unsuccessful in obtaining clearance from regulatory authorities to proceed into clinical development. In order to commence clinical development, we will need to identify success criteria and endpoints such that the FDA, the EMA or other regulatory authorities will be able to determine the clinical efficacy and safety profile of any product candidates we may develop. As we are initially seeking to identify and develop product candidates to treat diseases in which there is little clinical experience using new technologies, and while we may have opportunities to discuss our clinical development plans with regulatory authorities prior to commencing clinical development, there is heightened risk that the FDA, the EMA or other regulatory authorities may not consider the clinical trial endpoints that we propose to provide clinically meaningful results (reflecting a tangible benefit to patients). In addition, the resulting clinical data and results may be difficult to analyze. Even if the FDA does find our success criteria to be sufficiently validated and clinically meaningful, we may not achieve the pre-specified endpoints to a degree of statistical significance. This may be a particularly significant risk for many of the genetically defined diseases for which we plan to develop product candidates because many of these diseases such as Friedreich's Ataxia have small patient populations, and designing and executing a rigorous clinical trial with appropriate statistical power is more difficult than with diseases that have larger patient populations. Furthermore, even if we do achieve the pre-specified criteria, we may produce results that are unpredictable or inconsistent with the results of the non-primary endpoints or other relevant data. The FDA also weighs the benefits of a product against its risks, and the FDA may view the efficacy results in the context of safety as not being supportive of regulatory approval. Other regulatory authorities in the European Union and other countries may make similar comments with respect to these endpoints and data.

Any product candidates we may develop will be based on a novel technology that makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval. No gene editing therapeutic product has been approved in the United States or in Europe. Within the broader genome product field, only a limited number of gene therapy products, such as uniQure N.V.'s Glybera and Abecma from Bristol Myers Squibb and bluebird bio, have received marketing authorization or marketing approval from the European Commission or the FDA. Some of these products have taken years to register and have had to deal with significant issues in their post-marketing experience.

We are very early in our development efforts and may not be successful in identifying and developing potential product candidates. It will be many years before we or our collaborators commercialize a product candidate or generate any revenues, if ever.

The success of our business depends primarily upon our ability to identify, develop and commercialize product candidates. We are very early in our development efforts and have focused our research and development efforts to date on our Prime Editing platform, developing our Prime Editors and identifying our initial targeted disease indications. Although we believe we can demonstrate many of the key advantages of Prime Editing, because we are very early in our development efforts, we are not yet certain of the results we may achieve, which may be important for registration and commercialization of our products. Such uncertainties include but are not limited to the actual size of the set of pathogenic mutations we can address, the level of editing efficiency we can produce, the degree of unwanted byproducts we may encounter, our ability to achieve editing success in a single administration or the permanence of our edits. We have also not yet shown that preclinical editing efficacy can result in clinically important effects, nor that results of biomarker studies in our preclinical models can translate into positive results in clinical trials. One particular form of Prime Editing that uses recombinases to insert targeted “gene-sized” DNA into the genome, is in an even earlier stage of research and development than our immediate target indications and our differentiation indications. We believe this promising form of Prime Editing needs more than one source of DNA as a template and may deliver with less efficacy.

All of our product development programs are still in the research or preclinical stage of development. Our research methodology may be unsuccessful in identifying potential product candidates, our potential product candidates may be shown to have harmful side effects in preclinical *in vitro* experiments or animal model studies, they may not show promising signals of therapeutic effect in such experiments or studies or they may have other characteristics that may make the product candidates impractical to manufacture, unmarketable, or unlikely to receive marketing approval. We have not achieved preclinical proof of concept for our programs and there is no guarantee that we will achieve it. Our proposed delivery methods with potential product candidates have never been evaluated in human clinical trials. Moreover, we are not aware of any clinical trials involving Prime Editing technology. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of any product candidates we may develop, which may never occur. We currently generate no revenue from sales of any product, and we may never be able to develop or commercialize a marketable product.

In addition, although we believe Prime Editing will position us to rapidly expand our portfolio of product candidates beyond the initial product candidates we may develop after only minimal changes to the product candidate construct, we have not yet successfully developed any product candidate and our ability to expand our portfolio may never materialize.

Commencing clinical trials in the United States is also subject to acceptance by the FDA of our IND application and finalizing the trial design based on discussions with the FDA and other regulatory authorities. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence our clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional studies or trials or impose stricter approval conditions than we currently expect. There are equivalent processes and risks applicable to clinical trial applications in other countries, including in Europe.

Some of our approaches may require interaction and approval from regulatory authorities beyond the specific requirements for individual product candidates. For example, our “march up the chromosome” personalized

medicine approach may require the use of basket clinical studies, studies where more than one mutation in a disease are studied in a single clinical trial or even studies where mutations in different diseases are studied in a single clinical trial. Some of our approaches may also require studying more than one Prime Editor under a single IND or applying for registration for a suite of Prime Editor products to allow broad therapeutic coverage for a wide range of mutations in a single disease. It is also possible that using Prime Editing approaches in a wider, healthier population, as we propose in our “Blue Sky” approaches, may require different safety and regulatory thresholds from those required for smaller, more critically ill groups of patients.

Even if we complete the necessary clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize our potential product candidates in the United States or any other jurisdiction, if at all, and any such approval may be for a more narrow indication than we seek. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. We may conduct one or more of our clinical trials with one or more trial sites that are located outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to conditions imposed by the FDA, and there can be no assurance that the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and could delay or permanently halt our development of the applicable product candidates. Similarly, marketing approval by the FDA in the United States, if obtained, does not ensure approval by regulatory authorities in other countries or jurisdictions. Approval processes vary among countries and can involve additional product candidate testing and validation and additional administrative review periods.

Commercialization of any product candidates we may develop will also require obtaining manufacturing supply, capacity and expertise; building of a commercial organization; and significant marketing efforts. If we do not successfully commercialize any product candidates we may develop, we could experience a material harm to our business.

We may find it difficult to enroll patients in our clinical trials given the limited number of patients who have the diseases any product candidates we identify or develop are intended to target. If we experience delays or difficulties in the enrollment of patients in clinical trials, our clinical development activities and our receipt of necessary regulatory approvals could be delayed or prevented.

Although we are currently in preclinical development, as we progress our programs we may not be able to initiate or continue clinical trials for any product candidates we identify or develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA, the EMA or other analogous regulatory authorities outside the United States, or as needed to provide appropriate statistical power for a given trial. Enrollment may be particularly challenging for some of the rare genetically defined diseases we are targeting in our most advanced programs. In addition, if patients are unwilling to participate in our gene editing trials because of negative publicity from adverse events related to the biotechnology, gene therapy or gene editing fields, competitive clinical trials for similar patient populations, clinical trials in competing products or for other reasons, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of our potential product candidates may be delayed. Moreover, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as our potential product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors’ product candidates.

Patient enrollment is also affected by other factors, some of which may include:

- severity of the disease under investigation;
- size of the patient population and process for identifying patients, including proximity and availability of clinical trial sites for prospective patients with conditions that have small patient pools;
- design of the trial protocol, including efforts to facilitate timely enrollment in clinical trials;

- availability and efficacy of approved medications for the disease under investigation;
- availability of genetic testing for potential patients and ability to monitor patients adequately during and after treatment;
- ability to obtain and maintain patient informed consent;
- risk that enrolled patients will drop out before completion of the trial;
- eligibility and exclusion criteria for the trial in question;
- perceived risks and benefits of the product candidate under trial and gene editing as a therapeutic approach; and
- patient referral practices of physicians.

In addition, our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, some of which may include:

- difficulty in establishing or managing relationships with CROs and physicians;
- different standards for the conduct of clinical trials;
- different standard-of-care for patients with a particular disease;
- difficulty in locating qualified local consultants, physicians and partners; and
- potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment and of gene editing technologies.

Enrollment delays in our clinical trials may result in increased development costs for our potential product candidates, which would cause the value of our Company to decline and limit our ability to obtain additional financing. If we or our collaborators have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials or entire clinical programs, any of which would have an adverse effect on our business, financial condition, results of operations and prospects.

The gene editing field is relatively new and is evolving rapidly. We are focusing our research and development efforts on gene editing using Prime Editing technology, but other gene editing technologies may be discovered that provide significant advantages over Prime Editing, which could materially harm our business.

To date, we have focused our efforts on our Prime Editing platform. However, there are numerous other companies advancing gene editing and gene therapy product candidates that are in preclinical or clinical development. Some of these other companies have previously undertaken research and development of gene editing technologies using clustered regularly interspaced short palindromic repeats, or CRISPR, or other forms such as base editing, zinc finger nucleases, engineered meganucleases and transcription activator-like effector nucleases, or TALENs, but to date none has obtained marketing approval for a product candidate. There can be no certainty that Prime Editing technology will lead to the development of genetic therapies or that other gene editing technologies will not be considered better or more attractive for the development of therapies. For example, transposons, or “jumping genes,” can insert themselves into different places in the genome and carry specific DNA sequences to specific sites without the need for making double-stranded breaks in DNA, although such methods currently cannot target specific locations. In addition, Beam Therapeutics Inc., or Beam Therapeutics, is developing novel base editing technology. We have entered into a collaboration and license agreement with Beam Therapeutics, under which we grant Beam Therapeutics certain exclusive and non-exclusive rights in our Prime Editing technology in certain fields. Our license grant to Beam Therapeutics does not cover all fields and applications of Prime Editing and we retain the majority of rights to use the licensed Prime Editing technology outside of the fields licensed to Beam

Therapeutics. It is possible that base editing or other gene editing technology developed by Beam Therapeutics will be competitive with our business, and it is also possible that such editing technology may be considered more attractive than Prime Editing. Therefore, Beam Therapeutics may develop competing products using such technology. For more information regarding our agreement with Beam Therapeutics, see “Business—Our License and Collaboration Agreements—Strategic Relationship with Beam Therapeutics.”

Similarly, other new gene editing technologies that have not been discovered yet may be determined to be more attractive than Prime Editing. Moreover, if we decide to develop gene editing technologies other than those involving Prime Editing, we cannot be certain we will be able to obtain rights to such technologies. Although both of our co-founders who currently provide consulting and advisory services to us in the area of gene editing technologies have entered into agreements with us pursuant to which they assign to us any inventions with respect to the services they perform for us, such obligations are subject to limitations and do not extend to their work in other fields or to the intellectual property arising from their employment with their respective academic and research institutions. To obtain intellectual property rights assigned by these co-founders to such institutions, such as Broad Institute, HHMI and Harvard, we would need to enter into license agreements with such institutions, which may not be available on commercially reasonable terms or at all. Additionally, our consulting agreement with David Liu is subject to (i) the policies and regulations of certain institutions and (ii) certain agreements between such co-founder and certain third parties, including Beam Therapeutics, Inc. Furthermore, although our co-founders have long-term supporting or employment roles with us, a financial stake in our success and, in certain cases, non-competition clauses in their consulting or employment agreements, such non-competition obligation is limited to the field of any and all gene editing and technology. Therefore it is possible that they may in the future develop new technologies that are outside of the field of their non-competition obligations but may be competitive to our business. In addition, other companies may use Prime Editing to develop product candidates in areas they believe are not covered under our foundational patent applications or know-how. There are also a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we have research programs, using approaches other than gene editing approaches. Any of these factors could reduce or eliminate our commercial opportunity, and could have a material adverse effect on our business, financial condition, results of operations and prospects.

We are very early in our development efforts, and we have not yet completed IND-enabling studies or initiated clinical development of any product candidate. As a result, we expect it will be many years before we commercialize any product candidate, if ever. If we are unable to advance our current or future product candidates into and through clinical trials, obtain marketing approval and ultimately commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

We are very early in our development efforts and have focused our research and development efforts to date on research efforts and preclinical development. Currently, all of our programs are still in the research or preclinical stage of development. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development, marketing approval and eventual commercialization of our product candidates, which may never occur. We have not yet generated revenue from product sales or otherwise, and we may never be able to develop or commercialize a marketable product.

Commencing clinical trials in the United States is subject to acceptance by the FDA of an IND and finalizing the trial design based on discussions with the FDA and other regulatory authorities. In the event that the FDA requires us to complete additional preclinical studies or we are required to satisfy other FDA requests prior to commencing clinical trials, the start of our first clinical trials may be delayed or we may be unsuccessful obtaining clearance to proceed into clinical development. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence any clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials, delay the enrollment of our clinical trials, abandon our clinical development plans or meet stricter approval conditions than we currently expect. There are equivalent processes and risks applicable to clinical trial applications in other countries, including countries in the European Union.

Commercialization of any product candidates we may develop will require preclinical and clinical development; regulatory and marketing approval in multiple jurisdictions, including by the FDA and the EMA; manufacturing supply, capacity and expertise; a commercial organization; and significant marketing efforts. The success of product candidates we may identify and develop will depend on many factors, including the following:

- timely and successful completion of preclinical studies, including toxicology studies, biodistribution studies and minimally efficacious dose studies in animals, where applicable;
- effective INDs or comparable foreign applications that allow commencement of our planned clinical trials or future clinical trials for any product candidates we may develop;
- successful enrollment and completion of clinical trials, including under the FDA's current Good Clinical Practices, or GCPs, current Good Laboratory Practices, or GLPs, and any additional regulatory requirements from foreign regulatory authorities;
- positive results from our future clinical trials that support a finding of safety and effectiveness and an acceptable risk-benefit profile in the intended populations;
- receipt of marketing approvals from applicable regulatory authorities;
- establishment of arrangements through our own facilities or with third-party manufacturers for clinical supply and, where applicable, commercial manufacturing capabilities;
- establishment, maintenance, defense and enforcement of patent, trademark, trade secret and other intellectual property protection or regulatory exclusivity for any product candidates we may develop;
- commercial launch of any product candidates we may develop, if approved, whether alone or in collaboration with others;
- acceptance of the benefits and use of our product candidates we may develop, including method of administration, if and when approved, by patients, the medical community and third-party payers;
- effective competition with other therapies;
- maintenance of a continued acceptable safety, tolerability and efficacy profile of any product candidates we may develop following approval; and
- establishment and maintenance of healthcare coverage and adequate reimbursement by payers.

If we do not succeed in one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize any product candidates we may develop, which would materially harm our business. If we are unable to advance our product candidates to clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We have not tested any of our proposed delivery methods or gene editing approaches in clinical trials and any favorable results we may have may not be predictive of results that may be observed in later preclinical studies or clinical trials. If our potential product candidates, our Prime Editing technology or the delivery modes we rely on to administer them lack efficacy or cause serious adverse events, undesirable side effects or unexpected characteristics, such results could delay or prevent regulatory approval of the product candidates, limit the commercial potential or result in significant negative consequences following any potential marketing approval.

We are developing a broad set of delivery technologies to support our Prime Editing programs. This will lead to significant challenges to develop a corresponding set of technical capabilities in support of these programs. In particular, a variety of serious adverse events, undesirable side effects or unexpected characteristics may occur. Such events, side effects or characteristics could delay or prevent regulatory approval of any product candidates we may develop, limit the commercial potential or result in significant negative consequences following any potential

marketing approval. In addition, our Prime Editing technology itself, may lead to other issues, such as inability to deliver the desired efficacy or safety-related consequences as it is tested in clinical trials.

We have not tested any of our proposed delivery methods in clinical trials and any favorable results we may have may not be predictive of results that may be observed in later preclinical studies or clinical trials. Furthermore, we have not generated any clinical trial results to date. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates. Many product candidates that initially showed promise in early stage testing for treating a variety of diseases have later been found to lack efficacy or to cause side effects that prevented further clinical development of the product candidates.

Moreover, there have been only a very limited number of clinical trials involving the use of any gene editing technologies and none involving gene editing technology similar to our Prime Editing technology. It is impossible to predict when or if any product candidates we may develop will prove safe in humans. In the genetic therapy field, there have been several significant adverse events from gene therapy treatments in the past, including both the impact of the technology for editing, as well as the delivery methods used to convey the gene editing technology. These include a variety of safety concerns, including reported cases of leukemia, other cancers, significant morbidities and death. There can be no assurance that gene editing technologies such as our Prime Editing technology or the delivery methods we plan to use will not cause such undesirable side effects.

We cannot be sure that our Prime Editing technology or any of our planned delivery methods will not result in adverse effects in the long-term, such as improper editing of a patient's DNA that leads to lymphoma, leukemia, other cancers or other aberrantly functioning cells or other as yet unidentified findings. Many times, side effects manifest or are only detectable after investigational products are tested in larger scale, pivotal clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval. FDA guidance advises that patients treated with gene therapies undergo long-term follow-up observation for identification of potential adverse events for as long as 15 years. If additional clinical or long-term follow-up experience indicates that any of our potential product candidates have side effects or cause serious or life-threatening side effects, the development of the product candidate may fail or be delayed, or, if the product candidate has received regulatory approval, such approval may be revoked or limited. It is also possible that serious or life-threatening side effects may cause significant delay or altered perception of any product candidates we may develop, even if we are able to later show these effects are unrelated to our product candidates. Any adverse events may cause us to delay, limit or terminate other planned clinical trials, for example any that use a similar delivery method or those that use similar aspects of Prime Editing, any of which would have a material adverse effect on our business, financial condition, results of operations and prospects. In addition, many product candidates that initially showed promise in early-stage testing have later been found to cause later side effects that prevented further clinical development of the product candidates.

Additionally, a significant risk in any gene editing product candidate is that "off-target" edits, or edits far from the intended site of gene editing, may occur, which could cause serious adverse events, undesirable side effects or unexpected characteristics. One major causative factor leading to "off target" edits is the formation of double-strand breaks during gene editing. If double-strand breaks were to occur, they can also lead to decreased cell viability in edited cells, and an increase large deletions or structural rearrangements of DNA, chromosomal translocations or joining of one chromosome to another. In certain uses of Prime Editing, such as the use of dual flaps methods, or in some cases of use of nick-guide RNAs, more than one edit occurs along the target site. Although our preliminary data suggests otherwise, it is possible that the use of these variations of Prime Editing could result in adverse effects similar to those observed with double-strand breaks. However, our current understanding of our mechanism of action, which is designed to prevent double-strand breaks with Prime Editing, and preliminary data in our experiments suggest this risk may be low. We have performed initial experiments using assays that can detect off-target edits, even when such edits occur at very low frequencies. Using these assays, as well as reviewing published results, off-target edits have been noted. Except for initial experiments, we have not yet performed these experiments with our potential product candidates, so it is possible that we will detect more such off-target edits. However, our current information is limited, and we cannot be certain that Prime Editing with any product candidates we may develop will not cause rare double-strand breaks or that off-target editing will not occur and

cause serious adverse events in any of our future clinical trials. Furthermore, the lack of observed serious side effects in any preclinical studies to date does not guarantee that such side effects will not occur in human clinical trials of any product candidates we may develop, which would adversely impact our product development programs and business.

There is also the potential risk of delayed adverse events following exposure to Prime Editing therapy due to the permanence of edits to DNA or due to other components of product candidates used to carry the genetic material. In addition, because Prime Editing makes a permanent change, the therapy cannot be withdrawn, even after a side effect is observed. These risks also apply to “on-target” mis-edits, also often called “indels,” or edits that are not intended but occur at the target site of gene correction, which might also have all of the above consequences, as well as yet unforeseen adverse effects.

Although we and others have demonstrated the ability to engineer gene editors which are designed to improve the specificity of their edits in a laboratory setting, we cannot be sure that our engineering efforts will be effective in any product candidates that we may develop. For example, we might not be able to engineer an editor to make the desired change, could diminish the effectiveness of an edit that we make or lead to adverse effects. To date, these types of adverse effects have not been observed in our ongoing experiments and programs. Some Prime Editing approaches, such as those that use mismatch repair, or MMR, inhibition, may potentially also lead to adverse effects. Since our inhibition of MMR for use in Prime Editing is likely to be transient, lasting at most hours to days, we believe the risk related to MMR inhibition is small.

We also cannot be sure that our Prime Editing technology or any of our planned delivery methods will not result in adverse effects including allergic reactions, other changes in safety parameters, increases in liver function tests or many other potential concerns noted in clinical trials. It is also possible that our Prime Editors or our delivery methods will result in significant immunogenicity that may lead to adverse effects and could also prevent any chance of reapplication of a delivery method, or gene editing method in the future, if needed.

In certain of our programs, we plan to use lipid nanoparticles, or LNPs, to deliver our Prime Editors. LNPs have been shown to induce oxidative stress in the liver at certain doses, as well as initiate systemic inflammatory responses that can be fatal in some cases. While we aim to continue to optimize our LNPs, there can be no assurance that our LNPs will not have undesired effects. Our LNPs could contribute, in whole or in part, to one or more of the following: immune reactions, infusion reactions, complement reactions, opsonation reactions, antibody reactions including IgA, IgM, IgE or IgG or some combination thereof, or reactions to the PEG from some lipids or PEG otherwise associated with the LNP. Certain aspects of our investigational therapies may induce immune reactions from either the mRNA or the lipid as well as adverse reactions within liver pathways or degradation of the mRNA or the LNP, any of which could lead to significant adverse events in one or more of our future clinical trials. Many of these types of side effects have been seen for legacy LNPs. There may be uncertainty as to the underlying cause of any such adverse event, which would make it difficult to accurately predict side effects in future clinical trials and would result in significant delays in our programs.

Our viral vectors including adeno-associated viruses, or AAVs, or lentiviruses, which are relatively new approaches used for disease treatment, also have known side effects, and for which additional risks could develop in the future. In past clinical trials that were conducted by others with non-AAV vectors, several significant side effects were caused by gene therapy treatments, including reported cases of leukemia and death. Other potential side effects could include an immunologic reaction and insertional oncogenesis, which is the process whereby the insertion of a functional gene near a gene that is important in cell growth or division results in uncontrolled cell division, which could potentially enhance the risk of malignant transformation. AAV vectors may also persist in the cell for long periods, potentially permanently, and may result in long-term adverse effects. If the vectors we use demonstrate a similar side effect or other adverse events, we may be required to halt or delay further clinical development of any potential product candidates. Furthermore, the FDA has stated that lentiviral vectors possess characteristics that may pose high risks of delayed adverse events. Such delayed adverse events may occur in other viral vectors, including AAV vectors, at a lower rate.

In addition to side effects and adverse events caused by any product candidates we may develop, the conditioning, administration process or related procedures which may be used in our electroporation pipeline also

can cause adverse side effects and adverse events. A gene therapy patient is generally administered cytotoxic drugs to remove stem cells from the bone marrow to create sufficient space in the bone marrow for the modified stem cells to engraft and produce new cells. This procedure compromises the patient's immune system. In the future, if we are unable to demonstrate that such adverse events were caused by the conditioning regimens used, administration process or related procedure, the FDA, the EMA or other regulatory authorities could order us to cease further development of, or deny approval of, any product candidates we may develop for any or all target indications. Even if we are able to demonstrate that adverse events are not related to the drug product or the administration of such drug product, such occurrences could affect patient recruitment, the ability of enrolled patients to complete the clinical trial or the commercial viability of any product candidates that obtain regulatory approval.

We are subject to additional development challenges and risks due to the novel nature of our gene editing technology.

Because our *in vivo* technology may involve gene editing across multiple cell and tissue types, we are subject to many of the challenges and risks that other gene editing therapeutics and gene therapies face, some of which may include:

- regulatory guidance governing gene and gene editing therapy products have changed and may continue to change in the future;
- to date, only a limited number of products that involve *in vivo* gene transfer have been approved globally;
- improper modulation of a gene sequence, including unintended editing events or insertion of a sequence into certain locations in a patient's chromosome, could lead to cancer, other aberrantly functioning cells or other diseases, including death;
- corrective expression of a missing protein in a patient's cells could result in the protein being recognized as foreign and lead to a sustained immunological reaction against the expressed protein or expressing cells, which could be severe or life-threatening; and
- regulatory agencies may require extended follow-up observation periods of patients who receive treatment using gene editing products such as the FDA's recommended 15-year follow-up observation period for such patients, which will require us to adopt such observation periods for any product candidates we develop if required by the relevant regulatory agencies, which could vary by country or region.

Furthermore, because any *ex vivo* product candidates we may develop involve editing human cells and then delivering modified cells to patients, we are subject to many of the challenges and risks that engineered cell therapies face. For example, clinical trials using engineering cell-based gene therapies require complex logistics for autologous therapies and such personalized manufacturing may be inefficient and cost-prohibitive, which could lead to delays or even termination of our product development programs in the future which could materially harm our business.

We may also consider additional delivery modes, which may carry additional known and unknown risks.

We may also consider additional delivery modes, which may carry additional known and unknown risks. For example, we intend to use novel split intein technology for AAV gene therapy that allows us to deliver the Prime Editor and guide RNA construct by co-infection with two viruses, where each virus contains one half of the editor. The scientific evidence to support the feasibility of developing product candidates based on this technology is both preliminary and limited. We also intend to use LNPs to deliver some of our Prime Editors. While LNPs have been used to deliver smaller molecules, such as RNAi, they have not been clinically proven to deliver large RNA molecules, such as the ones we intend to use for our Prime Editors. Furthermore, as with many AAV-mediated gene therapy approaches, certain patients' immune systems might prohibit the successful delivery, thereby potentially limiting treatment outcomes of these patients. Even if initial clinical trials in any of our potential product candidates we may develop are successful, these product candidates we may develop may fail to show the desired safety and efficacy in later stages of clinical development despite having successfully advanced through preclinical studies and initial clinical trials.

In the future, if we are unable to demonstrate that any of the above adverse events were caused by factors other than our product candidates or our delivery methods, the FDA, the EMA or other regulatory authorities could order us to cease further development of, or deny approval of, any product candidates we are able to develop for any or all targeted indications. Even if we are able to demonstrate that all future serious adverse events are not product- and/or delivery-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial or may cause significant delays to our programs and potential registration. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trials, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to identify and develop product candidates, and may harm our business, financial condition, result of operations and prospects significantly.

We face significant competition in an environment of rapid technological change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours, which may harm our financial condition and our ability to successfully market or commercialize any product candidates we may develop.

The development and commercialization of new drug products is highly competitive. Moreover, the gene editing field is characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We will face competition with respect to any product candidates that we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent or other intellectual property protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we have research programs. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, while others are based on entirely different approaches.

There are several companies utilizing CRISPR/Cas9 nuclease technology, including Caribou Biosciences, Inc., Editas Medicine, Inc., CRISPR Therapeutics AG, Intellia Therapeutics, Inc. and Graphite Bio, Inc., among others. Several additional companies such as Sangamo Therapeutics, Inc., Precision BioSciences, Inc. and bluebird bio, Inc. utilize alternative nuclease-based genome editing technologies, including Zinc Fingers, Arcuses and TAL Nucleases. Beam Therapeutics Inc. utilizes base editing technology. In addition, other private companies such as Tessara Therapeutics Pty. Ltd. and Tome Biosciences, Inc. have announced their work in recombinase DNA and RNA gene writers, although little is known publicly about their science or portfolio. Other companies have announced intentions to enter the gene editing field, such as Moderna, Inc. and Pfizer Inc. Most recently, new epigenetic editing companies have emerged, such as Chroma Medicine, Inc. and Tune Therapeutics, Inc. In addition, we face competition from companies utilizing gene therapy, oligonucleotides and cell therapy therapeutic approaches. Several companies such as Arbor Biotechnologies, Inc., Scribe Therapeutics Inc., Mammoth Biosciences, Inc. and Metagenomi, Inc. are actively searching for novel genome editing components and have reported the discovery of new DNA-cutting enzymes. Other companies are active in LNP delivery technologies and advancing those into therapeutics using genetic therapies, including Recode Therapeutics, Inc., Verve Therapeutics, Inc., Generation Bio Co. and Beam Therapeutics Inc., among others.

Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future that are approved to treat the same diseases for which we may obtain approval for any product candidates we may develop. This may include other types of therapies, such as small molecule, antibody and/or protein therapies.

Many of our current or potential competitors, either alone or with their collaboration partners, may have significantly greater financial resources and expertise in research and development, manufacturing, conducting preclinical studies and clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and gene therapy industries may result in even more

resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize product candidates that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any product candidates that we may develop or that would render any product candidates that we may develop obsolete or non-competitive. Our competitors also may obtain FDA or other regulatory approval for their product candidates more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, as a result of the expiration or successful challenge of our patent or other intellectual property rights, we could face risks relating to our ability to successfully prevent or delay launch of competitors' products. The availability of our competitors' products could limit the demand and the price we are able to charge for any product candidates that we may develop and commercialize.

Adverse public perception of genetic therapies and of gene editing and Prime Editing in particular, may negatively impact regulatory approval of, and/or demand for, our potential products.

Our potential therapeutic products involve editing the human genome and making permanent changes that may not be reversible. The clinical and commercial success of our potential products will depend in part on public understanding and acceptance of the use of gene editing therapy for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene editing is unsafe, unethical or immoral, and, consequently, any product candidates we may develop may not gain the acceptance of the public or the medical community. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

In addition, gene editing technology is subject to public debate and heightened regulatory scrutiny due to ethical concerns relating to the application of gene editing technology to human embryos or the human germline. For example, academic scientists in several countries, including the United States, have reported on their attempts to edit the gene of human embryos as part of basic research. In addition, in November 2018, Dr. Jiankui He, a Chinese biophysics researcher who was an associate professor in the Department of Biology of the Southern University of Science and Technology in Shenzhen, China, reportedly claimed he had created the first human genetically edited babies, twin girls. This claim, and another that Dr. He had helped create a second gene-edited pregnancy, was subsequently confirmed by Chinese authorities and was negatively received by the public, in particular those in the scientific community. News reports indicate that Dr. He was sentenced to three years in prison and fined \$430,000 in December 2019 by the Chinese government for illegal medical practice in connection with such activities. In the wake of the claim, the World Health Organization established a new advisory committee to create global governance and oversight standards for human gene editing. The Alliance for Regenerative Medicine also released principles for the use of gene editing in therapeutic applications endorsed by a number of companies that use gene editing technologies.

Moreover, in an annual worldwide threat assessment report delivered to the U.S. Congress in February 2016, the U.S. Director of National Intelligence stated that research into gene editing that is conducted under different regulatory standards than those of Western countries probably increases the risk of the creation of potentially harmful biological agents or products, including weapons of mass destruction. He noted that given the broad distribution, low cost and accelerated pace of development of gene editing technology, its deliberate or unintentional misuse could have far-reaching economic and national security implications.

Although we do not, and will not use our technologies to edit human embryos or the human germline, such public debate about the use of gene editing technologies in human embryos and heightened regulatory scrutiny could

prevent or delay our development of product candidates. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair our development and commercialization of product candidates or demand for any product candidates we may develop. Adverse events in our preclinical studies or clinical trials or those of our competitors or of academic researchers utilizing gene editing technologies, even if not ultimately attributable to product candidates we may identify and develop, and negative publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of potential product candidates we may identify and develop, stricter labeling requirements for those product candidates that are approved, and a decrease in demand for any such product candidates.

If the market opportunities for any product candidates we may develop are smaller than we believe they are, our potential revenues may be adversely affected and our business may suffer. Because the target patient populations for many of the product candidates we may develop are small, we must be able to successfully identify patients and achieve market acceptance in the medical community in order to secure a significant market share to maintain profitability and growth.

We focus our research and product development on treatments for rare genetically defined diseases. Many of the product candidates we may develop are expected to target a single, often predominant mutation; as a result, the relevant patient population may therefore be small. Although we believe we can expand beyond our immediate target indications, this approach will require regulatory approval as discussed in the risk factor entitled “We are very early in our development efforts and may not be successful in identifying and developing potential product candidates. It will be many years before we or our collaborators commercialize a product candidate or generate any revenues, if ever.” Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with product candidates we may develop, are based on estimates. These estimates may prove to be incorrect and new studies may change the estimated incidence or prevalence of these diseases. The number of patients in the United States, Europe and elsewhere may turn out to be lower than expected, and patients may not be amenable to treatment with the product candidates we may develop, or may become increasingly difficult to identify or gain access to, all of which would adversely affect our business, financial condition, results of operations and prospects. Additionally, because of the potential that any product candidates we develop could cure a target disease, we may not receive recurring revenues from patients and may deplete the patient population prevalence through curative therapy.

Clinical trial and product liability lawsuits against us could divert our resources and could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We will face an inherent risk of clinical trial and product liability exposure related to the testing of our product candidates in human clinical trials, and we will face an even greater risk if we commercially sell any products that we may develop. While we currently have no products in clinical trials or that have been approved for commercial sale, the future use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies or others selling such products. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- termination of clinical trials;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend any related litigation;
- substantial monetary awards to trial participants or patients;

- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

We currently do not hold any clinical trial liability insurance coverage. We may need to obtain insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to obtain and maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If a successful clinical trial or product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We and any contract manufacturers and suppliers we engage are subject to numerous federal, state, and local environmental, health, and safety laws, regulations, and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air, and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research and product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We carry specific biological or hazardous waste insurance coverage (under which we currently have an aggregate of approximately \$2.0 million in coverage). However, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, we may incur substantial costs in order to comply with current or future environmental, health, and safety laws, regulations, and permitting requirements. These current or future laws, regulations, and permitting requirements may impair our research, development, or production efforts. Failure to comply with these laws, regulations, and permitting requirements also may result in substantial fines, penalties, or other sanctions or business disruption, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Any third-party contract manufacturers and suppliers we engage will also be subject to these and other environmental, health, and safety laws and regulations. Liabilities they incur pursuant to these laws and regulations could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Genetic therapies are novel, and any product candidates we develop may be complex and difficult to manufacture. We could experience delays in satisfying regulatory authorities or production problems that result in delays in our development programs, limit the supply of the product candidates we may develop or otherwise harm our business.

Any product candidates we may develop will likely require processing steps that are more complex than those required for most chemical pharmaceuticals. For example, one component of our Prime Editors is guide RNA, known as a Prime Editing guide RNA, or pegRNA we currently obtain from partners and vendors; future needs could require additional pegRNA lengths or increased purity, beyond what our partners and vendors can currently supply. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as the product candidates we intend to develop generally cannot be fully characterized. As a result, assays of the finished product candidate may not be sufficient to ensure that the product candidate will perform in the intended manner. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims, insufficient inventory or potentially delay progression of our potential IND filings. If we successfully develop product candidates, we may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet the FDA, the EMA or other comparable applicable foreign standards or specifications with consistent and acceptable production yields and costs. For example, the current approach of manufacturing AAV vectors may fall short of supplying required number of doses needed for advanced stages of preclinical studies or clinical trials, and the FDA may ask us to demonstrate that we have the appropriate manufacturing processes in place to support the higher-dose group in our preclinical studies or clinical trials. In addition, any product candidates we may develop will require complicated delivery methods, such as electroporation, LNPs or viral vectors, each of which will introduce additional complexities in the manufacturing process.

In addition, the FDA, the EMA and other regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, the EMA or other regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay clinical trials or product launches, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects.

Furthermore, we intend to use novel technology for gene editing. Our novel Prime Editors have two main components that act together to edit DNA: (i) a Prime Editor protein, comprising a fusion between a Cas protein and a reverse transcriptase enzyme, and (ii) a pegRNA, that targets the Prime Editor to a specific genomic location and provides a template for making the desired edit to the target DNA sequence. Prime Editing leverages the established DNA-targeting capabilities of CRISPR-Cas proteins modified to nick, but not cause double-stranded DNA breaks, and combines these with the DNA synthesis capabilities of reverse transcriptase enzymes, which have been engineered to efficiently and precisely copy a pegRNA-encoded edited sequence into target DNA. The scientific evidence to support the feasibility of developing product candidates based on this technology is both preliminary and limited and has yet to be produced at a clinical scale.

We also may encounter problems hiring and retaining the experienced scientific, quality control and manufacturing personnel needed to manage our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements.

Given the nature of biologics manufacturing there is a risk of contamination during manufacturing. Any contamination could materially harm our ability to produce product candidates on schedule and could harm our results of operations and cause reputational damage. Some of the raw materials that we anticipate will be required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of any product candidates we may develop could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially harm our development timelines and our business, financial condition, results of operations and prospects.

Any problems in our manufacturing process or the facilities with which we contract could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs. Problems in third-party manufacturing process or facilities also could restrict our ability to ensure sufficient clinical material for any clinical trials we may be conducting or are planning to conduct and meet market demand for any product candidates we develop and commercialize.

If preclinical studies or clinical trials of any product candidates we may identify and develop fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of any product candidates we may identify and develop, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete, and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results.

Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates.

We and our collaborators, if any, may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize any product candidates we may identify and develop, including:

- delays in reaching a consensus with regulators on trial design;
- regulators, institutional review boards, or IRBs, or independent ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- delays in reaching or failing to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective CROs and clinical trial sites;
- clinical trials of any product candidates we may develop may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development or research programs;
- difficulty in designing well-controlled clinical trials due to ethical considerations which may render it inappropriate to conduct a trial with a control arm that can be effectively compared to a treatment arm;
- difficulty in designing clinical trials and selecting endpoints for diseases that have not been well-studied and for which the natural history and course of the disease is poorly understood;
- the number of patients required for clinical trials of any product candidates we may develop may be larger than we anticipate; enrollment of suitable participants in these clinical trials, which may be particularly challenging for some of the rare genetically defined diseases we are targeting in our most advanced programs, may be delayed or slower than we anticipate; or patients may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators, IRBs, or independent ethics committees may require that we or our investigators suspend or terminate clinical research or clinical trials of any product candidates we may develop for various reasons, including noncompliance with regulatory requirements, a finding of undesirable side effects or other

unexpected characteristics, or that the participants are being exposed to unacceptable health risks or after an inspection of our clinical trial operations or trial sites;

- the cost of clinical trials of any product candidates we may develop may be greater than we anticipate;
- the supply or quality of any product candidates we may develop or other materials necessary to conduct clinical trials of any product candidates we may develop may be insufficient or inadequate, including as a result of delays in the testing, validation, manufacturing, and delivery of any product candidates we may develop to the clinical sites by us or by third parties with whom we have contracted to perform certain of those functions;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- clinical trial sites dropping out of a trial;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- occurrence of serious adverse events associated with any product candidates we may develop that are viewed to outweigh their potential benefits;
- occurrence of serious adverse events in trials of the same class of agents conducted by other sponsors; and
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

If we or our collaborators are required to conduct additional clinical trials or other testing of any product candidates we may develop beyond those that we currently contemplate, if we or our collaborators are unable to successfully complete clinical trials or other testing of any product candidates we may develop, or if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we or our collaborators may:

- be delayed in obtaining marketing approval for any such product candidates we may develop or not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to changes in the way the product is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw, or suspend, their approval of the product or impose restrictions on its distribution in the form of a Risk Evaluation and Mitigation Strategy, or REMS, or through modification to an existing REMS;
- be sued; or
- experience damage to our reputation.

Product development costs will also increase if we or our collaborators experience delays in clinical trials or other testing or in obtaining marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured, or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize any product candidates we may develop, could allow our competitors to bring products to market before we do, and could impair our ability to

successfully commercialize any product candidates we may develop, any of which may harm our business, financial condition, results of operations, and prospects.

Social media campaigns and demand for expanded access to our potential product candidates could negatively affect our reputation and harm our business.

We are developing product candidates in areas of unmet medical need where there are currently limited or no available therapeutic options and may receive requests in the future for right to try access or expanded access on a compassionate use basis to certain of our potential product candidates. It is possible for individuals or groups to target companies with disruptive social media campaigns related to a request for access to unapproved drugs for patients with significant unmet medical need. If we experience a similar social media campaign regarding our decision to provide or not provide access to any of our potential product candidates under an expanded access policy, our reputation may be negatively affected and our business may be harmed.

In addition, some patients who receive access to drugs prior to their commercial approval through compassionate use, expanded access programs or right to try access have life-threatening illnesses and have exhausted all other available therapies. The risk for serious adverse events in this patient population is high, which could have a negative impact on the safety profile of our potential product candidates if we were to provide them to these patients, which could cause significant delays or an inability to successfully commercialize our potential product candidates, which could materially harm our business. If we were to provide patients with our potential product candidates under an expanded access program, we may in the future need to restructure or pause any compassionate use and/or expanded access programs in order to perform the controlled clinical trials required for regulatory approval and successful commercialization of our potential product candidates, which could prompt adverse publicity or other disruptions related to current or potential participants in such programs.

Risks Related To Our Relationships with Third Parties

We may enter into collaborations with collaborators and strategic partners such as Beam Therapeutics or other third parties for the research, development, delivery, manufacturing and commercialization of Prime Editing technology and certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to capitalize on the market potential of our Prime Editing platform or product candidates.

We may seek third-party collaborators and strategic partners for the research, development, delivery, manufacturing and commercialization of certain of the product candidates we may develop. If we enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to collaboration, including the development, delivery, manufacturing or commercialization of any product candidates we may seek to develop with them. Our ability to generate revenues from these arrangements will depend on our collaborators' and strategic partners' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our research, development, expansion of our technology or for any product candidates we may develop pose numerous risks to us, including the following:

- Collaborators and strategic partners have significant discretion in determining the efforts and resources that they will apply to these collaborations, may not pursue development and commercialization of any product candidates we may develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities.
- Collaborators and strategic partners may have significant overlap in their areas of interest and capabilities, research and development activities and product candidates with us, which may result in potential conflicts of interest.
- The transfer of key technology between our collaborators and strategic partners and us may be incomplete, delayed or not meet our standards of quality.

- Collaborators and strategic partners may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing.
- Collaborators and strategic partners could independently develop or develop with third parties, products that compete directly or indirectly with our therapies or product candidates we may develop if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.
- Collaborators and strategic partners with marketing and distribution rights to one or more therapies may not commit sufficient resources to the marketing and distribution of such therapy or therapies.
- Collaborators and strategic partners may have rights or may believe they have rights to sub-license our Prime Editing technology more broadly than anticipated for the collaboration.
- Collaborators and strategic partners may not properly obtain, maintain, enforce or defend our intellectual property or proprietary rights or may use our intellectual property or proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation.
- Collaborators and strategic partners may not properly use our technology, perform activities below quality standards or wrongly interpret results, any of which may result in adverse public perception of Prime Editing or negatively impact the regulatory approval of, and/or demand for, our potential product candidates.
- There may be areas of ambiguity in the interpretation of obligations and deliverables under any collaboration agreements we have entered or may enter into, including disputes that may arise between the collaborators and strategic partners and us that result in the delay or termination of the research, development or commercialization of our therapies or product candidates or that result in costly litigation or arbitration that diverts management attention and resources.
- We may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control.
- Collaborations may be terminated and, if terminated, may leave incomplete some or all of the goals that were set for such collaboration or result in a need for additional capital to pursue further development or commercialization of the applicable product candidates we may develop.
- Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished or terminated.

If our collaborations do not result in successful research or delivery approaches or successful development and commercialization of product candidates, or if one of our collaborators or strategic partners terminates its agreement with us, there may be adverse consequences. For example, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of product candidates could be delayed, and we may need additional resources to develop product candidates. In addition, if one of our collaborators or strategic partners terminates its agreement with us, we may find it more difficult to find a suitable replacement or attract a new collaboration, lose access to key technology or our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, regulatory approval and commercialization described in this prospectus apply to the activities of our collaborators and strategic partners.

These relationships, or those like them, may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, result in a loss of value to our

stock or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators and strategic partners and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement will depend, among other things, upon our assessment of the collaborator's and strategic partner's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of several factors. If we license rights to any product candidates we may develop we or our collaborators and strategic partners may develop, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture.

If conflicts arise between us and our collaborators or strategic partners, these parties may act in a manner adverse to us and could limit our ability to implement our strategies.

If conflicts arise between our corporate or academic collaborators or strategic partners and us, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. Some of our academic collaborators and strategic partners are conducting multiple product development efforts within each area that is the subject of the collaboration with us. Our collaborators or strategic partners, however, may develop, either alone or with others, products in related fields that are competitive with the product candidates we may develop that are the subject of these collaborations with us. Competing products, either developed by the collaborators or strategic partners or to which the collaborators or strategic partners have rights, may result in the withdrawal of partner support for any product candidates we may develop.

Some of our collaborators or strategic partners could also become our competitors in the future. For example, Beam Therapeutics, currently one of our strategic partners, may develop product candidates in areas where both companies have freedom to pursue development. For more information regarding our agreement with Beam Therapeutics, see "Business—Our License and Collaboration Agreements" and the risk factor entitled "The gene editing field is relatively new and is evolving rapidly. We are focusing our research and development efforts on gene editing using Prime Editing technology, but other gene editing technologies may be discovered that provide significant advantages over Prime Editing, which could materially harm our business."

Our collaborators or strategic partners could develop competing products, preclude us from entering into collaborations with their competitors, fail to obtain timely regulatory approvals, prevent us from obtaining timely regulatory approvals, terminate their agreements with us prematurely or fail to devote sufficient resources to the collaboration efforts, including development, delivery, manufacturing and commercialization of products. Any of these developments could harm our company and product development efforts.

We expect to rely on third parties to conduct our clinical trials and some aspects of our research, as well as some aspects of our delivery methods, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.

We currently, and expect to continue to, rely on third parties, such as CROs, clinical data management organizations, medical institutions, preclinical laboratories and clinical investigators, to conduct some aspects of our research. For example, we may rely on a third party to conduct electroporation, to supply LNPs or AAVs, or to conduct some of our preclinical animal experiments. Any of these third parties may terminate their engagements with us at any time under certain criteria. If we need to enter into alternative arrangements, it may delay our product development activities.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA, the EMA and other regulatory authorities require us and the study sites and investigators we work with to comply with standards, commonly referred to as GLPs and GCPs for conducting, recording and reporting the results of preclinical studies and clinical trials to assure, amongst other things, that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. In the United States, we also are required to register certain clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Although we intend to design the clinical trials for our potential product candidates, CROs will conduct some or all of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct preclinical studies and future clinical trials will also result in less direct control over the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Among other reasons that may delay or impact the development of our potential product candidates, outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our preclinical studies and clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CROs and other third parties do not perform such preclinical studies and future clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our potential product candidates may be delayed, we may not be able to obtain regulatory approval and commercialize our potential product candidates or our development programs may be materially and irreversibly harmed. If we are unable to rely on preclinical and clinical data collected by our CROs and other third parties, we could be required to repeat, extend the duration of or increase the size of any preclinical studies or clinical trials we conduct and this could significantly delay commercialization and require greater expenditures.

We may also expect to rely on other third parties to store and distribute drug supplies for our future clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of any product candidates we may develop or commercialization of our therapies, producing additional losses and depriving us of potential product revenue.

We contract with third parties for the manufacture of materials for our research programs and expect to continue to do so for clinical trials and for any commercialization of product candidates that we may develop. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials, product candidates or any therapies that we may develop and commercialize, or that such supply will not be available to us on time or at an acceptable cost.

We do not have any manufacturing facilities at the present time. We currently rely on third-party manufacturers to manufacture many of our materials for research and may continue to do so for preclinical studies and possibly even clinical trials. We have not yet formulated our plans for commercial supply of any product candidates that we may develop or for which we or our collaborators may in the future obtain marketing approval, but our future decisions may be subject to similar risks to the ones discussed below.

We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, some of which may include:

- the possible breach of the manufacturing agreement by the third party;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- reliance on the third party for regulatory compliance, quality assurance, safety and pharmacovigilance and related reporting.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or therapies, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our therapies and harm our business, financial condition, results of operations and prospects.

Any therapies that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply for bulk drug substances. If any third party-manufacturer with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the facilities or resources, or enter into an agreement with a different third party-manufacturer, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or product candidates may be unique or proprietary to the original third party-manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change third party-manufacturers for any reason, we will be required to verify that the new third party-manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our potential product candidates according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new third party-manufacturer could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a third party-manufacturer may possess technology related to the manufacture of our product candidate that such third party-manufacturer owns independently. This would increase our reliance on such third party-manufacturer or require us to obtain a license from such third party-manufacturer in order to have another third party-manufacturer manufacture our product candidates, which may not be available on commercially reasonable terms, or at all. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials.

Our current and anticipated future dependence upon others for the manufacture of any product candidates or therapies we may develop may adversely affect our future profit margins and our ability to commercialize any therapies that receive marketing approval on a timely and competitive basis.

If we are not able to establish collaborations on a timely basis, on commercially reasonable terms, or at all, we may have to alter, reduce or delay our development and commercialization plans or increase our expenditures to fund development or commercialization activities at our own expense.

For some of the product candidates we may develop, we may decide to collaborate with other pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates, which is a complex and time-consuming process to negotiate and document. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator or strategic partner's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator or strategic partner's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, the EMA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator or strategic partner may

also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us. In addition, we and the collaborator or strategic partner may have differences in risk tolerance, which may affect the development and execution of such collaborations with respect to timing and other considerations.

We may also be restricted under existing collaboration agreements from entering into future collaboration agreements on certain terms with potential collaborators. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators, which further increases competition we face in seeking potential collaborations.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to develop product candidates or bring them to market and generate product revenue.

Risks Related To Our Intellectual Property

If we are unable to obtain and maintain patent and other intellectual property protection for any product candidates we develop and for our Prime Editing technology, or if the scope of the patent and other intellectual property protection obtained is not sufficiently broad, third parties could develop and commercialize products and technology similar or identical to ours and our ability to successfully commercialize any product candidates we may develop and our Prime Editing technology may be adversely affected.

Our commercial success will depend in large part on our ability to obtain and maintain patent, trademark, trade secret and other intellectual property protection of our Prime Editing technology, product candidates and other technology, methods used to manufacture them and methods of treatment, as well as to successfully defend our patent and other intellectual property rights against third-party challenges. It is difficult and costly to protect our Prime Editing technology and product candidates, and we may not be able to ensure their protection. The development of our product candidates and technology is at an early stage and consequently, our patent portfolio is also at an early stage. For example, we do not currently own or in-license any issued patents relating to our technology and product candidates and many of our and our licensors' patent applications are either at the provisional stage or at an early stage in prosecution. Our ability to stop unauthorized third parties from making, using, selling, offering to sell, importing or otherwise commercializing our product candidates we may develop is dependent upon the extent to which we have established rights under valid and enforceable patents or trade secrets that cover these activities.

We seek to protect our proprietary position by in-licensing intellectual property relating to our platform technology and filing patent applications in the United States and abroad related to our Prime Editing technology and product candidates that are important to our business. If we or our licensors are unable to obtain or maintain patent protection with respect to our Prime Editing technology and product candidates we may develop, or if the scope of the patent protection secured is not sufficiently broad, third parties could develop and commercialize products and technology similar or identical to ours and our ability to commercialize any product candidates we may develop may be adversely affected.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, enforce, defend or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and

other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned or licensed pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. If a third party can establish that we or our licensors were not the first to make or the first to file for patent protection of such inventions, our owned or licensed patent applications may not issue as patents and even if issued, may be challenged and invalidated or rendered unenforceable.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has been the subject of much litigation in recent years. The field of genome editing has been the subject of extensive patenting activity and litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain and we may become involved in complex and costly litigation. Our pending and future patent applications may not result in patents being issued which protect our Prime Editing technology and product candidates we may develop or which effectively prevent others from commercializing competitive technologies and product candidates. For example, our provisional applications may never result in issued patents. A provisional patent application is not eligible to become an issued patent until, among other things, we file a non-provisional patent application within 12 months of filing the related provisional patent application. If we do not timely file non-provisional patent applications, we may lose our priority dates with respect to our provisional patent applications and any patent protection on the inventions disclosed in our provisional patent applications. While we intend to timely file non-provisional patent applications relating to our provisional patent applications, we cannot predict whether any of our patent applications for our technology and product candidates will result in the issuance of patents that effectively protect our technology and product candidates. Any failure to obtain or maintain patent protection with respect to our technology and product candidates would have a material adverse effect on our business, financial condition, results of operations and prospects.

No consistent policy regarding the scope of claims allowable in the field of genome editing, including for Prime Editing technologies such as our Prime Editing technology, has emerged in the United States. The scope of patent protection outside of the United States is also uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions, obtain, maintain, enforce and defend our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patent rights. With respect to both in-licensed and owned intellectual property, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will be valid and enforceable and provide sufficient protection from third parties.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we license or own currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patent applications that we own or in-license may, if issued as patents, be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether any of our platform advances and product candidates we may develop will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents that may be issued from our patent applications by developing similar or alternative technologies or products in a non-infringing manner. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents that may be issued protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Some of our owned and in-licensed patent applications are, and may in the future be, co-owned with third parties. With respect to any patent applications co-owned by third parties, we may require exclusive licenses to such

co-owners' interest to such patents. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patent applications, we may be unable to prevent such co-owner from licensing their rights under the patent applications to other third parties, including our competitors, and our competitors may be able to market competing products and technology. In addition, we may need the cooperation of any such co-owners of our future patents in order to enforce such future patents against third parties, and such cooperation may not be provided to us.

Our rights to develop and commercialize our Prime Editing platform technology and product candidates are subject to the terms and conditions of licenses granted to us by others. If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We do not currently own any issued patents and are heavily reliant upon certain patent rights and proprietary technology we have licensed from third parties that are important or necessary to the development of our Prime Editing technology and product candidates. For example, we are a party to a license agreement with Broad Institute. In September 2019, we entered into a license agreement with Broad Institute, and in May 2020 and February 2021, we entered into amendments to such license agreement. Under the amended license agreement, or the Broad License Agreement, Broad Institute grants us certain rights and licenses under certain patent rights it owns or controls relating to our Prime Editing technology and product candidates. The Broad License Agreement imposes various diligence, milestone payment, royalty, insurance and other obligations on us. Our licenses are subject to Broad Institute's inclusive innovation model, pursuant to which Broad Institute retains the right, in certain circumstances, to grant to third parties (other than specified competitors of ours) licenses under the licensed patent rights that would otherwise fall within the scope of the exclusive license granted to us. All gene targets, which are any human genes to which a program is directed, are subject to Broad Institute's march-in license, which means Broad Institute has the right to terminate our license to gene targets under certain conditions and could make one or more gene targets unavailable to us. However, once we initiate a program for a gene target, in accordance with the terms of the Broad License Agreement, Broad Institute loses the right to use its march-in license for such gene target, provided we continue to use commercially reasonable efforts to continue to progress such development. As such, Broad Institute cannot exercise its march-in license with respect to any of our current programs for gene targets because such programs have been initiated in accordance with the terms and requirements of the Broad License Agreement. Internally, we determine when a program for a gene target has been initiated by considering factors such as whether a gene target has been identified as the subject of a program, how much time or resources have been dedicated to researching, developing, and/or designing and using reagents for a program, and the amount of preclinical testing in process for such program. For more information regarding the scope of our rights and obligations under the Broad License Agreement, see the section titled "Business—Our License and Collaboration Agreements—License Agreement with Broad Institute." If we fail to comply with these or other obligations in our current or future license agreements, our licensors may have the right to terminate our license, in which event we would not be able to develop or market our Prime Editing technology or any other technology or product candidates covered by the intellectual property licensed under this agreement. Our business would be seriously harmed if any current or future licenses terminate, if our licensors fail to abide by the terms of the license, if our licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. If our license agreements terminate, or we experience a reduction or elimination of licensed rights under these agreements, we may have to negotiate new or reinstated licenses with less favorable terms or we may not have sufficient intellectual property rights to operate our business. Moreover, if certain of our license agreements terminate, we may be required to continue to license or assign certain of our intellectual property to the applicable counterparty.

Certain of the patent rights that we license from Broad Institute are co-owned by Broad Institute with Harvard and certain of the licensed patent rights are co-owned by Broad Institute, Harvard, and Massachusetts Institute of Technology, or MIT. In addition, some of the inventors of the licensed patent applications are or were employees of HHMI, which retains certain rights to patents and patent applications invented by their employees. Our rights to our in-licensed patent applications from Broad Institute are dependent, in part, on inter-institutional or other operating agreements between Broad Institute, Harvard, MIT and HHMI. If Broad Institute, Harvard, MIT or HHMI breaches or terminates such inter-institutional or operating agreements, our rights to such in-licensed patent applications may

be adversely affected. We have also licensed certain improvements to Prime Editing from Dr. Liu's laboratory at Broad Institute. For example, Dr. Liu's laboratory at Broad Institute recently developed engineered pegRNAs, or epegRNAs, which we have exclusively in-licensed. Dr. Liu has entered into an agreement with us pursuant to which he is obligated to assign to us any inventions with respect to the services he performs for us. However, such obligations are subject to limitations and do not extend to his work in other fields or to the intellectual property arising from his employment with Harvard, HHMI and Broad Institute. To obtain such intellectual property rights, we would need to enter into license agreements with such institutions, including negotiations under the Broad Option Agreement, which may expire in November 2022, and such license agreements may not be available on commercially reasonable terms or at all.

Additionally, in September 2019, we established a strategic relationship with Beam Therapeutics, a biotechnology company developing gene editing products using its proprietary base editing technology. Under our license and collaboration agreement with Beam, or the Beam Collaboration Agreement, each party grants to the other certain exclusive and non-exclusive licenses and rights to certain Prime Editing, CRISPR and delivery technologies for use in certain specified fields. Activities performed by Prime and Beam under the Beam Collaboration Agreement may lead to co-owned patents and patent applications. For more information regarding the Broad License Agreement and the Beam Collaboration Agreement and our other material agreements related to our technology, see the section titled "Business—Our License and Collaboration Agreements."

These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our Prime Editing technology and product candidates in the future. Some licenses granted to us are expressly subject to certain preexisting rights held by the licensors or certain third parties. As a result, we may not be able to prevent third parties from developing and commercializing competitive products in certain territories or fields. For example, the rights granted to us under the Broad License Agreement are subject to certain retained rights of Broad Institute, MIT, Harvard, HHMI and the U.S. federal government, and the rights granted to us under the Beam Collaboration Agreement are subject to certain third party agreements and certain rights retained by third parties. Additionally, the Broad License Agreement provides that our field of use is limited to the field of prevention or treatment of human disease, and most licenses granted to us under the Broad License are further limited to the prevention or treatment of human disease by editing (including modifying or converting) or targeting DNA *ex vivo*, *in vivo*, or through xeno-transplantation methods and includes other specified exclusions. If we determine that rights to additional fields, including the specifically excluded fields, are necessary to commercialize our product candidates or maintain our competitive advantage, we may need to obtain a license from Broad Institute and/or other third parties in order to continue developing, manufacturing or marketing our product candidates. We may not be able to obtain such a license on an exclusive basis, on commercially reasonable terms, or at all, which could prevent us from commercializing our product candidates or allow our competitors or other third parties the chance to access technology that is important to our business.

We do not control the preparation, filing, prosecution and maintenance of the patent applications covering the technology that we license from Broad Institute or Beam Therapeutics. For example, pursuant to our licenses with Broad Institute and Beam Therapeutics, our licensors retain control of preparation, filing, prosecution and maintenance of their wholly-owned patent applications. We rely on such licensors to determine inventorship and perfect priority of their patent applications. We cannot be certain that these patent applications will be prepared, filed, prosecuted, maintained and defended in a manner consistent with the best interests of our business. If Broad Institute or Beam Therapeutics fails to prosecute or maintain such patent applications or loses rights to such patent applications, the rights we have licensed may be reduced or eliminated, our right to develop and commercialize any of our product candidates we may develop that are the subject of such licensed rights could be adversely affected and we may not be able to prevent third parties from making, using and selling competing products. In addition, we do not control all enforcement of the patent applications we license from Broad Institute. It is possible that our licensors' enforcement of patents against infringers or defense of such patents against challenges of validity or claims of enforceability may be less vigorous than if we had conducted them ourselves, or may not be conducted in accordance with our best interests.

Our licensors have also relied on third-party collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patent rights we have in-licensed. For example, our optioned patent

applications directed to the use of MMR inhibition for prime editing is jointly owned by Broad Institute, Harvard, The Trustees of Princeton University, or Princeton, and The Regents of the University of California, or University of California. The exclusivity of such option is solely with respect to Broad Institute and Harvard, and if we are unable to secure licenses to the rights of all co-owners of such patent applications, including Princeton and University of California, the license granted to us in jurisdictions where the consent of a co-owner is necessary to grant such a license may not be valid, and such co-owners for which we do not secure exclusive licenses may be able to license such patent rights to third parties, including our competitors, and such third parties may be able to market competing products and technology.

Furthermore, inventions contained within some of our in-licensed patent applications were made using U.S. government funding. We rely on our licensors to ensure compliance with applicable obligations arising from such funding, such as timely reporting, an obligation associated with our in-licensed patent applications. The failure of our licensors to meet their obligations may lead to a loss of rights or the unenforceability of relevant patents that may issue from such applications. For example, the U.S. government could have certain rights in such in-licensed patent applications, including a non-exclusive license authorizing the U.S. government to use the invention or to have others use the invention on its behalf. If the U.S. government decides to exercise these rights, it is not required to engage us as its contractor in connection with doing so. The U.S. government's rights may also permit it to disclose the funded inventions and technology to third parties and to exercise march-in rights to use or allow third parties to use the technology we have licensed that was developed using U.S. government funding. The U.S. government may also exercise its march-in rights if it determines that action is necessary because we or our licensors failed to achieve practical application of the U.S. government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. For example, if the U.S. government determines it is necessary, the U.S. government may exercise its march-in rights and license to third-party manufacturers any or all of our future products or current or future product candidates covered by in-licensed patents and patent applications made using U.S. government funding. In addition, our rights in such in-licensed U.S. government-funded inventions may be subject to certain requirements to manufacture product candidates embodying such inventions in the United States. Any of the foregoing could harm our business, financial condition, results of operations and prospects significantly.

In the event that any of our third-party licensors determines that, in spite of our efforts, we have materially breached a license agreement or have failed to meet certain obligations thereunder, it may elect to terminate the license agreement or, in some cases, one or more license(s) under the applicable license agreement and such termination would result in us no longer having the ability to develop and commercialize product candidates and technology covered by that license agreement or license. In the event of such termination of a third-party in-license, or if the underlying patent rights under a third-party in-license fail to provide the intended exclusivity, third parties may be able to seek regulatory approval of, and to market, products identical to ours. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. Any of these events could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

Pursuant to our license agreements with Beam Therapeutics and Broad Institute, we are generally responsible for bringing any actions against any third party for infringing on certain of the patent rights we have licensed from such counterparty, subject to certain conditions. Certain provisions of the Broad License Agreement also require us to meet development thresholds within specified timeframes to maintain the license, including establishing a set timeline for developing and commercializing products, while some provisions of the Beam Collaboration Agreement require us to use commercially reasonable efforts to conduct development activities for collaboration products. For more information regarding the scope of our rights and obligations under the Broad License Agreement and the Beam Collaboration Agreement, see the section titled "Business—Our License and Collaboration Agreements." In spite of our efforts, Broad Institute, Beam Therapeutics, or any future licensor from whom we may seek to license intellectual property rights might conclude that we have materially breached our obligations under such license agreements and might therefore terminate the license agreements, thereby removing or limiting our ability to develop and commercialize products and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying patent rights fail to provide the intended exclusivity, competitors or other third

parties may be able to seek regulatory approval of, and to market, products identical to ours and we may be required to cease our development and commercialization of our Prime Editing technology or product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and growth prospects. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent rights to third parties under our collaborative development relationships;
- our diligence obligations under the license agreement with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensor and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property rights from Beam Therapeutics and Broad Institute are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise under our existing license agreements or future license agreements into which we may enter could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology or broaden what we believe to be the scope of the licensor's rights to our intellectual property and technology, or increase what we believe to be our financial or other obligations under the relevant agreement, any of which could have a material adverse effect on our business, financial condition, results of operations and prospects. For example, we have exclusively licensed and sublicensed certain of our owned and licensed intellectual property rights to Beam under the Beam Collaboration Agreement in certain fields. Such agreement may be susceptible to multiple interpretations and the resolution of any contract interpretation disagreement could expand the field of exclusivity or other rights we have granted to Beam and therefore, narrow our field of exclusivity or rights with respect to such licensed intellectual property rights. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. As a result, any termination of or disputes over our intellectual property licenses could result in the loss of our ability to develop and commercialize our Prime Editing technology or other product candidates or we could lose other significant rights, any of which could have a material adverse effect on our business, financial conditions, results of operations and prospects. It is also possible that a third party could be granted limited licenses to some of the same technology, in certain circumstances.

Our owned and in-licensed patent applications may not provide sufficient protection of our Prime Editing technologies and our future product candidates or result in any competitive advantage.

We own and have in-licensed a number of patent applications that cover Prime Editing and related technologies. We and our licensors have filed patent applications intended to specifically cover our Prime Editing technology and uses with respect to treatment of particular diseases and conditions, but we do not currently own or in-license any issued U.S. patents.

Our owned and in-licensed patent applications contain claims directed to compositions of matter for our Prime Editing product candidates, as well as methods directed to the use of such product candidates for gene therapy treatment. Method-of-use patents do not prevent a competitor or other third party from developing or marketing an identical product for an indication that is outside the scope of the patented method. Moreover, with respect to method-of-use patents, even if competitors or other third parties do not actively promote their product for our

targeted indications or uses for which we may obtain patents, providers may recommend that patients use these products off-label, or patients may do so themselves.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our future patents may be challenged in the courts or patent offices in the United States and abroad. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries. For example, while our or our licensors' patent applications are pending, such patent applications may now or in the future be subject to a third party pre-issuance submission of prior art to the United States Patent and Trademark Office, or USPTO, or become involved in interference or derivation proceedings or equivalent proceedings in foreign jurisdictions. For example, prior art was submitted by a third party with respect to certain of our PCT patent applications in-licensed from Broad Institute directed to Prime Editing. Even if our or our licensors' patents do successfully issue, third parties may challenge their inventorship, priority of invention, validity, enforceability or scope, including through opposition, revocation, reexamination, post-grant and *inter partes* review proceedings and litigation. Moreover, we, or one of our licensors, may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post grant challenge proceedings, such as oppositions in a foreign patent office, that challenge priority of invention or other features of patentability. An adverse determination in any such submission, proceeding or litigation may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, limit the duration of the patent protection of our technology and product candidates, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Furthermore, even if they are unchallenged, our patent rights may not adequately protect our intellectual property or prevent others from designing around our platform technology or product candidates. If the breadth or strength of protection provided by patents that may issue from the patent applications we own or in-license with respect to our Prime Editing technology and product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in development, testing and regulatory review of new product candidates, the period of time during which we could market our product candidates under patent protection would be reduced.

Given that patent applications in the United States and other countries are confidential for a period of time after filing, at any moment in time, we cannot be certain that we or our licensors were in the past or will be in the future the first to file any patent application related to our Prime Editing technology or product candidates. In addition, some patent applications in the United States may be maintained in secrecy until the patents are issued. As a result, there may be prior art of which we or our licensors are not aware that may affect the validity or enforceability of a patent claim, and we or our licensors may be subject to priority disputes. For our in-licensed patent portfolios, we rely on our licensors to determine inventorship and to obtain and file inventor assignments of priority applications before their conversion as PCT applications. A failure to do so in a timely fashion may give rise to a challenge to entitlement of priority for foreign applications nationalized from such PCT applications. We or our licensors may in the future become a party to proceedings or priority disputes in Europe or other foreign jurisdictions. The loss of priority for, or the loss of, any European or other foreign patent rights could have a material adverse effect on the conduct of our business.

We may be required to disclaim part or all of the term of certain patents that may issue from our owned or in-licensed patent applications. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we or our licensors are aware, but which we or our licensors do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that, if challenged, our patent applications, if issued, would be declared by a court, patent office or other governmental authority to be valid or enforceable, or that even if the patent claims were found to be not invalid or unenforceable, a third party's technology or product would be found by a court to infringe our patent rights. Moreover, even if our patent applications, if issued, are declared to be valid and enforceable and a third party's technology or product found to infringe our patent rights, a court or other governmental authority may refuse to prevent a third party's technology or

product from being marketed, and the court or governmental authority would determine the royalty rate to be paid by the third party to us. We analyze patents or patent applications of third parties that we believe are relevant to our activities, but third parties may achieve issued claims, including in patents we consider to be unrelated, that block our efforts or potentially result in our product candidates or our activities infringing such claims. It is possible that third parties may have filed, and may in the future file, patent applications covering our products or gene editing technology similar to ours. Those patent applications may have priority over our owned and in-licensed patent applications, which could require us to obtain rights to issued patents covering such technologies. The possibility also exists that others will develop products that have the same effect as our product candidates on an independent basis that do not infringe patents that may issue from our own or in-licensed patent applications, or other intellectual property rights, or will design around the claims of our patents that may issue from our owned or in-licensed patent applications that cover our product candidates.

Likewise, our currently owned and in-licensed patent applications, if issued as patents, directed to our in-licensed and company-owned Prime Editing technologies and our product candidates are expected to expire between 2040 and 2042, without taking into account any possible patent term adjustments or extensions. Our owned or in-licensed patent applications, if issued as patents, may expire before, or soon after, our first product candidate achieves marketing approval in the United States or foreign jurisdictions. Additionally, no assurance can be given that the USPTO or relevant foreign patent offices will grant any of the pending patent applications we own or in-license currently or in the future. Upon the expiration of such patents that may issue from our current owned or in-licensed patent applications, we may lose the right to exclude others from practicing these inventions. The expiration of these patent rights could also have a similar material adverse effect on our business, financial condition, results of operations and prospects.

Our owned and in-licensed patent applications and other intellectual property may be subject to priority, inventorship or ownership disputes and similar proceedings. If we or our licensors are unsuccessful in any of these proceedings, we may be required to obtain licenses from third parties, which may not be available on commercially reasonable terms or at all, or to cease the development, manufacture and commercialization of one or more of our product candidates, which could have a material adverse impact on our business.

We or our licensors may be subject to claims that former employees, collaborators, or other third parties have an interest in our owned or in-licensed patent applications or other intellectual property as an inventor or co-inventor. If we or our licensors are unsuccessful in any interference proceedings or other priority, validity (including any patent oppositions), inventorship or ownership disputes to which we or they are subject, we may lose valuable intellectual property rights through the loss of part or all of our owned or licensed patent rights, the loss of exclusive ownership of or the exclusive right to use our owned or in-licensed patent rights, or the narrowing, invalidation, or unenforceability of our or our licensors' patent claims. In the event of loss of patent rights as a result of any of these disputes, we may be required to obtain and maintain licenses from third parties, including parties involved in any such interference proceeding or other priority, inventorship or ownership disputes. Such licenses may not be available on commercially reasonable terms or at all, or may be non-exclusive. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture and commercialization of one or more of our product candidates. The loss of exclusivity or the narrowing of our patent rights could limit our ability to stop others from using or commercializing similar or identical technology and product candidates. Even if we or our licensors are successful in an inventorship or ownership dispute, it could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could result in a material adverse effect on our business, financial condition, results of operations, or prospects.

We have limited foreign intellectual property rights and may not be able to protect our intellectual property and proprietary rights throughout the world.

We have limited intellectual property rights outside the United States. Filing, prosecuting and defending patents on our Prime Editing technologies and product candidates in all countries throughout the world would be prohibitively expensive and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. The laws of foreign countries do not protect intellectual property rights to the same extent as federal and state laws of the United States, even in jurisdictions where we or our licensors do pursue patent protection. In addition, our intellectual property license agreements may not always include worldwide

rights. Consequently, we or our licensors may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Third parties may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as that in the United States. These products may compete with our product candidates and patents that may issue from our or our licensors' pending patent applications or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology and pharmaceutical products, which could make it difficult for us to stop the infringement of our future patents or marketing of competing products by third parties in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our or our licensors' future patents and intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our or our licensors' future patents at risk of being invalidated or interpreted narrowly and our or our licensors' patent applications at risk of not issuing and could provoke third parties to assert claims against us or our licensors. We may not prevail in any lawsuits that we or our licensors initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Moreover, the initiation of proceedings by third parties to challenge the scope or validity of our or our licensors' patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. Accordingly, our or our licensors' efforts to enforce our or our licensors' intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or our licensors are forced to grant one or more licenses to third parties with respect to any future patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

We may not be successful in acquiring or in-licensing necessary rights to key technologies or any product candidates we may develop.

We currently have rights to intellectual property, through licenses from third parties, to identify and develop product candidates, and we expect to seek to expand our product candidate pipeline in part by in-licensing additional rights to key technologies. The future growth of our business will depend in part on our ability to in-license or otherwise acquire the rights to additional product candidates and technologies. Although we have succeeded in licensing technologies from Beam Therapeutics and Broad Institute in the past, we cannot guarantee that we will be able to in-license or acquire additional rights to any product candidates or technologies from Beam Therapeutics, Broad Institute, or other third parties on acceptable terms or at all. For example, Broad Institute is developing improvements to the Prime Editing technology for which we may find it necessary or useful to obtain a license. In addition, our agreements with Beam Therapeutics and Broad Institute provide that our fields of use excludes particular fields. If we determine that rights to such fields are necessary to commercialize our technology or product candidates or maintain our competitive advantage, we may need to obtain a license from Beam Therapeutics or Broad Institute in order to continue developing, manufacturing or marketing our technology or product candidates. In addition, we may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties (potentially including our competitors) to receive licenses to a portion of the intellectual property that is subject to our existing licenses. Additionally, upon our finalization of our product candidates, we may determine that there are third parties who possess technologies related to gene editing or other technologies which we may need to in-license, including intellectual property covering the use of Cas proteins and reverse transcriptases. We may not be able to obtain such a license on an exclusive basis, on commercially reasonable terms, or at all, which could prevent us from commercializing our

product candidates or allow our competitors or other third parties the chance to access technology that is important to our business.

Furthermore, there has been extensive patenting activity in the field of gene editing. Pharmaceutical companies, biotechnology companies and academic institutions are competing with us or are expected to compete with us in the field of gene editing technology and filing patent applications potentially relevant to our business and we are aware of certain third-party patent applications that, if issued, may allow the third party to circumvent our patent rights. For example, we are aware of several third-party patents and patent applications, that if issued, may be construed to cover or be relevant to our Prime Editing technology and product candidates. In order to market our product candidates, we may find it necessary or prudent to obtain licenses from such third-party intellectual property holders. However, we may be unable to secure such licenses or otherwise acquire or in-license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for product candidates we may develop and our Prime Editing technology. We may also require licenses from third parties for certain additional technologies, including technologies relating to Prime Editing, such as guide RNA modification, target sequences, Cas proteins such as Cas9, reverse transcriptases, as well as delivery technologies for product candidates we may develop.

Additionally, we may collaborate with academic institutions to accelerate our research or development under written agreements with these institutions. In certain cases, these institutions may provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Even if we hold such an option, we may be unable to negotiate a license from the institution within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, such institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program.

The licensing or acquisition of third-party intellectual property rights is a highly competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

The intellectual property landscape around the technologies we use or plan to use, including gene editing technology, is highly dynamic, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating their intellectual property rights, the outcome of which would be uncertain and may prevent, delay or otherwise interfere with our product discovery and development efforts.

The field of gene editing is still in its infancy, and no such therapeutic product candidates have reached the market. Due to the intense research and development that is taking place by several companies, including us and our competitors, in this field, the intellectual property landscape is evolving and in flux, and it may remain uncertain for the coming years. There may be significant intellectual property related litigation and proceedings relating to our owned and in-licensed, and other third-party, intellectual property and proprietary rights in the future.

Our commercial success depends upon our ability and the ability of our collaborators and present and future licensees to develop, manufacture, market and sell any product candidates that we may develop and use our proprietary technologies without infringing, misappropriating, or otherwise violating the intellectual property and proprietary rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post grant review and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be subject to and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our Prime Editing technology and product candidates we may

develop, including interference proceedings, post-grant review, *inter partes* review and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions such as oppositions before the European Patent Office, or EPO. Numerous U.S. and foreign issued patents and pending patent applications that are owned by third parties exist in the fields in which we are developing our product candidates and they may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit.

As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our Prime Editing technology and product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of therapies, products or their methods of use or manufacture. There may be third-party patents of which we are currently unaware with claims to technologies, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents.

Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. Our product candidates make use of CRISPR-based technology, which is a field that is highly active for patent filings. As of June 2019, it was reported that approximately 2072 patent families worldwide related to CRISPR gene editing inventions and their uses. The extensive patent filings related to CRISPR make it difficult for us to assess the full extent of relevant patents and pending applications that may cover our Prime Editing technology and product candidates and their use or manufacture. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our Prime Editing platform technology and product candidates. We are aware of multiple patents and patent applications directed to CRISPR technologies, Cas molecules, including Cas9, and their uses in gene editing. For example, we are aware of a patent portfolio that is co-owned by the University of California, University of Vienna and Emmanuelle Charpentier, which we refer to together as CVC, which contains multiple patents and pending applications directed to gene editing. We are also aware of patents and patent applications directed to gene editing owned or co-owned by Broad Institute, MIT, Rockefeller University and Harvard, which we refer to together as the Boston Licensing Parties, Toolgen Inc. and Sigma-Aldrich. Additional patents and patent applications that we are aware of and directed to gene-editing are owned or co-owned by The General Hospital Corporation, BASF, SNIPR Technologies Ltd., Novartis, Columbia University, Agilent Technologies, Thermo Fisher Scientific, Life Technologies Corporation and Intellia.

Our ability to commercialize our product candidates may be adversely affected if we require but cannot obtain a license to these patents. We may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be nonexclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, we may be unable to commercialize our Prime Editing technology or product candidates or such commercialization efforts may be significantly delayed, which could in turn significantly harm our business.

Several patents and pending applications with claims directed to foundational aspects of gene editing are currently involved in interference proceedings at the USPTO. The Patent Trial and Appeal Board (PTAB) of the USPTO declared a second interference between 10 pending applications co-owned by the CVC and 13 patents and one pending application co-owned by the Boston Licensing Parties on June 24, 2019, after the first interference between the two parties was terminated in 2018. Toolgen subsequently joined the patent dispute and two more interferences were declared in December 2020, between a pending application owned by Toolgen and several pending applications co-owned by the CVC or patents and pending applications co-owned by the Boston Licensing Parties. More recently, in June 2021, two additional interferences were declared between patents and applications co-owned by the Boston Licensing Parties or pending applications co-owned by the CVC and pending applications owned by Sigma-Aldrich. It is presently unclear who will prevail in these proceedings and own or partially own the patents subject to such interferences. If it is necessary for us to obtain a license to one or more of the patents currently involved in such interference proceedings, such patents may not be available to license on commercially reasonable terms or at all. For example, we are aware that the Boston Licensing Parties and CVC have previously

licensed certain of such patents to third parties. Our ability to commercialize our product candidates in the United States and abroad may be adversely affected if we cannot obtain a license on commercially reasonable terms to relevant third-party patents that cover our product candidates or Prime Editing technology.

Because of the large number of patents issued and patent applications filed in our field, third parties may allege they have patent rights encompassing our product candidates, technologies or methods. Third parties may assert that we are employing their proprietary technology without authorization and may file patent infringement claims or lawsuits against us, and if we are found to infringe such third-party patents, we may be required to pay damages, cease commercialization of the infringing technology, or obtain a license from such third parties, which may not be available on commercially reasonable terms or at all. In addition, we have in the past, and may in the future, receive an offer for license from third parties regarding their proprietary intellectual property for which they may believe encompass our product candidates and technologies. We will evaluate such offers for relevance to our business.

Even if we believe third-party claims that we or our technology or product candidates are infringing, misappropriating or otherwise violating such third party's intellectual property are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, enforceability, or priority. A court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could materially and adversely affect our ability to commercialize our product candidates and any other product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. Further, even if we were successful in defending against any such claims, such claims could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business. If we are found to infringe a third party's intellectual property rights, and we are unsuccessful in demonstrating that such patents are invalid or unenforceable, we could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product candidates. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. We also could be required to obtain a license from such third party to continue developing, manufacturing and marketing product candidates we may develop and our technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, we may be unable to commercialize our Prime Editing technology or product candidates or such commercialization efforts may be significantly delayed, which could in turn significantly harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations and prospects.

In addition, our agreements with certain suppliers with whom we do business require us to defend or indemnify such parties to the extent they become involved in patent infringement claims. We could also voluntarily agree to defend or indemnify third parties in instances where we are not obligated to do so if we determine it would be important to our business relationships. If we are required or agree to defend or indemnify third parties in connection with any infringement claims, we could incur significant costs and expenses that could adversely affect our business, operating results or financial condition.

Defense of third-party claims of infringement of misappropriation, or violation of intellectual property rights involves substantial litigation expense and would be a substantial diversion of management and employee time and resources from our business. Some third parties may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, financial condition, results of operations and prospects. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Any of the

foregoing events could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may become involved in lawsuits to protect or enforce our future patents or the future patents of our licensors, which could be expensive, time consuming and unsuccessful and could result in a finding that such patents are unenforceable or invalid.

Competitors and other third parties may infringe, misappropriate or otherwise violate our future patents or the future patents of our licensors, or we may be required to defend against claims of infringement, misappropriation or other violation. In addition, our future patents or the future patents of our licensors also may become involved in inventorship, priority, validity or enforceability disputes. Countering or defending against such claims can be expensive and time consuming. In an infringement proceeding, a court may decide that a patent owned or in-licensed by us is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our future owned and in-licensed patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our future owned or in-licensed patents at risk of being invalidated or interpreted narrowly.

In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. These types of mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). These types of proceedings could result in revocation or amendment to our future patents such that they no longer cover our product candidates. The outcome for any particular patent following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our licensor, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our technology and/or product candidates. Defense of these types of claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

Conversely, we may choose to challenge the patentability of claims in a third party's U.S. patent by requesting that the USPTO review the patent claims in re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). We may choose to challenge third-party patents in patent opposition proceedings in the EPO or another foreign patent office. Even if successful, the costs of these opposition proceedings could be substantial and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office then we may be exposed to litigation by a third party alleging that their patent may be infringed by our product candidates, Prime Editing technology or other proprietary technologies.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Certain third parties, including our competitors, may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and

more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and applications are due to be paid to the USPTO and foreign patent agencies outside of the United States over the lifetime of our owned or licensed patents applications and patents that may issue from such applications. In certain circumstances, we rely on our licensors to pay these fees due to U.S. and non-U.S. patent agencies. The USPTO and foreign patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. We are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. While an inadvertent lapse or non-compliance with such requirements can sometimes be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations, however, in which non-compliance can result a partial or complete loss of patent rights in the relevant jurisdiction. Were a noncompliance event to occur, third parties might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Changes in patent law in the United States and in non-U.S. jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our Prime Editing platform technology and product candidates.

As is the case with other biotech and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain.

Changes in either the patent laws or interpretation of the patent laws could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of our future issued patents. For example, in March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, the United States transitioned from a “first to invent” to a “first-to-file” patent system. Under a “first-to-file” system, assuming that other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on an invention regardless of whether another inventor had made the invention earlier. A third party that files a patent application in the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either file any patent application related to our technology or product candidates or invent any of the inventions claimed in our or our licensors’ patent applications. The America Invents Act also includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted, allowing third party submission of prior art and establishing a new post-grant review system including post-grant review, *inter partes* review and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. The effects of these changes are currently unclear as the USPTO continues to promulgate new regulations and procedures in connection with the America Invents Act and many of the substantive changes to patent law, including the “first-to-file” provisions, only became effective in March 2013. In addition, the courts have yet to address many of these provisions and the applicability of the act and new regulations on the specific patents discussed in this filing have not been determined and would need to be reviewed. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our future issued patents.

In addition, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce patents that we might obtain in the future. For example, in the case, *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.*, the U.S. Supreme Court held that certain claims to DNA molecules are not patentable. We cannot predict how this and future decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patent applications. Similarly, foreign courts have made, and will likely continue to make, changes in how the patent laws in their respective jurisdictions are interpreted. We cannot predict future changes in the interpretation of patent laws or changes to patent laws that might be enacted into law by U.S. and foreign legislative bodies. Any similar adverse changes in the patent laws of other jurisdictions could also have a material adverse effect on our business, financial condition, results of operations and prospects.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. The terms of individual patents depend upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest non-provisional filing date in the applicable country. However, the actual protection afforded by a patent varies from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. Various extensions including patent term extensions, or PTEs, and patent term adjustments, or PTAs, may be available, but the life of a patent and the protection it affords is limited. For more information regarding PTA and PTE, see the section titled “Business—Intellectual Property”. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting our product candidates might expire before or shortly after we or our partners commercialize those candidates. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we do not obtain PTE and data exclusivity for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of product candidates we may develop, one or more of our U.S. patents may be eligible for limited PTE under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments. The Hatch-Waxman Amendments provides a PTE term of up to five years as compensation for patent term lost during the FDA regulatory review process. A PTE cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent per product may be extended and only those claims covering the approved product, a method for using it, or a method for manufacturing it may be extended. However, even if we were to seek a PTE, it may not be granted because of, for example, the failure to exercise due diligence during the testing phase or regulatory review process, the failure to apply within applicable deadlines, the failure to apply prior to expiration of relevant patents, or any other failure to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. In addition, to the extent we wish to pursue a PTE based on a patent that we in-license from a third party, we would need the cooperation of that third party, which may not be available. If we are unable to obtain PTE or term of any such extension is less than we request, third parties may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations and prospects could be materially harmed.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patent protection for our technology and product candidates, we also rely on know-how and trade secret protection, as well as confidentiality agreements, non-disclosure agreements and invention assignment agreements with our employees, consultants and third-parties, to protect our confidential and proprietary information, especially where we do not believe patent protection is appropriate or obtainable.

It is our policy to require our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements generally provide that all confidential information concerning our business or financial affairs developed by or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties, except in certain specified circumstances. In the case of employees, the agreements generally provide that all inventions conceived by the individual, and that are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In the case of consultants and other third parties, the agreements generally provide that all inventions conceived in connection with the services provided are our exclusive property. However, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes or who were involved in the development of intellectual property. Additionally, the assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. We may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements. Monitoring unauthorized uses and disclosures is difficult and we do not know whether the steps we have taken to protect our proprietary technology will be effective. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable.

In addition to contractual measures, we try to protect the confidential nature of our proprietary information through other appropriate precautions, such as physical and technological security measures. However, trade secrets and know-how can be difficult to protect and we do not have a formal trade secret policy at this time. These measures may not, for example, in the case of misappropriation of a trade secret by an employee or third party with authorized access, provide adequate protection for our proprietary information. Our security measures may not prevent an employee or consultant from misappropriating our trade secrets and providing them to a third party, and any recourse we might take against this type of misconduct may not provide an adequate remedy to protect our interests fully. In addition, trade secrets may be independently developed by others in a manner that could prevent us from receiving legal recourse. If any of our confidential or proprietary information, such as our trade secrets, were to be disclosed or misappropriated, or if any of that information was independently developed by a third party, our competitive position could be harmed.

In addition, some courts inside and outside the United States are sometimes less willing or unwilling to protect trade secrets. If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. Even if we are successful, these types of lawsuits may consume our time and other resources. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Third parties may assert that our employees, consultants, or advisors have wrongfully used or disclosed confidential information or misappropriated trade secrets.

As is common in the biotechnology and biopharmaceutical industries, we employ individuals who were previously employed at universities or other biotechnology or biopharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, and although we try to ensure that our employees, consultants, independent contractors or other third parties do not use the proprietary

information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants, independent contractors or other third parties have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Certain third parties, including our competitors, may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We do not currently own any registered trademarks. Our unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations and growth prospects.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- our product candidates will eventually become commercially available in generic or biosimilar product forms;
- others may be able to make gene therapy products that are similar to our product candidates or utilize similar gene editing technology but that are not covered by the claims of the patent applications that we own or license or the patents that we may own or license in the future;
- we, our licensors, or our current or future collaborators, might not have been the first to make the inventions covered by the pending patent applications that we license or may own in the future;
- we, our licensors, or our current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- we, our licensors, or our current or future collaborators, may fail to meet our obligations to the U.S. government regarding any in-licensed patent applications funded by U.S. government grants, leading to the loss or unenforceability of patent rights;

- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our pending, owned or licensed patent applications or those that we may own in the future will not lead to issued patents;
- it is possible that there are prior public disclosures that could invalidate our owned or in-licensed patent rights, or parts of our owned or in-licensed patent rights;
- it is possible that there are unpublished patent applications or patent applications maintained in secrecy that may later issue with claims covering our product candidates or technology similar to ours;
- it is possible that our owned or in-licensed patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause patents issuing from these patent applications to be held invalid or unenforceable;
- issued patents that we obtain in the future may be held invalid, unenforceable, or narrowed in scope, including as a result of legal challenges by third parties, including our competitors;
- the claims of our owned or in-licensed patents, if and when issued, may not cover our product candidates;
- the laws of foreign countries may not protect our proprietary rights or the proprietary rights of license partners or current or future collaborators to the same extent as the laws of the United States;
- the inventors of our owned or in-licensed patent applications may become involved with competitors, develop products or processes that design around our patent applications, or become hostile to us or the patent applications or patents that may issue from such patent applications on which they are named as inventors;
- third parties might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we have engaged in scientific collaborations in the past and will continue to do so in the future and our collaborators may develop adjacent or competing products that are outside the scope of our patent applications;
- we may not develop additional proprietary technologies that are patentable;
- any product candidates we develop may be covered by third-parties' patents or other exclusive rights;
- the patents of others may harm our business; or
- we may choose not to file a patent in order to maintain certain trade secrets or know-how and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related To Regulatory and Other Legal Compliance Matters

The FDA, the EMA and the National Institutes of Health, or NIH, have demonstrated caution in their regulation of gene therapy treatments, and ethical and legal concerns about gene therapy and genetic testing may result in additional regulations or restrictions on the development and commercialization of any product candidates we may develop, which may be difficult to predict.

The FDA, the EMA and the NIH have each expressed interest in further regulating biotechnology, including gene therapy and genetic testing. For example, the EMA advocates a risk-based approach to the development of a

gene therapy product. Agencies at both the federal and state level in the United States, as well as the U.S. congressional committees and other governments or governing agencies, have also expressed interest in further regulating the biotechnology industry. Such action may delay or prevent commercialization of any product candidates we may develop. Additionally, gene therapies may be associated with undesirable or unacceptable side effects, unexpected characteristics or other serious adverse events, including death, off-target cuts of DNA, or the introduction of cuts in DNA at locations other than the target sequence. These off-target cuts could lead to disruption of a gene or a genetic regulatory sequence at an unintended site in the DNA, or, in those instances where we also provide a segment of DNA to serve as a repair template, it is possible that following off-target cut events, DNA from such repair template could be integrated into the genome at an unintended site, potentially disrupting another important gene or genomic element. There also is the potential risk of delayed adverse events following exposure to gene therapies due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material. Due to concerns from regulatory agencies on the development of gene therapies and their potential for unknown long-term effects, participants in gene-therapy clinical trials may also require long-term follow-up for as long as 15 years.

Regulatory requirements in the United States and in other jurisdictions governing gene therapy products have changed frequently and may continue to change in the future. In January 2020, the FDA issued several new guidance documents on gene therapy products. The FDA established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research to consolidate the review of gene therapy and related products and established the Cellular, Tissue and Gene Therapies Advisory Committee to advise this review. In addition to the government regulators, the IBC and IRB of each institution at which we will conduct clinical trials of our potential product candidates, or a central IRB if appropriate, would need to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of gene therapy product candidates conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of any of our potential product candidates. Similarly, the EMA governs the development of gene therapies in the European Union and may issue new guidelines concerning the development and marketing authorization for gene therapy products and require that we comply with these new guidelines. These regulatory review agencies and committees and the new requirements or guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of any product candidates we may develop or lead to significant post-approval limitations or restrictions. As we advance our potential product candidates, we will be required to consult with these regulatory agencies and committees and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our potential product candidates can be costly and could negatively impact our or our collaborators' ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

Even if we, or any of our collaborators or strategic partners, obtain marketing approvals for any product candidates we may develop, the terms of approvals and ongoing regulation of such product candidates could require the substantial expenditure of resources and may limit how we, or they, manufacture and market such product candidates, which could materially impair our ability to generate revenue.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA, the EMA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, facility registration and drug listing requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, applicable product tracking and tracing requirements and requirements regarding the distribution of samples to physicians and recordkeeping. In addition, our manufacturing and testing facilities will be required to undergo pre-license inspections and pre-approval inspections. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the products may be

marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the products.

Accordingly, assuming we, or any collaborators we may have, receive marketing approval for one or more product candidates we develop, we, and such collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we and such collaborators are not able to comply with post-approval regulatory requirements, we and such collaborators could have the marketing approvals for our products withdrawn by regulatory authorities and our, or such collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Furthermore, the cost of compliance with post-approval regulations may have a negative effect on our business, operating results, financial condition and prospects.

Reductions in government operations may delay necessary manufacturing facility inspections by regulators and adversely affect the supply of any product candidates we may develop. Since March 2020 when foreign and domestic inspections of facilities were largely placed on hold, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. Since April 2021, the FDA has conducted limited inspections and employed remote interactive evaluations, using risk management methods, to meet user fee commitments and goal dates. Ongoing travel restrictions and other uncertainties continue to impact oversight operations both domestic and abroad and it is unclear when standard operational levels will resume. The FDA is continuing to complete mission-critical work, prioritize other higher-tiered inspectional needs (e.g., for-cause inspections), and carry out surveillance inspections using risk-based approaches for evaluating public health. Should FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the ongoing COVID-19 pandemic and may experience delays in their regulatory activities.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved, or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for biologics or modifications to approved biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Healthcare and other reform legislation may increase the difficulty and cost for us and any collaborators we may have to obtain marketing approval of and commercialize any product candidates we may develop and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been and continue to be ongoing efforts to implement legislative and regulatory changes regarding the healthcare system. Such changes could prevent or delay marketing approval of any product candidates that we may develop, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Although we

cannot predict what healthcare or other reform efforts will be successful, such efforts may result in more rigorous coverage criteria, in additional downward pressure on the price that we, or our future collaborators, may receive for any approved products or in other consequences that may adversely affect our ability to achieve or maintain profitability.

Within the United States, the federal government and individual states have aggressively pursued healthcare reform, as evidenced by the passing of the Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, and the ongoing efforts to modify or repeal that legislation. The ACA substantially changed the way healthcare is financed by both governmental and private insurers and contains a number of provisions that affect coverage and reimbursement of drug products and/or that could potentially reduce the demand for pharmaceutical products such as increasing drug rebates under state Medicaid programs for brand name prescription drugs and extending those rebates to Medicaid managed care and assessing a fee on manufacturers and importers of brand name prescription drugs reimbursed under certain government programs, including Medicare and Medicaid. Other aspects of healthcare reform, such as expanded government enforcement authority and heightened standards that could increase compliance-related costs, could also affect our business. Modifications have been implemented under the former Trump administration and additional modifications or repeal may occur.

There have been executive, judicial and congressional challenges to certain aspects of the ACA. On February 10, 2021, the Biden administration withdrew the federal government's support for overturning the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, from February 15, 2021 through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden administration or other efforts, if any, to challenge, repeal or replace the ACA will impact our business. There is no assurance that federal or state health care reform will not adversely affect our future business and financial results, and we cannot predict how future federal or state legislative, judicial or administrative changes relating to healthcare reform will affect our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, on March 22, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100 percent of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. Furthermore, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. Specifically, the Joint Select Committee on Deficit Reduction, asked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2 percent per fiscal year, which went into effect in April 2013, and, due to subsequent legislative amendments, will remain in effect through 2030 unless additional Congressional action is taken. However, COVID-19 relief legislation suspended the 2 percent Medicare sequester reductions from May 1, 2020 through December 31, 2021. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. The Bipartisan Budget Act, or BBA, also amended the ACA, effective January 1, 2019, by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole."

Furthermore, the prices of prescription pharmaceuticals in the United States and foreign jurisdictions is subject to considerable legislative and executive actions and could impact the prices we obtain for our products, if and when licensed. At the U.S. federal level, the former Trump administration used several means to propose or implement

drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. As a result, the FDA released a final rule on September 24, 2020, effective November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Furthermore, on November 20, 2020, the U.S. Department of Health and Human Services, or HHS, finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Medicare Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed until January 1, 2023. On November 20, 2020, CMS, issued an interim final rule implementing the Trump administration's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the U.S. District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. It is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. In addition to pricing regulations, reforms of regulatory approval frameworks may adversely affect our pricing strategy. For example, on July 9, 2021, President Biden issued an executive order directing the FDA to, among other things, continue to clarify and improve the approval framework for biosimilars, including the standards for interchangeability of biological products, facilitate the development and approval of biosimilar and interchangeable products, clarify existing requirements and procedures related to the review and submission of BLAs, and identify and address any efforts to impede biosimilar competition. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. It is difficult to predict the future legislative landscape in healthcare and the effect on our business, results of operations, financial condition and prospects. However, we expect that additional state and federal healthcare reform measures will be adopted in the future, particularly in light of the new presidential administration. Furthermore, it is possible that additional governmental action is taken in response to the ongoing COVID-19 pandemic. At the state level, legislatures have also been increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our potential product candidates. In markets outside of the United States and the European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of any product candidates we may develop to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

While we intend to seek designations for our potential product candidates with the FDA and comparable foreign regulatory authorities that are intended to confer benefits such as a faster development process or an accelerated regulatory pathway, there can be no assurance that we will successfully obtain such designations. In addition,

even if one or more of our potential product candidates are granted such designations, we may not be able to realize the intended benefits of such designations.

The FDA and comparable foreign regulatory authorities offer certain designations for product candidates that are designed to encourage the research and development of product candidates that are intended to address conditions with significant unmet medical need. These designations may confer benefits such as additional interaction with regulatory authorities, a potentially accelerated regulatory pathway and priority review. However, there can be no assurance that we will successfully obtain such designations for any product candidates. In addition, while such designations could expedite the development or approval process, they generally do not change the standards for approval. Even if we obtain such designations for one or more of our potential product candidates, there can be no assurance that we will realize their intended benefits. For example, we may seek Fast Track Designation for some of our potential product candidates. If a therapy is intended for the treatment of a serious or life threatening condition and the therapy nonclinical or clinical data demonstrates the potential to address unmet medical needs for this condition, the therapy sponsor may apply for Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a Fast Track Designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Additionally, we may seek a Breakthrough Therapy Designation for some of our potential product candidates. A breakthrough therapy is defined as a therapy that is intended, alone or in combination with one or more other therapies, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For therapies that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Therapies designated as breakthrough therapies by the FDA may also be eligible for accelerated approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our potential product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our potential product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification. In addition, we may seek a regenerative medicine advanced therapy, or RMAT, designation for some of our potential product candidates. An RMAT is defined as cell therapies, therapeutic tissue engineering products, human cell and tissue products and combination products using any such therapies or products. Gene therapies, including genetically modified cells that lead to a durable modification of cells or tissues may meet the definition of a regenerative medicine therapy. The RMAT program is intended to facilitate efficient development and expedite review of RMATs, which are intended to treat, modify, reverse or cure a serious or life-threatening disease or condition. A new drug application or a BLA for an RMAT may be eligible for priority review or accelerated approval through (1) surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit or (2) reliance upon data obtained from a meaningful number of sites. Benefits of such designation also include early interactions with FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A regenerative medicine therapy that is granted accelerated approval and is subject to post-approval requirements may fulfill such requirements through the submission of clinical evidence, clinical trials, patient registries or other sources of real world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post-approval monitoring of all patients treated with such therapy prior to its approval. RMAT designation is within the discretion of the FDA. Accordingly, even if we believe one of our potential product candidates meets the criteria for designation as a regenerative medicine advanced therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of RMAT designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our potential product candidates qualify as

for RMAT designation, the FDA may later decide that the biological products no longer meet the conditions for qualification.

In the future, we may also seek approval of product candidates under the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it is designed to treat a serious or life-threatening disease or condition and generally provides a meaningful advantage over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. If the sponsor fails to conduct such studies in a timely manner or if such post-approval studies fail to verify the drug's predicted clinical benefit, the FDA may withdraw its approval of the drug on an expedited basis. In addition, for products being considered for accelerated approval, the FDA generally requires, unless otherwise informed by the Agency, that all advertising and promotional materials intended for dissemination or publication within 120 days of marketing approval be submitted to the Agency for review during the pre-approval review period. There can be no assurance that FDA would allow any of the product candidates we may develop to proceed on an accelerated approval pathway, and even if FDA did allow such pathway, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. Moreover, even if we received accelerated approval, any post-approval studies required to confirm and verify clinical benefit may not show such benefit, which could lead to withdrawal of any approvals we have obtained.

If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. We may request priority review for the product candidates that we may develop. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily result in an expedited regulatory review or approval process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or at all.

In addition, in the European Union, we may seek to participate in the PRIME scheme for our product candidates. The PRiority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation, where the marketing authorization application will be made through the centralized procedure in the European Union. Eligible products must target conditions for which there is an unmet medical need (there is no satisfactory method of diagnosis, prevention or treatment in the European Union or, if there is, the new medicine will bring a major therapeutic advantage) and they must demonstrate the potential to address the unmet medical need by introducing new methods of therapy or improving existing ones. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. There is no guarantee, however, that our product candidates would be deemed eligible for the PRIME scheme and even if we do participate in the PRIME scheme, where during the course of development a medicine no longer meets the eligibility criteria, support under the PRIME scheme may be withdrawn.

We may not be able to obtain orphan drug designation or exclusivity for our potential product candidates, and even if we do, that designation may not provide an expedited development or regulatory review or approval process and any orphan drug exclusivity we may receive for approved products may not prevent the FDA or the EMA from approving other competing products.

Under the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition. A similar regulatory scheme governs approval of orphan product candidates by the EMA in the European Union. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for another similar product candidate for the same orphan therapeutic indication for that time period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation, in particular if the product is sufficiently profitable so that market exclusivity is no longer justified.

In order for the FDA to grant orphan drug exclusivity to one of our potential product candidates, the agency must find that the product candidate is indicated for the treatment of a condition or disease that affects fewer than 200,000 individuals in the United States or that affects 200,000 or more individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product candidate available for the disease or condition will be recovered from sales of the product in the United States. The FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet this standard. Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different product candidates can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product candidate for the same condition if the FDA concludes that the later product candidate is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care compared with the product that has orphan exclusivity. Orphan drug exclusivity may also be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, consultants and commercial partners, and, if we commence clinical trials, our principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the EMA and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA, the EMA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. Upon the effectiveness of this registration statement, we will adopt a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations and prospects, including the imposition of significant fines or other sanctions.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain product candidates outside of the United States and require us to develop and implement costly compliance programs.

We are subject to numerous laws and regulations in each jurisdiction outside the United States in which we operate. The creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

Similarly, the U.K. Bribery Act 2010 has extra-territorial effect for companies and individuals having a connection with the United Kingdom. The U.K. Bribery Act prohibits inducements both to public officials and private individuals and organizations. Compliance with the FCPA and the U.K. Bribery Act is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Our expansion outside of the United States has required, and will continue to require, us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing or selling certain drugs and drug candidates outside of the United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

We are subject to stringent laws, rules, regulations, policies, standards and contractual obligations related to data privacy and security and changes in such laws, rules, regulations, policies, standards and contractual obligations could adversely affect our business.

We are subject to data privacy and protection laws, rules, regulations, policies, standards and contractual obligations that apply to the collection, transmission, storage, use, disclosure, transfer, maintenance and other processing of sensitive, personal and personally-identifying information, which, among other things, impose certain requirements relating to the privacy, security, transmission and other processing of personal information, including comprehensive regulatory systems in the United States and European Union. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. However, our data privacy program is in its early stages and we have not yet assessed the applicability of and our compliance with data privacy-related laws, rules and regulations. As a result, we cannot guarantee that we are and have been in

compliance with all applicable data privacy and protection laws, rules regulations, policies and standards, and we may need to expend significant resources to implement privacy compliance measures. Additionally, we rely on certain third-party vendors to process certain confidential, sensitive or personal information on our behalf. Failure by us or our third-party vendors to comply with any of these laws, rules, regulations, contractual obligations or standards could result in notification obligations, enforcement actions, regulatory investigations or inquiries, significant fines, imprisonment of company officials and public censure, litigation and claims for damages by affected individuals, customers or business partners, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

There are numerous U.S. federal and state laws, rules and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to the Health Insurance Portability and Accountability Act of 1996, or HIPAA, establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Additionally, laws in all 50 states require businesses to provide notice to customers whose personally identifiable information has been disclosed as a result of a data breach. Determining whether personal information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation.

If we are unable to properly protect the privacy and security of personal information, we could be alleged or actually found to have breached our contracts. Furthermore, if we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face significant civil and criminal penalties. HHS has the discretion to impose penalties without attempting to resolve violations through informal means, and such enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these laws, rules and regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws, rules and regulations at the international, federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

We make public statements about our use, collection, disclosure and other processing of personal information through our privacy policies, information provided on our website and press statements. Although we endeavor to comply with our public statements and documentation, we may at times fail to do so or be alleged to have failed to do so. The publication of our privacy policies and other statements that provide promises and assurances about data privacy and security can subject us to potential government or legal action if they are found to be deceptive, unfair or misrepresentative of our actual practices.

Data privacy remains an evolving landscape at both the domestic and international level, with new laws, rules and regulations coming into effect and continued legal challenges, and our efforts to comply with the evolving data protection laws, rules and regulations may be unsuccessful. It is possible that these laws, rules and regulations may be interpreted and applied in a manner that is inconsistent with our practices. The laws are not consistent, and compliance in the event of a widespread data breach is costly and time-consuming. States are also frequently amending existing laws, requiring attention to frequently changing regulatory requirements. We must devote significant resources to understanding and complying with this changing landscape. Failure by us or our third-party vendors to comply with laws, rules and regulations regarding data privacy and protection would expose us to risk of enforcement actions taken by data protection authorities and carries with it the potential for significant penalties if we are found to be non-compliant. Similarly, failure to comply with federal and state laws, rules and regulations in the United States regarding privacy and security of personal information could expose us to penalties under such laws, rules and regulations. Any such failure to comply with data protection and privacy laws, rules and regulations could result in significant government-imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. Even if we are not determined to have violated these laws, rules or regulations, government investigations into these issues typically require the expenditure of significant

resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects.

Risks Related To Employee Matters, Managing Growth and Information Technology

Our future success depends on our ability to retain our President and Chief Executive Officer, our Co-Founders, our Chief Scientific Officer, our Chief Technical Officer and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on Keith Gottesdiener, our President and Chief Executive Officer, David R. Liu and Andrew Anzalone, our Co-Founders, Jeremy Duffield, our Chief Scientific Officer, Ann Lee, our Chief Technical Officer, as well as the other principal members of our management and scientific teams. Dr. Gottesdiener, Dr. Liu, Dr. Anzalone and Dr. Lee and such other principal members are engaged “at will,” meaning we or they may terminate the relationship at any time. We do not maintain “key person” insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Following this offering, Dr. Liu will continue to serve on our Scientific Advisory Board and as our paid consultant and will retain his position and affiliation with Harvard, HHMI and Broad Institute. Furthermore, Dr. Liu is one of our principal stockholders. Dr. Liu’s positions at Harvard, HHMI and Broad Institute could result in, or may create the appearance of, conflicts of interest related to our license of intellectual property rights from Harvard, HHMI and Broad Institute and other contractual relationships we may enter into from time to time with Harvard, HHMI and Broad Institute. For more information, see “Business—Team— Relationship with David Liu, Ph.D.”

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. In addition, our company-building efforts and establishment of a company culture will also be important to developing an innovative company in a high-evolving area. We may not be able to succeed in these efforts to build Prime Medicine as an attractive and exciting place to build a career or to attract and retain these types of personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors, including our scientific co-founders, may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. The inability to recruit, or loss of services of, certain executives, key employees, consultants or advisors, may impede the progress of our research, development and commercialization objectives and have a material adverse effect on our business, financial condition, results of operations and prospects.

We expect to expand our research, development, delivery, manufacturing, commercialization, regulatory and future sales and marketing capabilities over time, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of December 31, 2021, we had 81 full-time employees, of which 50 have M.D. or Ph.D. degrees. Within our workforce, 69 employees are engaged in research and development and 12 are engaged in business development, finance, legal, and general management and administration. In connection with the growth and advancement of our pipeline and becoming a public company, we expect to increase the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities, and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expected expansion of our operations or recruit and train additional qualified personnel. Moreover, the expected physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

As a growing biotechnology company, we are actively pursuing new platforms and product candidates in many therapeutic areas and across a wide range of diseases. Successfully developing product candidates for and fully understanding the regulatory and manufacturing pathways to all of these therapeutic areas and disease states requires a significant depth of talent, resources and corporate processes in order to allow simultaneous execution across multiple areas. Due to our limited resources, we may not be able to effectively manage this simultaneous execution and the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, legal or regulatory compliance failures, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our potential product candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to compete effectively and commercialize any product candidates we may develop will depend in part on our ability to effectively manage the future development and expansion of our company.

The administrator of the 2019 Plan is authorized to exercise its discretion to effect the repricing of stock options and stock appreciation rights and there may be adverse consequences to our business if the administrator of the 2019 Plan exercises such discretion.

Pursuant to our 2019 Plan, we are authorized to grant equity awards, including stock options and stock appreciation rights, to our employees, directors and consultants. The administrator of the 2019 Plan (which we expect will be, as is customary, our compensation committee) is authorized to exercise its discretion to reduce the exercise price of stock options or stock appreciation rights or effect the repricing of such awards. Although we do not anticipate needing to exercise this discretion in the near term, or at all, if the administrator of the 2019 Plan were to exercise such discretion without seeking prior stockholder approval, certain proxy advisory firms or institutional investors may be unsupportive of such actions and publicly criticize our compensation practices, and proxy advisory firms may recommend an “against” or “withhold” vote for members of our compensation committee. In addition, if we are required to hold an advisory vote on named executive officer compensation (known as the “say-on-pay” vote) at the time of, or subsequent to, any such repricing, it is likely that proxy advisory firms would issue an “against” recommendation on our say on pay vote and institutional investors may not be supportive of our say-on-pay vote. If proxy advisory firms or institutional investors are successful in aligning their views with our broader stockholder base and we are required to make changes to the composition of our board and its committees, or if we need to make material changes to our compensation and corporate governance practices, our business might be disrupted and our stock price might be negatively impacted. Even if we are able to successfully rationalize the exercise of such discretionary power, defending against any “against” or “withhold” recommendation for members of our compensation committee, any “against” recommendation on our say on pay vote or public criticism could be distracting to management, and responding to such positions from such firms or investors, even if remedied, can be costly and time-consuming.

In addition, if the administrator of the 2019 Plan does determine to reprice stock options or stock appreciation rights, even absent negative reactions from proxy advisory firms and institutional investors, management attention may be diverted and we could incur significant costs, including accounting and administrative costs and attorneys’ fees. We may also be required to recognize incremental compensation expense as a result of such repricing. These actions could cause our stock price to decrease and experience periods of increased volatility, which could result in material adverse consequences to our business.

Our board of directors has determined not to make any further awards under the 2019 Plan following the closing of this offering.

Our internal computer and information technology systems, or those of our third-party vendors, collaborators, contractors, consultants or other third parties, may fail or suffer security incidents or data breaches, which could result in a material disruption of our product development programs, compromise confidential, sensitive or

personal information related to our business or prevent us from accessing critical information, potentially exposing us to liability or otherwise adversely affecting our business.

Our internal computer and information technology systems and those of our current and any future third-party vendors, collaborators, contractors, consultants or other third parties, are vulnerable to damage or interruption from, among other things, computer viruses, computer hackers, phishing attacks, ransomware, malware, social engineering, malicious code, employee theft, fraud, misconduct or misuse, denial-of-service attacks, sophisticated nation-state and nation-state-supported actors, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we seek to protect our information technology systems from system failure, accident and security breach, we have in the past and may in the future experience phishing and other security incidents which could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary, personal or confidential information or other disruptions. For example, the loss of clinical trial data from future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

Controls employed by our information technology department and other third parties could prove inadequate, and our ability to monitor such third parties' data security practices is limited. Due to applicable laws, rules, regulations and standards or contractual obligations, we may be held responsible for any information security failure or cybersecurity attack attributed to our third-party vendors as they relate to the information we share with them.

If we were to experience a cybersecurity breach or other security incident relating to our information systems or data, the costs, time and effort associated with the investigation, remediation and potential notification of the breach to counterparties, regulators and data subjects could be material. We may incur significant costs in an effort to detect and prevent security incidents, and we may face increased costs and requirements to expend substantial resources in the event of an actual or perceived security incident. In addition, techniques used to sabotage or to obtain unauthorized access to networks in which data is stored or through which data is transmitted change frequently, become more complex over time and generally are not recognized until launched against a target. As a result, we and our third-party vendors may be unable to anticipate these techniques or implement adequate preventative measures quickly enough to prevent either an electronic intrusion into our systems or services or a compromise of critical information. We cannot guarantee that we will be able to detect or prevent any such incidents, and, our remediation efforts may not be successful or timely. Our efforts to improve security and protect data from compromise may also identify previously undiscovered instances of data breaches or other cybersecurity incidents. If we do not allocate and effectively manage the resources necessary to build and sustain the proper technology and cybersecurity infrastructure, we could suffer significant business disruption, including transaction errors, supply chain or manufacturing interruptions, processing inefficiencies, data loss or the loss of or damage to intellectual property or other proprietary, personal or confidential information. Additionally, we do not currently maintain cybersecurity insurance, and any insurance we may maintain in the future against the risk of this type of loss in the future may not be sufficient to cover actual losses, or may not apply to the circumstances relating to any particular loss.

To the extent that any disruption or security breach were to result in a loss of, or damage to, our or our third-party vendors', collaborators', contractors', consultants' or other third parties' data, including personal data, or applications or inappropriate disclosure, loss, destruction or alteration of, or access to, confidential, personal or proprietary information, we could incur significant liability including litigation exposure, substantial penalties and fines, we could become the subject of regulatory action, inquiry or investigation, our competitive position could be harmed, we could incur significant reputational damage and the further development and commercialization of any product candidates we may develop could be delayed. Any of the above could have a material adverse effect on our business, financial condition, results of operations or prospects.

Risks Related To This Offering and Ownership of Our Common Stock

We do not know whether a market will develop for our common stock or what the market price of our common stock will be, and, as a result, it may be difficult for you to sell your shares of our common stock.

Before this offering, there was no public trading market for our common stock. If a market for our common stock does not develop or is not sustained, it may be difficult for you to sell your shares of common stock at an

attractive price or at all. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations may be below the expectations of public market analysts and investors, and, as a result of these and other factors, the price of our common stock may fall.

You will incur immediate and substantial dilution as a result of this offering.

If you purchase common stock in this offering, you will incur immediate and substantial dilution of \$ _____ per share, representing the difference between the assumed initial public offering price of \$ _____ per share, the midpoint of the price range set forth on the cover page of this prospectus, and our pro forma as adjusted net tangible book value per share as of December 31, 2021 after giving effect to this offering. Moreover, we issued options in the past that allow the holders to acquire common stock at prices significantly below the assumed initial public offering price. As of December 31, 2021, there were 9,335,220 shares subject to outstanding options with a weighted-average exercise price of \$1.27 per share. To the extent that these outstanding options are ultimately exercised, the underwriters exercise their option to purchase additional shares or further vesting of restricted stock occurs, you will incur further dilution. For a further description of the dilution you will experience immediately after this offering, see “Dilution.”

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. We do not currently have and may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock would likely decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

Future sales of our common stock in the public market could cause our stock price to fall.

Our stock price could decline as a result of sales of a large number of shares of our common stock after this offering or the perception that these sales could occur. These sales, or the possibility that these sales may occur, also might make it more difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

Upon completion of this offering, _____ shares of our common stock will be outstanding (or _____ shares of common stock will be outstanding assuming exercise in full of the underwriters’ option to purchase additional shares), based on our shares outstanding as of _____. All shares of common stock expected to be sold in this offering will be freely tradable without restriction or further registration under the Securities Act of 1933, as amended, or Securities Act, unless held by our “affiliates,” as that term is defined in Rule 144 under the Securities Act. The resale of the remaining _____ shares, or _____ percent of our outstanding shares after this offering, is currently prohibited or otherwise restricted as a result of securities law provisions, market standoff agreements entered into by our stockholders with us or lock-up agreements entered into by our stockholders with the underwriters. However, subject to applicable securities law restrictions and excluding shares of restricted stock that will remain unvested, these shares will be able to be sold in the public market beginning 180 days after the date of this prospectus. Shares of unvested restricted stock that were issued and outstanding as of the date of this prospectus will become available for sale immediately upon the vesting of such shares, as applicable, and the expiration of any applicable market stand-off or lock-up agreements. Shares issued upon the exercise of stock options pursuant to future awards that may be granted under our equity incentive plans or pursuant to future awards granted under those plans will become available for sale in the public market to the extent permitted by the provisions of applicable vesting schedules, any applicable market stand-off and lock-up agreements and Rule 144 and Rule 701 under the Securities Act. For more information see the section entitled “Shares Eligible for Future Sale” included elsewhere in this prospectus.

Upon completion of this offering, the holders of approximately _____ shares, or _____ percent, of our common stock, will have rights, subject to some conditions, to require us to file registration statements covering the sale of

their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also intend to register the offer and sale of all shares of common stock that we may issue under our equity compensation plans. Once we register the offer and sale of shares for the holders of registration rights and shares to be issued under our equity incentive plans, they can be freely sold in the public market upon issuance, subject to the lock-up agreements described in the section entitled “Underwriting” included elsewhere in this prospectus.

In addition, in the future, we may issue additional shares of common stock or other equity or debt securities convertible into common stock in connection with a financing, acquisition, litigation settlement, employee arrangements or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and could cause our stock price to decline.

Insiders will continue to have substantial influence over us after this offering, which could limit your ability to affect the outcome of key transactions, including a change of control.

After this offering, our directors and executive officers and their affiliates will beneficially own shares representing approximately percent of our outstanding common stock. As a result, these stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might affect the market price of our common stock.

The market price of our common stock may be volatile, which could result in substantial losses for investors purchasing shares in this offering.

The initial public offering price for our common stock was determined through negotiations with the underwriters. This initial public offering price may vary from the market price of our common stock after the offering. As a result, you may not be able to sell your common stock at or above the initial public offering price. The market price for our common stock may be influenced by those factors discussed in this “Risk Factors” section and many others, some of which may include:

- the success of existing or new competitive product candidates or technologies;
- the timing and results of preclinical studies and clinical trials for any product candidates we may develop;
- failure or discontinuation of any of our development and research programs;
- results of any preclinical studies, clinical trials or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- developments or changing views regarding the use of genetic therapies, including those that involve gene editing;
- commencement or termination of collaborations for our product development and research programs;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other intellectual property or proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our research programs, clinical development programs or product candidates that we may develop;
- the results of our efforts to develop product candidates;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts, if any, that cover our stock;

- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- expiration of market stand-off or lock-up agreements;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- the ongoing COVID-19 pandemic, natural disasters or major catastrophic events;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

In recent years, the stock market in general and the market for pharmaceutical and biotechnology companies in particular, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. These fluctuations may be even more pronounced in the trading market for our stock shortly following this offering. Following periods of such volatility in the market price of a company’s securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future.

Securities litigation could result in substantial costs and divert management’s attention and resources from our business.

We are an “emerging growth company” and a “smaller reporting company,” and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or SOX Section 404, not being required to comply with any requirement for a supplement to the auditor’s report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. As a result, the information we provide stockholders will be different than the information that is available with respect to other public companies. In this prospectus, we have not included all of the executive compensation related information that would be required if we were not an emerging growth company.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption, and, therefore, while we are an emerging growth company we will not be subject to the new or revised accounting standards at the same time that they become applicable to other public companies that are not emerging growth companies. As a result of this election, our financial statements may not be comparable to those of other public companies that comply with new or revised accounting pronouncements as of public company effective dates. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies.

We are also a “smaller reporting company,” meaning that the market value of our stock held by non-affiliates plus the proposed aggregate amount of gross proceeds to us as a result of this offering is less than \$700 million and our annual revenue is less than \$100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company after this offering if either (i) the market value of our stock held by non-affiliates is less than \$250 million or (ii) our annual revenue is less than \$100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than \$700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an “emerging growth company,” we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We expect that we will need to hire additional accounting, finance and other personnel in connection with our becoming, and our efforts to comply with the requirements of being, a public company. Our management and other personnel will need to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that the rules and regulations applicable to us as a public company may make it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We are currently evaluating these rules and regulations and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to SOX Section 404, we will be required to furnish a report by our management on our internal control over financial reporting beginning with our second filing of an Annual Report on Form 10-K with the SEC after we become a public company. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by SOX Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

We do not expect to pay any dividends for the foreseeable future. Investors in this offering may never obtain a return on their investment.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. In addition, any future credit facility may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

General Risks Factors

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect our business and our financial condition. In recent years, many such changes have been made and changes are likely to continue to occur in the future. We cannot predict whether, when, in what form or with what effective dates, tax laws, regulations and rulings may be enacted, promulgated or decided or whether they could increase our tax liability or require changes in the manner in which we operate in order to minimize increases in our tax liability.

If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. In connection with this offering, we intend to begin the process of documenting, reviewing and improving our internal controls and procedures for compliance with Section 404 of the Sarbanes-Oxley Act of 2002, or SOX, which will require annual management assessment of the effectiveness of our internal control over financial reporting.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy or consequent inability to produce accurate financial statements on a timely basis could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm our common share price and make it more difficult for us to effectively market and sell our service to new and existing customers.

We have identified a material weakness in our internal control over financial reporting. If we fail to remediate this material weakness or identify additional material weaknesses in the future or otherwise fail to maintain effective internal control over financial reporting in the future, we may not be able to accurately report our financial condition or results of operations which may adversely affect investor confidence in us and, as a result, the value of our common stock.

In preparing our financial statements as of and for the years ended December 31, 2019 and 2020, we identified a material weakness in our internal control over financial reporting that existed as of the end of those periods, and which remains unremediated as of December 31, 2021. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis.

Specifically, we did not design and maintain effective controls over segregation of duties commensurate with our financial reporting requirements, as certain personnel have access to edit financial information without an independent review. This material weakness did not result in a misstatement to the consolidated financial statements. However, this material weakness could result in a misstatement of substantially all of the financial statement accounts and disclosures that would result in a material misstatement to the annual or interim consolidated financial statements that would not be prevented or detected.

We cannot assure you that we will be successful in fully remediating this material weakness, or that additional material weaknesses in our internal control over financial reporting will not be identified in the future. Our failure to design, implement and maintain effective internal control over financial reporting could result in misstatements in our financial statements that could result in a restatement of our financial statements, and could cause us to fail to meet our reporting obligations.

The process of designing and implementing effective internal control over financial reporting is a continuous effort that requires us to anticipate and react to changes in our business and the economic and regulatory environments and to expend significant resources that are adequate to satisfy our reporting obligations. We have not performed a formal evaluation of our internal control over financial reporting, as required by the rules and regulations of the SEC, nor are we required to have an independent registered public accounting firm perform an audit of our internal control over financial reporting as of any balance sheet date or for any period reported in our financial statements. Presently, we are not an accelerated filer, as such term is defined by Rule 12b-2 of the Exchange Act, and therefore, our management is not presently required to perform an annual assessment of the effectiveness of our internal control over financial reporting. Our independent registered public accounting firm will first be required to attest to the effectiveness of our internal control over financial reporting for our Annual Report on Form 10-K for the first year we are no longer an "emerging growth company" or a "smaller reporting company". Failure to comply with the rules and regulations of the SEC could potentially subject us to sanctions or investigations by the SEC, the applicable stock exchange or other regulatory authorities, which would require additional financial and management resources. We have begun the process of compiling the system and processing documentation necessary to perform the evaluation needed to comply with the rules and regulations of the SEC in the future, but we may not be able to complete our evaluation, testing and any required remediation in a timely fashion. An independent assessment of the effectiveness of our internal control over financial reporting could detect deficiencies in our internal control over financial reporting that our management's assessment might not. Undetected material weaknesses in our internal control over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation.

Provisions in our third amended and restated certificate of incorporation, our amended and restated by-laws and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Our third amended and restated certificate of incorporation, amended and restated by-laws and Delaware law contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. Our third amended and restated certificate of incorporation and by-laws, which will become effective upon the closing of this offering, include provisions that:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors;
- prohibit stockholder action by written consent;

- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- provide that our directors may be removed only for cause;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorized our board of directors to make, alter, amend or repeal our amended and restated by-laws; and
- require supermajority votes of the holders of our common stock to amend specified provisions of our third amended and restated certificate of incorporation and amended and restated by-laws.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock.

In addition, because we are incorporated in the State of Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, or the DGCL, which prohibits a person who owns in excess of 15 percent of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15 percent of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Any provision of our third amended and restated certificate of incorporation, amended and restated by-laws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated bylaws that will become effective upon the effectiveness of our registration statement designate specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit stockholders' ability to obtain a favorable judicial forum for disputes with us.

Pursuant to our amended and restated bylaws that will become effective upon the effectiveness of our registration statement, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of or based on a breach of a fiduciary duty owed by any director, officer or other employee of ours to us or our stockholders; (iii) any action asserting a claim pursuant to any provision of the DGCL, our third amended and restated certificate of incorporation or our amended and restated bylaws; or (iv) any action asserting a claim governed by the internal affairs doctrine, or the Delaware Forum Provision. The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act. Our amended and restated bylaws further provide that unless we consent in writing to the selection of an alternative forum, the United States District Court for the District of Massachusetts shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or the Federal Forum Provision. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is deemed to have notice of and consented to the Delaware Forum Provision and the Federal Forum Provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

We recognize that the Delaware Forum Provision and the Federal Forum Provision in our amended and restated bylaws may impose additional litigation costs on stockholders in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware or the Commonwealth of Massachusetts, as applicable. Additionally, the forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to

bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage the filing of lawsuits against us and our directors, officers and employees, even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are “facially valid” under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the United States District Court for the District of Massachusetts may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

We have wide discretion in the use of the net proceeds from this offering and may not use them effectively.

We cannot specify with certainty the particular uses of the net proceeds we will receive from this offering. Our management will have wide discretion in the application of the net proceeds, including for any of the purposes described in “Use of Proceeds.” Accordingly, you will have to rely upon the judgment of our management with respect to the use of the proceeds, with only limited information concerning management’s specific intentions. Our management may spend a portion or all of the net proceeds from this offering in ways that our stockholders may not desire or that may not yield a favorable return. The failure by our management to apply these funds effectively could harm our business, financial condition, results of operations and prospects. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. A severe or prolonged economic downturn or additional global financial crises could result in a variety of risks to our business, including weakened demand for any product candidates we develop or our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Our operations are vulnerable to interruption by disasters, terrorist activity, pandemics and other events beyond our control, which could harm our business.

Our facilities are located in Massachusetts. We have not undertaken a systematic analysis of the potential consequences to our business and financial results from a major flood, power loss, terrorist activity, pandemics or other disasters and do not have a recovery plan for such events. In addition, we do not carry sufficient insurance to compensate us for actual losses from interruption of our business that may occur, and any losses or damages incurred by us could harm our business. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the sections entitled “Prospectus Summary,” “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” and “Business,” contains express or implied forward-looking statements that are based on our management’s belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this prospectus include, but are not limited to, statements about:

- the initiation, timing, progress and results of our research and development programs, preclinical studies and future clinical trials;
- our ability to demonstrate, and the timing of, preclinical proof-of-concept *in vivo* for multiple programs;
- our ability to advance any product candidates that we may identify and successfully complete any clinical studies, including the manufacture of any such product candidates;
- our ability to pursue our four strategic indication categories: immediate target indications, differentiation target indications, “blue sky” indications and “march up the chromosome” approaches;
- our ability to quickly leverage programs within our initial target indications and to progress additional programs to further develop our pipeline;
- the timing of our investigational new drug applications submissions;
- the implementation of our strategic plans for our business, programs and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our Prime Editing technology;
- developments related to our competitors and our industry;
- our ability to leverage the clinical, regulatory, and manufacturing advancements made by gene therapy and gene editing programs to accelerate our clinical trials and approval of product candidates;
- our ability to identify and enter into future license agreements and collaborations;
- developments related to our Prime Editing technology;
- regulatory developments in the United States and foreign countries;
- our ability to attract and retain key scientific and management personnel; and
- our use of proceeds from this offering, estimates of our expenses, capital requirements, and needs for additional financing.

In some cases, you can identify forward-looking statements by terminology such as “may,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue” or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section entitled “Risk Factors” and elsewhere in this prospectus. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future

performance. You should read this prospectus and the documents that we reference in this prospectus and have filed with the SEC as exhibits to the registration statement, of which this prospectus forms a part, completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

This prospectus also contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. While we are not aware of any misstatements regarding any third-party information presented in this prospectus, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors, including those discussed under the section entitled “Risk factors” and elsewhere in this prospectus.

USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of _____ shares of our common stock in this offering will be approximately \$ _____ million, or approximately \$ _____ million if the underwriters exercise in full their option to purchase additional shares, assuming an initial public offering price of \$ _____ per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

A \$1.00 increase (decrease) in the assumed initial public offering price of \$ _____ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the net proceeds to us from this offering by \$ _____ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase (decrease) of 1.0 million shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) net proceeds to us from this offering by \$ _____ million, assuming no change in the assumed initial public offering price per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We do not expect that a change in the offering price or the number of shares by these amounts would have a material effect on our intended uses of the net proceeds from this offering, although it may impact the amount of time prior to which we may need to seek additional capital.

As of December 31, 2021, we had cash and cash equivalents and short-term investments of \$269.6 million. We currently intend to use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows:

- approximately \$ _____ million for continued research and development of our immediate target indications and differentiation target indications, including through achieving preclinical proof-of-concept in several programs;
- approximately \$ _____ million to develop our early-stage manufacturing processes and build out our dedicated chemistry facility; and
- the remainder for general corporate purposes.

Based on our current plans, we believe our existing cash and cash equivalents and short-term investments, together with the net proceeds from this offering, will be sufficient to fund our operations and capital expenditure requirements into _____.

All of our programs are currently in preclinical stage of development. The expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our research and development, the status of and results from preclinical studies or clinical trials we may commence in the future, as well as any collaborations that we may enter into with third parties for our product candidates or strategic opportunities that become available to us, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering. We expect the net proceeds from this offering, together with our existing cash and cash equivalents, and short-term investments, will not be sufficient for us to advance any of our programs through regulatory approval, and we will need to raise additional capital to complete the development and potential commercialization of any of our programs.

Pending our use of proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation instruments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain any future earnings to fund the development and expansion of our business, and therefore we do not anticipate paying cash dividends on our common stock in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors and will depend on our results of operations, financial condition, capital requirements and other factors deemed relevant by our board of directors.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and our capitalization as of December 31, 2021:

- on an actual basis;
- on a pro forma basis to give effect to (i) the settlement of the consideration due to Myeloid in January 2022 consisting of a \$30.0 million payment and the issuance of 3,424,422 shares of common stock to settle our related party forward contract liability, (ii) the automatic conversion of all outstanding shares of our Series A and Series B convertible preferred stock into an aggregate of 161,420,799 shares of common stock immediately prior to the completion of this offering and (iii) the filing and effectiveness of our third amended and restated certificate of incorporation immediately prior to the completion of this offering, in each case as if such events had occurred on December 31, 2021; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of _____ shares of our common stock in this offering at an assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The pro forma as adjusted information below is illustrative only, and our capitalization following the completion of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read the information in this table together with our consolidated financial statements and the related notes included elsewhere in this prospectus and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” section of this prospectus.

	As of December 31, 2021		
	Actual	Pro forma	Pro forma as adjusted
	(in thousands, except share and per share data)		
Cash and cash equivalents	\$ 185,420	\$ 155,420	\$ _____
Related party forward contract liability	\$ 12,020	\$ —	\$ _____
Convertible preferred stock (Series A and B), \$0.00001 par value; 161,420,799 shares authorized; 161,420,799 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	395,800	—	_____
Stockholders’ equity (deficit):			
Preferred stock, \$0.00001 par value; no shares authorized, issued or outstanding, actual; 10,000,000 shares authorized and no shares issued or outstanding, pro forma and pro forma as adjusted	—	—	_____
Common stock, \$0.00001 par value; 293,258,790 shares authorized, 100,768,255 shares issued and outstanding, actual; 775,000,000 shares authorized, 265,613,476 shares issued and outstanding, pro forma; 775,000,000 shares authorized, _____ shares issued and outstanding, pro forma as adjusted	1	3	_____
Additional paid-in capital	15,162	422,980	_____
Accumulated other comprehensive loss	(27)	(27)	_____
Accumulated deficit	(171,376)	(171,376)	_____
Total stockholders' equity (deficit)	(156,240)	251,580	_____
Total capitalization	\$ 251,580	\$ 251,580	\$ _____

Each \$1.00 increase (decrease) in the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, total stockholders’ equity and total capitalization by \$ _____

million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase (decrease) of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, total stockholders' equity and total capitalization by \$ million, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The number of shares of our common stock in the table above is based on 265,613,476 shares (which includes 47,734,388 shares of unvested restricted common stock) of our common stock outstanding as of December 31, 2021, after giving effect to (i) the issuance of 3,424,422 shares our common stock to Myeloid in January 2022 and (ii) the automatic conversion of all outstanding shares of our Series A and Series B convertible preferred stock into an aggregate of 161,420,799 shares of our common stock immediately prior to the completion of this offering, and excludes:

- 9,335,220 shares of common stock issuable upon the exercise of stock options outstanding as of December 31, 2021, with a weighted-average exercise price of \$1.27 per share under our 2019 Stock Option and Grant Plan;
- 532,500 shares of common stock issuable upon the exercise of stock options granted after December 31, 2021, with a weighted-average exercise price of \$3.51 per share under our 2019 Stock Option and Grant Plan;
- 7,479,092 shares of common stock reserved for issuance under our 2019 Stock Option and Grant Plan as of December 31, 2021, which shares will cease to be available for issuance at the time our 2022 Stock Option and Incentive Plan becomes effective;
- shares of common stock reserved for future issuance under our 2022 Stock Option and Incentive Plan, which will become effective upon the date immediately preceding the date on which the registration statement of which this prospectus is a part is declared effective; and
- shares of common stock reserved for future issuance under our 2022 Employee Stock Purchase Plan, which will become effective upon the date immediately preceding the date on which the registration statement of which this prospectus is a part is declared effective.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book (deficit) as of December 31, 2021 was \$(157.7) million, or \$(2.97) per share of our common stock. Our historical net tangible book deficit per share is the amount of our total tangible assets less our total liabilities and the carrying values of our convertible preferred stock, which is not included within stockholders' deficit. Our historical net tangible book deficit per share represents historical net tangible book deficit divided by the 53,033,867 shares of our common stock outstanding (which excludes 47,734,388 shares of unvested restricted common stock) as of December 31, 2021.

Our pro forma net tangible book value as of December 31, 2021 was \$250.1 million, or \$1.15 per share of our common stock. Pro forma net tangible book value represents the amount of our total tangible assets less our total liabilities, after giving effect to: (i) the settlement of the consideration due to Myeloid in January 2022, consisting of a \$30.0 million payment and the issuance of 3,424,422 shares of common stock to settle our related party forward contract liability; and (ii) the automatic conversion of all outstanding shares of our Series A and Series B convertible preferred stock into an aggregate of 161,420,799 shares of common stock immediately prior to the completion of this offering. Pro forma net tangible book value per share represents pro forma net tangible book value divided by the total number of shares outstanding (which excludes 47,734,388 shares of unvested restricted common stock) as of December 31, 2021, after giving effect to the pro forma adjustment described above.

After giving further effect to our issuance and sale of shares of our common stock in this offering at an assumed initial public offering price of \$ _____ per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of December 31, 2021 would have been \$ _____ million, or \$ _____ per share. This amount represents an immediate increase in pro forma as adjusted net tangible book value per share of \$ _____ to our existing stockholders and immediate dilution of \$ _____ in pro forma as adjusted net tangible book value per share to new investors purchasing common stock in this offering.

Dilution per share to new investors is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis (without giving effect to any exercise by the underwriters of their option to purchase additional shares):

Assumed initial public offering price per share		\$
Historical net tangible book value (deficit) per share as of December 31, 2021	\$	(2.97)
Increase per share attributable to the pro forma adjustments described above	\$	4.12
Pro forma net tangible book value per share as of December 31, 2021	\$	1.15
Increase in pro forma as adjusted net tangible book value per share attributable to new investors participating in this offering		
Pro forma as adjusted net tangible book value per share immediately after this offering		
Dilution per share to new investors participating in this offering		\$

The dilution information discussed above is illustrative only and will change based on the actual initial public offering price and other terms of this offering determined at pricing. Each \$1.00 increase (decrease) in the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) our pro forma as adjusted net tangible book value per share after this offering by \$ _____ and dilution per share to new investors purchasing common stock in this offering by \$ _____, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this

prospectus, would increase our pro forma as adjusted net tangible book value per share after this offering by \$ [redacted] and decrease dilution per share to new investors purchasing common stock in this offering by \$ [redacted], assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each decrease of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would decrease our pro forma as adjusted net tangible book value per share after this offering by \$ [redacted] and increase dilution per share to new investors purchasing common stock in this offering by \$ [redacted], assuming no change in the assumed initial public offering price and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters exercise their option to purchase additional shares in full, our pro forma as adjusted net tangible book value per share after this offering would be \$ [redacted], representing an immediate increase in pro forma as adjusted net tangible book value per share of \$ [redacted] to existing stockholders and immediate dilution in pro forma as adjusted net tangible book value per share of \$ [redacted] to new investors purchasing common stock in this offering, based on the assumed initial public offering price of \$ [redacted] per share and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The following table summarizes on the pro forma as adjusted basis described above, the total number of shares of common stock purchased from us, including shares of unvested restricted stock, on an as converted to common stock basis, the total consideration paid or to be paid, and the average price per share paid or to be paid by existing stockholders and by new investors in this offering at an assumed initial public offering price of \$ [redacted] per share, which is the midpoint of the estimated price range set forth on the cover of this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. As the table shows, new investors purchasing common stock in this offering will pay an average price per share substantially higher than our existing stockholders paid.

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders	265,613,476		\$ 315,762,632		\$ 1.19
Investors participating in this offering					
Total	265,613,476	100 %	\$ 315,762,632	100 %	

The table above assumes no exercise of the underwriters' option to purchase additional shares in this offering. If the underwriters' option to purchase additional shares is exercised in full, the number of shares of our common stock held by existing stockholders would be reduced to [redacted] percent of the total number of shares of our common stock outstanding after this offering, and the number of shares of common stock held by new investors purchasing common stock in this offering would be increased to [redacted] percent of the total number of shares of our common stock outstanding after this offering.

The discussion and tables above are based on 265,613,476 shares (which includes 47,734,388 shares of unvested restricted common stock) of our common stock outstanding as of December 31, 2021, after giving effect to (i) the issuance of 3,424,422 shares of our common stock to Myeloid in January 2022 and (ii) the automatic conversion of all outstanding shares of our Series A and Series B convertible preferred stock into an aggregate of 161,420,799 shares of our common stock immediately prior to the completion of this offering, and excludes:

- 9,335,220 shares of common stock issuable upon the exercise of stock options outstanding as of December 31, 2021, with a weighted-average exercise price of \$1.27 per share under our 2019 Stock Option and Grant Plan;
- 532,500 shares of common stock issuable upon the exercise of stock options granted after December 31, 2021, with a weighted-average exercise price of \$3.51 per share under our 2019 Stock Option and Grant Plan;

- 7,479,092 shares of common stock reserved for issuance under our 2019 Stock Option and Grant Plan as of December 31, 2021, which shares will cease to be available for issuance at the time our 2022 Stock Option and Incentive Plan becomes effective;
- shares of common stock reserved for future issuance under our 2022 Stock Option and Incentive Plan, which will become effective upon the date immediately preceding the date on which the registration statement of which this prospectus is a part is declared effective; and
- shares of common stock reserved for future issuance under our 2022 Employee Stock Purchase Plan, which will become effective upon the date immediately preceding the date on which the registration statement of which this prospectus is a part is declared effective.

To the extent that new stock options are issued or any outstanding options are exercised, or we issue additional shares of common stock in the future, there will be further dilution to new investors. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes appearing at the end of this prospectus. This discussion and other parts of this prospectus contain forward-looking statements that involve risks and uncertainties, such as statements regarding our plans, objectives, expectations, intentions and projections. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the "Risk Factors" section of this prospectus. Our historical results are not necessarily indicative of the results that may be expected for any period in the future.

Overview

We are a biotechnology company committed to delivering a new class of differentiated one-time curative genetic therapies to address the widest spectrum of diseases by deploying our Prime Editing technology, which we believe is a versatile, precise, efficient and broad gene editing technology.

Genetic mutations implicated in disease are diverse and can range from errors of a single base, known as point mutations, to errors that extend beyond a single base, such as insertions, deletions, duplications, or combinations thereof. Other mutations can affect regulatory sequences that control the function of genes and can affect the function of larger biochemical and genetic pathways. Furthermore, natural genetic variations, revealed by population-level genomic studies, are known to protect against or to increase risk of disease. To maximize the impact of these genetic insights, we believe the ability to alter the human genome at the foundational level may confer the greatest therapeutic impact on human disease.

Since our inception in September 2019, we have devoted substantially all of our efforts on organizing and staffing our company, business planning, raising capital, research and development activities, developing our Prime Editing platform, building our intellectual property portfolio and providing general and administrative support for these operations. To date, we have financed our operations primarily with proceeds from sales of preferred stock. Through December 31, 2021, we had received gross proceeds of \$315.8 million from sales of preferred stock.

We have incurred significant operating losses since inception. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of any product candidates we may develop. We generated net losses of \$2.5 million, \$3.4 million, and \$165.4 million for the period from September 13, 2019 (inception) to December 31, 2019 and the years ended December 31, 2020 and 2021, respectively. As of December 31, 2021, we had an accumulated deficit of \$171.4 million. We expect to continue to incur significant expenses for at least the next several years if and as we:

- continue our current research programs and preclinical development of any product candidates we identify;
- seek to identify additional research programs and product candidates;
- initiate preclinical studies and clinical trials for any product candidates we may identify;
- experience any delays or interruptions due to the ongoing COVID-19 pandemic, including delays in preclinical testing and clinical trials or interruptions in the supply chain for any future product candidates;
- further develop our in-licensed and company-owned gene editing platform, which we call our Prime Editing platform;
- maintain, expand, enforce, defend and protect our intellectual property portfolio and provide reimbursement of third-party expenses related to our patent portfolio;
- seek marketing approvals for any product candidates for which we successfully complete clinical trials;

- develop, maintain and enhance a sustainable, scalable, reproducible and transferable manufacturing process for the product candidates we may develop;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any therapies for which we may obtain marketing approval;
- hire additional research and development personnel;
- hire clinical and commercial personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development;
- acquire or in-license product candidates, intellectual property and technologies;
- establish and maintain collaborations;
- should we decide to do so, build and maintain a commercial-scale current Good Manufacturing Practices, or cGMP, manufacturing facility; and
- operate as a public company.

We will not generate revenue from product sales unless and until we successfully initiate and complete clinical development and obtain regulatory approval for any product candidates. If we obtain regulatory approval for any of our product candidates and do not enter into a commercialization partnership, we expect to incur significant expenses related to developing our commercialization capability to support product sales, manufacturing, marketing, and distribution. Further, following the completion of this offering, we expect to incur additional costs associated with operating as a public company, including increased accounting, audit, legal, regulatory, compliance and director and officer insurance costs as well as investor and public relations expenses associated with being a public company.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of private and public equity offerings, debt financings, or other capital sources, which may include additional collaborations with other companies, marketing, distribution or licensing arrangements with third parties, or other strategic transactions. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, reduce or eliminate the development and commercialization of any product candidates that we may identify or delay our pursuit of potential in-licenses or acquisitions.

Because of the numerous risks and uncertainties associated with product development, we are unable to accurately predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents and short-term investments, will enable us to fund our operating expenses and capital expenditure requirements into the . We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See “—Liquidity and Capital Resources.” and “Risk Factors—Risks Related To Our Financial Position and Need for Additional Capital.”

Impact of COVID-19 on Our Operations

In March 2020, the World Health Organization declared the outbreak of COVID-19 a global pandemic. We are subject to a number of risks associated with the COVID-19 global pandemic, including potential delays associated

with our ongoing preclinical studies and anticipated clinical trials. COVID-19 may have an adverse impact on our operations, supply chains and distribution systems or those of our third-party vendors and collaborators, and increase expenses, including as a result of impacts associated with preventive and precautionary measures that are being taken, such as restrictions on travel and border crossings, quarantine policies and social distancing. For example, our laboratory-based personnel have been unable to maximize use of our existing laboratory space due to restrictions on density of people and other aspects of our work have been limited by the need for our staff to isolate. We and our third-party vendors and collaborators may experience disruptions in supply of items that are essential for our research and development activities. We cannot predict the scope and severity of any economic recovery after the COVID-19 pandemic abates, including following any additional “waves” or other intensifying of the pandemic will have on our financial condition, operations and business plans.

License Agreement with Broad Institute

In September 2019, we entered into a license agreement with Broad Institute, and in May 2020 and February 2021, we entered into amendments to the license agreement, for certain patents related to delivery or targeting of DNA, or the Broad License Agreement. Under the Broad License Agreement, Broad Institute grants to us (i) an exclusive, worldwide license under the licensed patent rights solely to offer for sale, sell, have sold and import products covered by such licensed patent rights, or licensed products, solely for use within the Prime Broad Field (subject to certain specified limitations and exclusions with respect to certain applications), (ii) a non-exclusive, worldwide license under the licensed patent rights solely to make, have made, offer for sale, sell, have sold, and import licensed products solely for use in the Prime Broad Field, (iii) a non-exclusive, worldwide license under the licensed patent rights solely to make, have made, offer for sale, sell, have sold and import other products that are enabled by (a) the licensed patent rights or (b) the use of certain materials transferred to us by Broad Institute, solely for the prevention or treatment of human diseases and (iv) a non-exclusive, worldwide license solely for internal research. Further, with respect to DNA delivery or targeting applications covered by the licensed patent rights, the exclusive license granted to us by Broad Institute is limited only to “prime editor” products and specifically excludes applications relating to the production or processing of small or large molecules, including for the prevention or treatment of human disease. Under the Broad License Agreement, we also have the right to grant sublicenses to our affiliates and third parties, subject to certain requirements. We are obligated to use commercially reasonable efforts to develop, seek marketing approval for, and commercialize licensed products in the field. As partial consideration for the license, we made an upfront payment of \$0.5 million to Broad Institute.

Concurrently with the Broad License Agreement, we entered into a subscription agreement with Broad Institute, or the Broad Subscription Agreement. Under the Broad Subscription Agreement, as additional consideration for the license, we issued 1,938,429 shares of common stock, with a fair value of \$39,000, to Broad Institute, representing 5.0 percent of our then outstanding capital stock on a fully diluted basis. The Broad Subscription Agreement also obligated us to issue additional shares of common stock to Broad Institute without additional consideration to maintain Broad Institute’s ownership of us at 5.0 percent on a fully-diluted basis, if at any time prior to the achievement of an equity financing up to \$100.0 million, we issue additional securities that would cause Broad Institute shares of common stock to be less than 5.0 percent of our outstanding capital stock on a fully-diluted basis, or the Anti-Dilution Obligation. Upon the achievement of the \$100.0 million of equity financing in connection with the closing of the fourth tranche of our Series A preferred stock, we fully settled the Anti-Dilution Obligation, which resulted in the issuance of 7,768,425 shares of common stock to Broad Institute with a fair value of \$7.5 million.

We also granted certain preemptive rights to Broad Institute, under which if after we reach the financing threshold of \$100.0 million, we propose to offer or sell any new securities, then Broad Institute shall have the right to purchase from us the portion of such new securities that would allow Broad Institute to maintain its 5.0 percent ownership in us. In April 2021, we exceeded the financing threshold with the fourth issuance of the Series A preferred stock. In connection with the fourth closing of Series A preferred stock, Broad Institute purchased an additional 761,844 shares of Series A preferred stock, at a price of \$1.00 per share for gross proceeds of \$0.8 million, to maintain its 5.0 percent ownership in us.

Under the Broad License Agreement, we are required to use commercially reasonable efforts to develop licensed products in the Prime Broad Field in accordance with a development plan that we prepared and submitted to Broad Institute. We are also obligated to pay Broad Institute an annual license maintenance fee ranging from the low

to mid five-figures to the low six-figures, depending on the particular calendar year, for the term of the agreement. Broad Institute is also entitled to receive clinical and regulatory milestone payments up to a total of \$20.0 million per licensed product, depending on the patient population to be treated by the licensed product achieving the applicable milestone. If we undergo a change of control at any time during the term of the Broad License Agreement, certain of the clinical and regulatory milestone payments will increase by a specified percentage. Broad Institute is also entitled to sales-based milestone payments up to a total of \$54.0 million per licensed product, depending on the patient population to be treated by the licensed product achieving the applicable milestone. Broad Institute is entitled to lower payments to the extent the clinical and regulatory milestones or sales-based milestones are achieved by enabled products, rather than licensed products.

Broad Institute is entitled to receive mid-single digit percentage royalties on net sales of licensed products, and low single-digit percentage royalties of enabled products. Royalties payable to Broad Institute are subject to customary offsets and reductions with respect to a product in a given country, to a floor. On a country-by-country and product-by-product basis, the royalty term for a product in a country will terminate on the latest of (i) the expiration of the last to expire valid claim of an issued patent or pending patent application within the licensed patent rights covering such product in such country, (ii) the period of regulatory exclusivity for such product in such country or (iii) 10 years after the first commercial sale of such product in such country.

Unless earlier terminated, the Broad License Agreement will remain in effect until the later of (i) the last to expire valid claim of an issued patent or pending patent application within the licensed patent rights covering our licensed products or (ii) the expiration of the last royalty term for a licensed product in a country. We can terminate the Broad License Agreement for our convenience following prior written notice to Broad Institute. Each party may terminate the Broad License Agreement for the other party's uncured material breach. Broad Institute may also immediately terminate the Broad License Agreement (i) to the extent we (or our affiliates or sublicensees) challenge a licensed patent right, (ii) upon our bankruptcy or insolvency or (iii) if we fail to procure and maintain insurance.

Exclusive Option Agreement with Broad Institute

In May 2021, we executed an exclusive option agreement with Broad Institute, or the Broad Option Agreement, pursuant to which, Broad Institute granted to us an exclusive option to negotiate an amendment to the Broad License Agreement to include certain additional patent rights relating to Prime Editing improvements to our license thereunder (subject to certain specific limitations and exclusions with respect to certain applications), or the Exclusive Option.

In connection with the Broad Option Agreement, Broad Institute also granted to us, during the option period, a limited, non-exclusive license under the new patent rights solely for research purposes to evaluate whether to exercise our option (subject to certain specified exceptions). We paid a upfront fee of \$0.1 million to Broad Institute under the agreement upon execution of the agreement.

We may terminate the Broad Option Agreement for convenience by giving advance written notice of termination to Broad Institute. Broad Institute has the right to terminate the agreement if we (i) fail to make a payment to Broad Institute under the option agreement and fail to cure such non-payment within a certain time period, (ii) are otherwise in material breach of the option agreement and fail to cure within a certain time period, or (iii) become insolvent.

Our option expires in November 2022, unless we mutually agree in writing with Broad Institute to extend such expiration date. As of December 31, 2021, we have not exercised our Exclusive Option.

Pledge to Broad Institute and Harvard

In February 2021, we committed to donate \$5.0 million to Broad Institute and Harvard annually for 14 years, commencing in 2021, or the Pledge. The Pledge is intended to be used for research and development related to new genome editing technologies, for example Prime Editing, improve on existing genome-editing technologies, identify delivery mechanisms for these technologies and apply these technologies to the understanding and treatment of rare genetic diseases. We can terminate the Pledge at our discretion, subject to providing one year of funding from the date of termination.

Related Party Beam Collaboration Agreement

In September 2019, we entered into a collaboration and license agreement, or the Beam Collaboration Agreement, with Beam Therapeutics, Inc., or Beam, to collaborate on the research, development, manufacture and commercialization of certain Prime Editing products within a specified field and provide each other with access and licenses to certain proprietary technology to advance the other's progress. Under the Beam Collaboration Agreement, each party agreed to provide each other with access to, and licenses under, certain technology, know-how and patent rights controlled by each party for a limited number of years after the effective date, known as the initial term, and certain improvements thereto. Under the Beam Collaboration Agreement, we grant to Beam an exclusive (even as to us and our affiliates), worldwide license under (i) certain prime editing technology, know-how and patent rights that we control during the initial term, and improvements thereto that we control for a specified number of years following the initial term, and (ii) our interest in certain jointly-owned collaboration technology, in each case, solely to develop, make, have made, use, offer for sale, sell, import and commercialize licensed products only in the Beam field. Beam also grants to us certain non-exclusive, worldwide licenses under certain technology, know-how and patent rights, including under certain CRISPR or delivery-related technology, know-how and patent rights, that it controls during the initial term, and improvements thereto that Beam controls for a specified number of years following the initial term, solely to develop, make, have made, use, offer for sale, sell, import and commercialize products only in the Prime field. As partial consideration for the Beam Collaboration Agreement, Beam agreed to pay us, upon its election to continue its collaboration with us on the first anniversary of the Beam Collaboration Agreement, \$5.0 million worth of its own shares of common stock which such shares were issued to us on October 6, 2020.

Before and within a short period of time after the filing of an IND for a development candidate being developed under the Beam Collaboration Agreement, Beam has the option to designate up to a mid-single digit number of licensed products for which we are not permitted to exercise our profit share right, or the Beam Option (described below). Under the Beam Collaboration Agreement, a licensed product for which we have not exercised our profit share option or for which Beam has exercised the Beam Option is referred to as a protected product. Beam must exercise its option within 30 days following the filing of an IND for such product. Unless we exercise our profit sharing option for a licensed product, Beam is solely responsible for the development and commercialization of licensed products in the Beam field under the Beam Collaboration Agreement. If Beam exercises its option for a protected product, Beam will owe us a payment of \$5.0 million if the product is developed for non-sickle cell disease or \$10.0 million if the product is developed for sickle cell disease.

On a licensed product-by-licensed product basis, we have the right to elect to share equally with Beam in the profits and losses in the United States for Beam's licensed products. We may exercise such right for each licensed product within a specified period of time. Any such licensed product for which we exercise our right we refer to as a collaboration product. If we exercise such right, we agree to share equally in the costs, profits and losses of each such collaboration product in the United States, rather than receiving milestones and royalties based on development and sales thereof by Beam in the United States. For clarity, we are still entitled to receive milestones and royalties on the development and sale of each such collaboration product outside the United States. We also have the right to elect, within a specified time period, at least one year prior to the expected filing of an NDA, to co-promote with Beam each collaboration product in the United States, in addition to sharing in the profits and losses. To the extent we exercise our co-promote option with respect to a given collaboration product, we and Beam must use commercially reasonable efforts to commercialize such collaboration product, in each case, in the Beam field in the major markets in which marketing authorization has been obtained. After we have exercised our right to profit share on a collaboration product, we are able to, at any time during the term of the Beam Collaboration Agreement, on a collaboration product-by-collaboration product basis, opt-out of the profit and loss share and co-promotion activities with respect to any collaboration product with prior written notice to Beam within a certain time period.

We are entitled to receive development milestone payments from Beam on Beam's development of protected products (which, for clarity, includes any licensed product for which we have not exercised our profit share option) and collaboration products. For protected products, we are entitled to receive up to a total of \$35.5 million on a protected product-by-protected product basis based on Beam's development of such protected product and, for collaboration products, up to a total of \$17.8 million on a collaboration product-by-collaboration product basis based on Beam's development of such collaboration product outside of the United States, in each case, with such amounts

lowered if such licensed product achieves a given milestone for use in treating an orphan disease. We are also entitled to receive sales-based milestone payments from Beam based on net sales of licensed products. For protected products, we are entitled to receive up to a total of \$84.5 million on a protected product-by-protected product basis based on net sales of such protected product worldwide, and, for collaboration products, up to a total of \$42.3 million on a collaboration product-by-collaboration product basis based on net sales of collaboration products outside of the United States.

The sickle cell disease product partnered with Beam is a licensed product under the Beam Collaboration Agreement. Beam has not designated this product as a protected product and we have not received any development or sales-based milestones with respect to Beam's exploitation thereof.

Beam is obligated to pay to us tiered royalties ranging from a high-single digit percentage to a low double-digit percentage, but less than teens on net sales of protected products worldwide on a protected product-by-protected product basis and net sales of collaboration products outside of the United States on a collaboration product-by-collaboration product basis. Our royalties are subject to customary offsets and reductions, to a floor that takes into account any royalties we are obligated to pay to our third party licensors, including Broad Institute. In addition, certain of the rights licensed under the Beam Collaboration Agreement are sublicensed from third parties, and Beam agrees to reimburse us for certain payments we are required to make to our third party licensors attributable to Beam's exercise of any sublicense we grant to Beam, including payments we make to Broad Institute under the Broad License Agreement.

If we develop a product that is covered by the technology, know-how or patent rights that Beam licenses to us under the Beam Collaboration Agreement, which we refer to as a Prime product, we are obligated to pay to Beam a low single digit percentage royalty on our worldwide net sales of such any product on a Prime product-by-Prime product and country-by-country basis, subject to certain customary reductions, to a floor.

Unless earlier terminated in accordance with its terms, the Beam Collaboration Agreement will expire on the later of (a) expiration of the last royalty term for a product on which a party is obligated to pay royalties to the other party or (b) with respect to any collaboration product, the date on which neither party is developing or commercializing any such collaboration product in the United States. See "Business—Our License and Collaboration Agreements."

In connection with the Beam Collaboration Agreement, concurrently in September 2019, we also entered into a mutual subscription agreement, or the Beam Mutual Subscription Agreement. Under the Beam Mutual Subscription Agreement, if Beam elected to continue its collaboration with us, on the first anniversary of the collaboration agreement, we were obligated to grant Beam 5,000,000 shares of our common stock that represented an amount equal to 5.0 percent of the 100 million shares of Series A preferred stock that we had issued or committed to issue as of the effective date, as part of our first preferred stock offering. In connection with the Beam Mutual Subscription Agreement, on October 6, 2020, we issued to Beam an aggregate of 5,000,000 shares of our common stock with a fair value of \$0.2 million.

Research Collaboration, Option and License Agreement with Myeloid Therapeutics, Inc.

In December 2021, we entered into a research collaboration and exclusive option agreement with Myeloid Therapeutics Inc., or Myeloid, and such agreement, the Myeloid Agreement. Under the Myeloid Agreement, we collaborate with Myeloid, a related party, on the research and development of LINE-1 retrotransposon technology. This retrotransposon-based approach is complementary to Prime Editing and, if successfully deployed alongside Prime Editing, could expand the applicability of our technologies towards our goal of more broadly addressing human diseases. In connection with the Myeloid Agreement, we also entered into a subscription agreement with Myeloid under which we were obligated to issue an aggregate of 3,424,422 shares of our common stock as additional consideration for the license.

Myeloid grants to us an exclusive option, exercisable during the research term and for 60 days thereafter, to obtain ownership of certain patent rights and know-how owned by Myeloid that relate to LINE-1 retrotransposon technology. If we exercise our option, in addition to assigning us ownership of the applicable patent rights and

know-how, Myeloid also agrees to grant us certain exclusive and non-exclusive licenses, including to certain improvements and other enabling technology.

Following the exercise of our option, we agree to grant Myeloid, in addition to certain other licenses, an exclusive, worldwide license under the assigned patent rights and know-how to develop and commercialize products in the field of myeloid cells and myeloid cell engineering, or the Myeloid Field. As of December 31, 2021, we have not exercised our option.

Upon entering into the Myeloid Agreement, Myeloid was entitled to receive an upfront payment of \$30.0 million in cash and an aggregate of 3,424,422 shares of our common stock, with a then fair value of \$12.0 million, both of which Myeloid received in January 2022. If the research agreement meets its goals, then (i) during the research term, Myeloid is entitled to cash payments of up to \$35.0 million in the aggregate upon the achievement of certain milestones reflecting the technology's development; and (ii) if we exercise our option, we agree to pay to Myeloid an option exercise fee of \$80.0 million in cash, and shares of our common stock with a then fair value of \$30.0 million. Additionally, if the research collaboration meets its goal and we exercise our option, and we are able to proceed with the development and commercialization of a product that is covered by (a) the patent rights or know-how subject to our option or (b) the patent rights or know-how developed by one or both of the parties during the research term related to LINE-1 retrotransposon technology, or, collectively, a Prime Product, Myeloid would be eligible to receive, for the first five Prime Products, development and regulatory milestone payments of up to \$120.0 million on a Prime Product-by-Prime Product basis and sales-based milestone payments of up to \$210.0 million on a Prime Product-by-Prime Product basis.

Myeloid is also eligible to receive tiered low to mid single-digit percentage royalties on our annual aggregate global net sales of Prime Products on a Prime Product-by-Prime Product and country-by-country basis, subject to customary offsets and reductions to a floor. On a country-by-country and Prime Product-by-Prime Product basis, the period during which royalties will be paid will continue until the latest of (i) the expiration date of the last to expire valid claim of an issued patent or pending patent application within the patent rights subject to our option or the patent rights developed by one or both of the parties during the research term related to LINE-1 retrotransposon technology, in each case, covering the applicable Prime Product, (ii) loss of regulatory exclusivity for such Prime Product in such country, or (iii) ten (10) years after the first commercial sale of such Prime Product in such country.

Following the exercise of our option and for a period of two years thereafter, Myeloid will have the right to select up to three targets, subject to certain exclusions, for the development and commercialization of products directed at such targets in all fields and we will be eligible to receive the development, regulatory and sales-based milestone payments and royalty payments as set forth above from Myeloid with respect to such products.

Unless earlier terminated based on customary termination rights, the Myeloid Agreement will continue on a Prime Product-by-Prime Product and country-by-country basis until the expiration of the royalty term for such Prime Product in such country. If we exercise our option, neither party will have the right to terminate the Myeloid Agreement for any reason.

Components of Our Results of Operations

Related Party Collaboration Revenue

We have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products for the foreseeable future. Our revenues to date have been generated through the Beam Collaboration Agreement, as set forth above. In the future, we may generate additional revenue from collaboration, grant or license agreements we have entered into, or may enter into, with respect to our product candidates, as well as product sales from any approved product. Our ability to generate product revenues will depend on the successful development and eventual commercialization of any product candidates that we identify. If we fail to complete the development of any future product candidates in a timely manner or to obtain regulatory approval for such product candidates, our ability to generate future revenue and our results of operations and financial position would be materially adversely affected.

We concluded that the Beam Collaboration Agreement and the Beam Mutual Subscription Agreement should be combined and treated as a single arrangement for accounting purposes as the agreements were entered into contemporaneously and in contemplation of one another. We determined that the combined agreements are accounted for under Topic 606, *Revenue recognition*, or ASC 606. We identified the following performance obligations: (i) exclusive, worldwide license to certain Prime patents (ii) non-exclusive, worldwide license to CRISPR technology and (iii) joint research committee participation.

We also evaluated whether the Beam Option and our right to elect collaboration products in the Beam Collaboration Agreement represented material rights that would give rise to a performance obligation and concluded that neither the Beam Option nor our right to elect collaboration products convey a material right to Beam and therefore are not considered separate performance obligations within the Beam Collaboration Agreement. There have been no protected products or collaborations products to date. Under the Beam Collaboration Agreement, we are eligible to receive certain milestones and royalties regardless of whether any options are exercised, which are considered variable consideration. At each reporting period, we evaluate whether milestones are considered probable of being reached and, to the extent that a significant reversal would not occur in future periods, estimate the amount to be included in the transaction price. During the years ended December 31, 2020 and 2021, we did not receive any milestone payments and all variable consideration related to the Beam Collaboration Agreement remained fully constrained.

We recognized revenue for the license performance obligations at a point in time, that is upon the first anniversary of the effective date when Beam elected to continue its collaboration with us. We determined that the joint research committee performance promise is immaterial in the context of the contract.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred in connection with the development and research of our immediate target indications and our differentiation target indications. These expenses include:

- the cost allocated to acquire in-process research and development, or IPR&D, with no alternative future use associated with asset acquisitions or transactions to license intellectual property, such as our Myeloid Agreement and Broad License Agreement;
- expenses incurred in connection with our Pledge to Broad Institute;
- personnel-related expenses, including salaries, bonuses, benefits and stock-based compensation for employees engaged in manufacturing, research and development functions;
- expenses incurred in connection with continuing our current research programs and preclinical development of any product candidates we may identify, including under agreements with third parties, such as consultants and contractors;
- the cost of developing and validating our manufacturing process for use in our preclinical studies and future clinical trials;
- laboratory supplies and research materials; and
- facilities, depreciation and other expenses related to research and development activities, which include direct or allocated expenses for rent and maintenance of facilities, and utilities.

We measure and recognize asset acquisitions or licenses to intellectual property that are not deemed to be business combinations based on the cost to acquire or license the asset or group of assets, which includes transaction costs. Goodwill is not recognized in asset acquisitions or transaction to license intellectual property. In an asset acquisition or license to intellectual property, the cost allocated to acquire in-process research and development, or IPR&D, with no alternative future use is recognized as research and development expense on the acquisition date. For the period from September 13, 2019 (inception) to December 31, 2019, we recorded \$0.7 million of research and

development expense related to the acquired IPR&D from Broad Institute, which consisted of the initial upfront payment of \$0.5 million, the \$39,000 fair value of common stock issued to Broad Institute and the initial fair value of the Anti-Dilution Obligation of \$0.2 million. For the year ended December 31, 2021, we recorded \$42.0 million of research and development expense related to the acquired IPR&D from Myeloid, which consisted of the accrued initial upfront payment of \$30.0 million and the \$12.0 million fair value of common stock to be issued to Myeloid.

Upfront and milestone payments made are accrued for and expensed when the achievement of the milestone is probable up to the point of regulatory approval. Milestone payments made upon regulatory approval will be capitalized and amortized over the remaining useful life of the related product.

We expense all research and development costs in the periods in which they are incurred. Most of our research and development expenses have been related to early stage development activities. We have not reported program costs because we have not historically tracked or recorded our research and development expenses on a program-by-program basis, as we do not currently have any product candidates. In the future, external research and development costs for any individual product candidate will be tracked commencing upon product candidate nomination. We do not allocate employee costs, costs associated with our discovery efforts, laboratory supplies, and facilities expenses, including depreciation or other indirect costs, to specific product development programs because these costs are deployed across multiple programs and our platform and, as such, are not separately classified.

We expect our research and development expenses to increase substantially for the foreseeable future as we continue to invest in research and development activities related to developing any future product candidates, including investments in manufacturing, as we advance any product candidates we may identify and begin to conduct clinical trials. The success of product candidates we may identify and develop will depend on many factors, including the following:

- timely and successful completion of preclinical studies, including toxicology studies, biodistribution studies and minimally efficacious dose studies in animals, where applicable;
- effective INDs or comparable foreign applications that allow commencement of our planned clinical trials or future clinical trials for any product candidates we may develop;
- successful enrollment and completion of clinical trials, including under the FDA's current Good Clinical Practices, or GCPs, current Good Laboratory Practices, or GLPs, and any additional regulatory requirements from foreign regulatory authorities;
- positive results from our future clinical trials that support a finding of safety and effectiveness and an acceptable risk-benefit profile in the intended populations;
- receipt of marketing approvals from applicable regulatory authorities;
- establishment of arrangements through our own facilities or with third-party manufacturers for clinical supply and, where applicable, commercial manufacturing capabilities;
- establishment, maintenance, defense and enforcement of patent, trademark, trade secret and other intellectual property protection or regulatory exclusivity for any product candidates we may develop; and
- maintenance of a continued acceptable safety, tolerability and efficacy profile of any product candidates we may develop following approval.

Any changes in the outcome of any of these variables with respect to the development of product candidates that we may identify could mean a significant change in the costs and timing associated with the development of such candidates. For example, if the FDA or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect, or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time to complete clinical development of that therapeutic candidate. We may never obtain regulatory approval for any of our candidates, and, even if we do, drug commercialization takes several years and millions of dollars in development costs.

Following consummation of this offering, certain bonuses will become payable, and certain performance-based restricted stock awards and options to purchase common stock will vest and we will record approximately \$0.8 million of compensation expense as research and development expenses on the closing date of the offering.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and personnel-related costs, including stock-based compensation, for our personnel in executive, legal, finance and accounting, human resources and other administrative functions. General and administrative expenses also include legal fees relating to patents and corporate matters; professional fees paid for accounting, auditing, consulting and tax service; insurance costs; office and information technology costs; and facilities, depreciation and other general and administrative expenses, which include direct or allocated expenses for rent and maintenance of facilities and utilities.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support development of product candidates and our continued research activities. We also anticipate that we will incur increased accounting, audit, legal, regulatory, compliance and director and officer insurance costs as well as investor and public relations expenses associated with being a public company. We also expect to incur additional intellectual property-related expenses as we file patent applications to protect innovations arising from our research and development activities.

Following consummation of this offering, certain performance-based restricted stock awards will vest and we will record approximately \$44,000 of compensation expense as general and administrative expenses on the closing date of the offering.

Other Income (Expense)

Change in Fair Value of Preferred Stock Tranche Liability

Our Series A preferred stock purchase agreement obligated the Series A investors to participate in subsequent offerings of Series A preferred stock upon satisfaction of certain conditions, or the preferred stock tranche right. The preferred stock tranche right was classified as a liability and initially recorded at fair value upon the issuance date of the right. The liability was subsequently remeasured to fair value at each reporting date and immediately prior to being settled, and changes in fair value of the preferred stock tranche right liability were recognized as a component of other income (expense), net in our consolidated statements of operations and comprehensive loss. In 2020, we closed the second tranche Series A preferred stock financing and in April 2021, we closed the third and fourth tranche Series A preferred stock financings, resulting in full settlement of the preferred stock tranche right, upon both of which we issued additional shares of Series A preferred stock. Immediately prior to the issuance of such shares, the preferred stock tranche right liability was remeasured to fair value with the change in fair value recognized as a component of other income (expense), net.

As a result of the preferred stock tranche right settlement in April 2021, we will no longer recognize changes in the fair value of the preferred stock tranche liability in our consolidated statements of operations and comprehensive loss.

Change in Fair Value of Anti-Dilution Obligation

In connection with the Broad License Agreement, we entered into the Broad Subscription Agreement, in which we granted Broad Institute 1,938,429 shares of common stock, which represented a 5.0 percent of our then outstanding capital stock on a fully-diluted basis. The Broad Subscription Agreement obligated us to issue additional shares of common stock to Broad Institute without additional consideration to maintain Broad Institute's ownership of us at 5.0 percent on a fully-diluted basis, if at any time prior to the achievement of an equity financing up to \$100.0 million, we issue additional securities that would cause Broad Institute shares of common stock to be less than 5.0 percent of our outstanding capital stock on a fully-diluted basis, which we refer to collectively as the Anti-Dilution Obligation. We classified the Anti-Dilution Obligation as a liability on our consolidated balance sheet that we remeasured to fair value at each reporting date, and we recognized changes in the fair value of the liability

associated with the Anti-Dilution Obligation as a component of other income (expense) in our consolidated statement of operations and comprehensive loss.

As a result of the achievement of \$100.0 million in equity financing upon the fourth Series A preferred stock closing, we fully settled the Anti-Dilution Obligation and will no longer recognize changes in the fair value of the Anti-Dilution Obligation in our consolidated statements of operations and comprehensive loss.

Change in Fair Value of Related Party Short-Term Investment

In connection with the Beam Collaboration Agreement, Beam issued 200,307 shares of Beam common stock to us on October 6, 2020. Our related party short-term investment is recorded at fair value based upon quoted market prices at each reporting date. Unrealized and realized gains and losses on this investment subsequent to its initial recognition are recognized as a component of other income (expense) in the consolidated statements of operations and comprehensive loss.

Other Income (Expense), Net

Other income (expense), net consists of the change in the fair value of the shares we were entitled to receive from our related party Beam from the first anniversary of the Beam Collaboration Agreement through the date we received the shares from Beam, October 6, 2020. In connection with the Beam Collaboration Agreement, Beam granted 200,307 shares of Beam common stock to us. We were entitled to receive the shares of Beam upon the first anniversary of the Beam Collaboration Agreement in September 2020. We received the shares of Beam on October 6, 2020. The change in the fair value of the shares from September through our receipt on October 6, 2020 is included as other income (expense), net in the consolidated statements of operations and comprehensive loss. As the shares were received on October 6, 2020, we no longer recognize changes in the fair value of the Beam shares we were entitled to receive.

Income Taxes

For the period from September 13, 2019 (inception) to December 31, 2019 and the years ended December 31, 2020 and 2021, we recorded an income tax provision (benefit) of \$4,000, \$1.9 million and \$(0.5) million, respectively. We recorded a full valuation allowance of our net deferred tax assets positions as of December 31, 2021 as we believed it was more likely than not we would not be able to utilize our deferred tax assets prior to their expiration.

As of December 31, 2021, we had U.S. federal NOL carryforwards of \$41.8 million, which may be available to reduce future taxable income which do not expire. In addition, as of December 31, 2021, we had state NOL carryforwards of \$40.8 million, which may be available to reduce future taxable income, and expire at various times beginning in 2039. As of December 31, 2021, we also had U.S. federal and state research and development tax credit carryforwards of \$1.3 million and \$0.4 million, respectively, which may be available to reduce future tax liabilities and expire at various dates beginning in 2040 and 2035, respectively.

Results of Operations

Comparison of Years Ended December 31, 2020 and 2021

The following table summarizes our results of operations for the years ended December 31, 2020 and 2021:

	Years Ended December 31,		Change
	2020	2021	
	(in thousands)		
Related party collaboration revenue	\$ 5,210	\$ —	\$ (5,210)
Operating expenses:			
Research and development	2,980	70,550	67,570
General and administrative	3,162	13,924	10,762
Total operating expenses	6,142	84,474	78,332
Income (loss) from operations	(932)	(84,474)	(83,542)
Other income (expense):			
Change in fair value of preferred stock tranche right liability	(10,904)	(74,319)	(63,415)
Change in fair value of anti-dilution obligation	(700)	(6,681)	(5,981)
Change in fair value of related party short-term investment	10,867	(391)	(11,258)
Other income (expense), net	126	12	(114)
Total other expense, net	(611)	(81,379)	(80,768)
Net loss before income taxes	(1,543)	(165,853)	(164,310)
Benefit from income taxes	1,867	(486)	(2,353)
Net loss	\$ (3,410)	\$ (165,367)	\$ (161,957)

Related Party Collaboration Revenue

Related party collaboration revenue was \$5.2 million for the year ended December 31, 2020, consisting of \$5.4 million of consideration received in the form of Beam shares in connection with the Beam Collaboration Agreement, offset by shares of our common stock that we issued to Beam with a then fair value of \$0.2 million, and was recognized upon the first anniversary of the effective date of the agreement, when Beam elected to continue its collaboration with us. No collaboration revenue was recognized for the year ended December 31, 2021.

Operating Expenses

Research and Development Expenses

	Years Ended December 31,		Change
	2020	2021	
	(in thousands)		
License, intellectual property fees and other	\$ 50	\$ 47,346	\$ 47,296
Personnel related (including stock-based compensation)	1,124	10,683	9,559
Professional and consultant fees	163	650	487
Facility related and other	1,120	5,729	4,609
Lab supplies	523	6,142	5,619
Total research and development expenses	\$ 2,980	\$ 70,550	\$ 67,570

Research and development expenses were \$3.0 million for the year ended December 31, 2020, compared to \$70.6 million for the year ended December 31, 2021. The increase of \$67.6 million was primarily due to an increase of \$47.3 million in license, intellectual property fees and other primarily due to \$42.0 million of an upfront expense

under the Myeloid Agreement and \$5.3 million under the Broad License Agreement (including amounts associated with the Pledge, as described above), an increase of \$9.6 million in personnel-related expense driven by approximately 50 new hires in research and development, an increase of \$5.6 million lab supplies expense due to continued discovery efforts and expansion of our research and development activities and an increase of \$4.6 million facility related expense primarily due to the expansion of our office and laboratory space through new facilities being leased.

General and Administrative Expenses

	Years Ended December 31,		Change
	2020	2021	
	(in thousands)		
Personnel related (including stock-based compensation)	\$ 1,030	\$ 3,622	\$ 2,592
Professional and consultant fees	1,951	8,088	6,137
Facility related and other	181	2,214	2,033
Total general and administrative expenses	\$ 3,162	\$ 13,924	\$ 10,762

General and administrative expenses were \$3.2 million for the year ended December 31, 2020, compared to \$13.9 million for the year ended December 31, 2021. The increase of \$10.8 million was primarily due to an increase of \$6.1 million in professional and consultant fees as we prepare to become and operate as a public company, an increase of \$2.6 million of personnel-related expense primarily due to compensation related costs related to eight new hires to expand upon our administrative staff functions and an increase of \$2.0 million of facility related expenses primarily due to newly signed office leases to support our expanded general and administrative staff.

Other Income (Expense)

	Years Ended December 31,		Change
	2020	2021	
	(in thousands)		
Change in fair value of preferred stock tranche right liability	\$ (10,904)	\$ (74,319)	\$ (63,415)
Change in fair value of anti-dilution obligation	(700)	(6,681)	(5,981)
Change in fair value of related party short-term investment	10,867	(391)	(11,258)
Other income (expense), net	126	12	(114)
Total other expense, net	\$ (611)	\$ (81,379)	\$ (80,768)

Change in Fair Value of Preferred Stock Tranche Right Liability

The change in fair value of the preferred stock tranche right liability increased by \$63.4 million from the year ended December 31, 2020 compared to the year ended December 31, 2021. The increase was primarily due to a \$1.55 increase in the per share fair value of the underlying preferred stock used to determine the fair value of the preferred stock tranche right from December 31, 2020 through the settlement date in April 2021, as compared to the \$0.33 increase in per share fair value of the underlying preferred stock used to determine the fair value of the preferred stock tranche right from December 31, 2019 to December 31, 2020.

Change in Fair Value of Anti-Dilution Obligation

The change in fair value of the Anti-Dilution Obligation increased by \$6.0 million from the year ended December 31, 2020 compared to the year ended December 31, 2021. The increase was primarily due to a \$0.86 increase in the per share fair value of our common stock used to determine the fair value of the Anti-Dilution Obligation from December 31, 2020 through the settlement date in connection with the fourth Series A preferred stock closing, as compared to the \$0.09 increase in the per share fair value of our common stock used to determine the fair value of the Anti-Dilution Obligation from December 31, 2019 to December 31, 2020.

Change in Fair Value of Related Party Short-Term Investment

The change in fair value of related party short-term investment decreased by \$11.3 million from the year ended December 31, 2020 compared to the year ended December 31, 2021. The decrease was primarily due to a \$1.95 decrease in the stock price of the Beam stock from December 31, 2020 to December 31, 2021 as compared to the \$54.25 increase in the per share value of our common stock used to determine the fair value of related party short-term investments from October 6, 2020, the date on which we received the Beam shares, to December 31, 2020.

Other Income (Expense), Net

The change in other income (expense), is due to the unrealized loss of \$0.1 million recognized in the year ended December 31, 2020 related to the change in the fair value of the Beam shares we were entitled to receive for the period from the first anniversary date of the Beam Collaboration agreement, or September 26, 2020, through October 6, 2020, when we received the Beam shares due to a decrease in the stock price of the Beam stock. There is no similar unrealized loss in the year ended December 31, 2021 as any change in the fair value of the shares received subsequent to October 6, 2020 is included in the change in fair value of related party short-term investment.

Income Taxes

For the years ended December 31, 2020 and 2021, we recorded an income tax provision (benefit) of \$1.9 million and \$(0.5) million, respectively. The deferred income tax provision for the year ended December 31, 2020 was attributable to releasing our valuation allowance on our deferred tax assets as we were in a net deferred tax liability position, primarily due to our recognition of an unrealized gain on our related party short term investment. The deferred income tax benefit for the year ended December 31, 2021 was attributable to recording a valuation allowance on our deferred tax assets and liabilities due to being in a net deferred tax asset position.

Comparison of Period from September 13, 2019 (Inception) to December 31, 2019 and the Year Ended December 31, 2020

The following table summarizes our results of operations for the period from September 13, 2019 (inception) to December 31, 2019 and the year ended December 31, 2020:

	Period from September 13, 2019 (Inception) to December 31,	Year Ended December 31,	
	2019	2020	Change
	(in thousands)		
Related party collaboration revenue	\$ —	\$ 5,210	\$ 5,210
Operating expenses:			
Research and development	920	2,980	2,060
General and administrative	1,252	3,162	1,910
Total operating expenses	<u>2,172</u>	<u>6,142</u>	<u>3,970</u>
Loss from operations	<u>(2,172)</u>	<u>(932)</u>	<u>1,240</u>
Other income (expense):			
Change in fair value of preferred stock tranche right liability	(353)	(10,904)	(10,551)
Change in fair value of anti-dilution obligation	—	(700)	(700)
Change in fair value of related party short term investment	—	10,867	10,867
Other income, net	—	126	126
Total other expense, net	<u>(353)</u>	<u>(611)</u>	<u>(258)</u>
Net Loss before income taxes	<u>(2,525)</u>	<u>(1,543)</u>	<u>982</u>
Provision for income taxes	4	1,867	1,863
Net loss	<u>\$ (2,529)</u>	<u>\$ (3,410)</u>	<u>\$ (881)</u>

Related Party Collaboration Revenue

Related party collaboration revenue was zero for the period from September 13, 2019 (inception) to December 31, 2019, compared to \$5.2 million for the year ended December 31, 2020. Collaboration revenue for the year ended December 31, 2020 consisted of \$5.4 million of consideration received in the form of Beam shares in connection with the Beam Collaboration Agreement, offset by shares of our common stock that we issued to Beam with a then fair value of \$0.2 million, and was recognized upon the first anniversary of the effective date of the agreement, when Beam elected to continue its collaboration with us.

Research and Development Expenses

	Period from September 13, 2019 (Inception) to December 31,	Year Ended December 31,	Change
	2019	2020	
	(in thousands)		
License, intellectual property fees and other	\$ 719	\$ 50	\$ (669)
Personnel related (including stock-based compensation)	156	1,124	968
Professional and consultant fees	45	163	118
Facility related and other	—	1,120	1,120
Lab supplies	—	523	523
Total research and development expenses	<u>\$ 920</u>	<u>\$ 2,980</u>	<u>\$ 2,060</u>

Research and development expenses were \$0.9 million for the period from September 13, 2019 (inception) to December 31, 2019, compared to \$3.0 million for the year ended December 31, 2020. The \$2.1 million increase in research and development expenses was primarily due to an increase of \$1.1 million in facility and other related costs due to our laboratory space lease in Cambridge, Massachusetts that was signed in March 2020, a \$1.0 million increase in personnel-related expense primarily due to increased headcount of nine new hires for research and development activities and an increase of \$0.5 million in lab supplies due to the expansion of our research and development staff and increased discovery and preclinical activities. These increases were offset by a \$0.7 million decrease in license and intellectual property fees primarily due to the consideration paid for the Broad License Agreement in September 2019, which consisted of upfront fees paid of \$0.5 million, the initial recognition of the Anti-Dilution Obligation of \$0.2 million and the issuance of shares of our common stock to Broad Institute, with a fair value of \$39,000. Personnel-related costs, consisting of employees and non-employees, included stock-based compensation of \$0.2 million and \$0.4 million for the period from September 13, 2019 (inception) to December 31, 2019 and the year ended December 31, 2020, respectively.

General and Administrative Expenses

	Period from September 13, 2019 (Inception) to December 31,	Year Ended December 31,	Change
	2019	2020	
	(in thousands)		
Personnel related (including stock-based compensation)	\$ —	\$ 1,030	\$ 1,030
Professional and consultant fees	1,247	1,951	704
Facility related and other	5	181	176
Total general and administrative expenses	<u>\$ 1,252</u>	<u>\$ 3,162</u>	<u>\$ 1,910</u>

General and administrative expenses were \$1.3 million for the period from September 13, 2019 (inception) to December 31, 2019 compared to \$3.2 million for the year ended December 31, 2020. The increase of \$1.9 million in general and administrative expenses was primarily due to an increase of \$1.0 million in personnel-related costs as a result of three hires, including our Chief Executive Officer, as we commenced our operations, an increase of \$0.7

million in professional and consultant fees primarily due to the Broad License Agreement that we entered into which required us to reimburse Broad Institute for certain patent costs, and an increase of \$0.2 million in facility-related and other expenses primarily due to an increase in our leased office space and other expenses primarily attributable to the increase in headcount. Personnel-related costs included stock-based compensation of \$0 and \$40,000 for the period from September 13, 2019 (inception) to December 31, 2019 and the year ended December 31, 2020, respectively.

Other Income (Expense)

	Period from September 13, 2019 (Inception) to December 31,	Year Ended December 31,	
	2019	2020	Change
	(in thousands)		
Change in fair value of preferred stock tranche right liability	\$ (353)	\$ (10,904)	\$ (10,551)
Change in fair value of anti-dilution obligation	—	(700)	(700)
Change in fair value of related party short-term investment	—	10,867	10,867
Other income (expense), net	—	126	126
Total other income (expense), net	\$ (353)	\$ (611)	\$ (258)

Change in Fair Value of Preferred Stock Tranche Right Liability

The change in fair value of the preferred stock tranche right liability expense was \$0.4 million for the period from September 13, 2019 (inception) to December 31, 2019, compared to \$10.9 million for the year ended December 31, 2020. The increase of \$10.5 million was related to the remeasurement to fair value of the Series A preferred stock tranche liability associated with the Series A preferred stock, which primarily was due to an increase in the fair value of the underlying preferred stock during the year ended December 31, 2020, used to determine the fair value of the preferred stock tranche right liability.

Change in Fair Value of Anti-Dilution Obligation

The change in fair value of the Anti-Dilution Obligation was zero for the period from September 13, 2019 (inception) to December 31, 2019, compared to \$0.7 million for the year ended December 31, 2020. The increase of \$0.7 million was related to the remeasurement to fair value of the Anti-Dilution Obligation associated with the Broad License Agreement, primarily due to an increase in the fair value of our common stock during the year ended December 31, 2020, used to determine the fair value of the Anti-Dilution Obligation.

Change in Fair Value of Related Party Short-Term Investment

The change in fair value of related party short-term investment is due to the change in fair value of the Beam shares held by us since October 6, 2020, which increased by \$10.9 million during the period from September 13, 2019 (inception) to December 31, 2019 to the year ended December 31, 2020. The increase was primarily due to a \$54.25 increase in the stock price of the Beam stock from October 6, 2020 to December 31, 2020.

Other Income (expense), Net

Other expense was zero for the period from September 13, 2019 (inception) to December 31, 2019 compared to \$0.1 million for the year ended December 31, 2020. The increase of \$0.1 million was due to the change in fair value of the Beam shares we were entitled to receive on September 26, 2020 and the fair value of the shares we received from Beam on October 6, 2020.

Income Taxes

For the period from September 13, 2019 (inception) to December 31, 2019 and the year ended December 31, 2020, we recorded an income tax provision of \$4,000 and \$1.9 million, respectively. The deferred income tax

provision for the year ended December 31, 2020 was attributable to releasing our valuation allowance on our deferred tax assets as we were in a net deferred tax liability position, primarily due to our recognition of an unrealized gain on our related party short term investment.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We expect to incur significant expenses and operating losses for the foreseeable future as we commence the clinical development of our programs and continue our platform development and early-stage research activities. We have not yet commercialized any products and we do not expect to generate revenue from sales of products for several years, if at all. To date, we have funded our operations primarily with proceeds from the sale of our convertible preferred stock. Through December 31, 2021, we had received gross proceeds of \$315.8 million from sales of our preferred stock. As of December 31, 2021, we had cash and cash equivalents and short-term investments of \$269.6 million, excluding our restricted cash.

Cash Flows

The following table summarizes our sources and uses of cash for each of the periods presented:

	Period from September 13, 2019 (Inception) to December 31,	Year Ended December 31,	
	2019	2020	2021
	(in thousands)		
Net cash used in operating activities	\$ (1,334)	\$ (5,544)	\$ (34,082)
Net cash used in investing activities	—	(1,062)	(73,626)
Net cash provided by financing activities	9,981	34,934	269,278
Net increase in cash, cash equivalents and restricted cash	\$ 8,647	\$ 28,328	\$ 161,570

Operating Activities

During the year ended December 31, 2021, operating activities used \$34.1 million of cash, resulting primarily from our net loss of \$165.4 million and a change in our deferred income taxes of \$0.6 million, partially offset by a change in fair value of preferred stock tranche right liability of \$74.3 million, non-cash research and development expense of \$12.0 million, a change in fair value of anti-dilution obligation of \$6.7 million, non-cash rent expense of \$4.3 million, stock-based compensation expense of \$1.7 million, amortization of premium and discount on short-term investments of \$0.7 million, depreciation and amortization expense of \$0.6 million and a change in fair value of related party short-term investment of \$0.4 million. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2021 was \$31.2 million which primarily consisted of an increase in accrued expenses and other current liabilities of \$35.2 million, and an increase in accounts payable of \$1.2 million, partially offset by a decrease in lease liability of \$4.3 million and prepaid expenses and other current assets of \$0.9 million due to increased spending during the year.

During the year ended December 31, 2020, operating activities used \$5.5 million of cash, resulting primarily from our net loss of \$3.4 million, a change in fair value of related party short-term investment of \$10.9 million and non-cash consideration received under related party collaboration arrangement of \$5.4 million, partially offset by non-cash expenses related to a change in fair value of preferred stock tranche right liability of \$10.9 million, deferred income taxes of \$1.9 million, a change in fair value of anti-dilution obligation of \$0.7 million, stock-based compensation of \$0.4 million, non-cash other income (expense) of \$0.1 million, and non-cash consideration paid to Beam of \$0.2 million. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2020 was \$0.2 million which primarily consisted of a net increase in accounts payable of \$0.3 million and accrued expenses of \$0.3 million due to increased spending during the year partially offset by a \$0.4 million increase in prepaid expenses and other current assets due to payment of deposits for new leases.

During the period from September 13, 2019 (inception) to December 31, 2019, operating activities used \$1.3 million of cash, resulting primarily from our net loss of \$2.5 million, partially offset by a change in fair value of

preferred stock tranche right liability of \$0.4 million, non-cash research and development expense for a Broad license of \$0.2 million, and non-cash expenses related to stock-based compensation of \$0.2 million. Net cash provided by changes in our operating assets and liabilities for the September 13, 2019 (inception) to December 31, 2019 was \$0.5 million, which primarily consisted of an increase in accrued expenses due to timing of payments to vendors.

Investing Activities

During the year ended December 31, 2021, net cash used in investing activities was \$73.6 million, primarily consisting of purchases of short-term investments of \$82.0 million, purchase of property and equipment of \$4.2 million and payment of security deposits of \$0.5 million all of which were offset by \$13.0 million from the maturities of short-term investments. The purchase of short-term investments consisted of U.S. treasuries using the proceeds from issuance of convertible preferred stock. The purchases of equipment were primarily related to laboratory equipment purchases, which increased as we expanded our discovery and preclinical activities. The payment of security deposits was due to our new leases signed during the period.

During the year ended December 31, 2020, net cash used in investing activities was \$1.1 million, primarily consisting of payments of security deposit of \$0.4 million related to our lab space and purchases of property and equipment of \$0.6 million. The purchases of equipment during the period were primarily related to laboratory equipment purchases, which increased as we expanded our discovery and preclinical activities. The payment of security deposits was due to our new leases signed during the period.

During the period from September 13, 2019 (inception) to December 31, 2019, there were no cash flows from investing activities.

Financing Activities

During the year ended December 31, 2021, net cash provided by financing activities was \$269.3 million, primarily consisting of net proceeds of \$270.4 million from our additional issuances of Series A preferred stock and issuance of Series B preferred stock in April 2021, net of issuance costs, partially offset by \$1.1 million of deferred offering costs.

During the year ended December 31, 2020, net cash provided by financing activities was \$35.0 million, primarily consisting of net proceeds from our additional issuance of Series A preferred stock in November 2020.

During the period from September 13, 2019 (inception) to December 31, 2019, net cash provided by financing activities was \$10.0 million, primarily consisting of net proceeds from our initial issuance of Series A preferred stock in September 2019.

Funding Requirements

To date, we have not generated any revenue from product sales. We do not expect to generate revenue from product sales unless and until we successfully complete preclinical and clinical development of, receive regulatory approval for, and commercialize a product candidate and we do not know when, or if at all, that will occur. We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities and studies and initiate clinical trials. In addition, if we obtain regulatory approval for any product candidates, we expect to incur significant expenses related to product sales, marketing, and distribution to the extent that such sales, marketing and distribution are not the responsibility of potential collaborators. Further, upon the completion of this offering, we expect to incur additional costs associated with operating as a public company. The timing and amount of our operating expenditures will depend largely on the factors set out above. For more information, see “Risk Factors—Risks Related To Our Financial Position and Need for Additional Capital.”

We believe that the anticipated net proceeds from this offering, together with our existing cash and cash equivalents and short-term investments, will enable us to fund our operating expenses and capital expenditure requirements through . We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. We expect that we will require additional

funding to: continue our current research development activities; identify product candidates; initiate preclinical testing and clinical trials for our future product candidates we identify; develop, maintain, expand and protect our intellectual property portfolio; further develop our Prime Editing platform; and hire additional research, clinical and scientific personnel. If we receive regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on where we choose to commercialize ourselves.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of private and public equity offerings, debt financings, additional collaborations, strategic alliances, and marketing, distribution or licensing arrangements with third parties. To the extent that we raise additional capital through the sale of equity or convertible debt securities, ownership interest may be materially diluted, and the terms of such securities could include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specified actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through collaborations, strategic alliances or marketing, or distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, any future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, reduce or eliminate our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Other Commitments

Leases

As of December 31, 2021, we have future remaining operating lease payments of \$10.6 million relating to leases we have recognized on our consolidated balance sheet, of which an aggregate \$7.4 million is payable before December 31, 2022. In addition, we have two leases that have been entered into but have not yet commenced, as of December 31, 2021, for which we expect to pay approximately \$218.5 million over the next 12 years. Refer to Note 10 – *Leases* to our consolidated financial statements appearing at the end of this prospectus for more information on our lease obligations.

License and Collaboration Agreements

Under the Broad License Agreement, we are obligated to pay to Broad Institute an annual license maintenance fee ranging from the low to mid-five figures to the low six-figures, depending on the particular calendar year for the term of the agreement. Broad Institute is also entitled to receive clinical and regulatory milestone payments up to a total of \$20.0 million per licensed product, depending on the patient population to be treated by the licensed product achieving the applicable milestone. If we undergo a change of control at any time during the term of the Broad License Agreement, certain of the clinical and regulatory milestone payments will increase by a specified percentage. Broad Institute is also entitled to sales-based milestone payments up to a total of \$54.0 million per licensed product, depending on the patient population to be treated by the licensed product achieving the applicable milestone. Broad Institute is entitled to lower payments to the extent the clinical and regulatory milestones or sales-based milestones are achieved by enabled products, rather than licensed products.

Broad Institute is entitled to receive mid-single digit percentage royalties on net sales of licensed products, and low single-digit percentage royalties of enabled products. Royalties payable to Broad Institute are subject to customary offsets and reductions with respect to a product in a given country, to a floor.

Under the Beam Collaboration Agreement, Beam has the option to designate up to a mid-single digit number of licensed products for which we are not permitted to exercise our profit sharing right. If Beam exercises its option for a protected product, Beam will owe us a payment of \$5.0 million if the product is developed for non-sickle cell disease or \$10.0 million if the product is developed for sickle cell disease.

We are entitled to receive development milestone payments from Beam on Beam's development of protected products (which, for clarity, includes any licensed product for which we have not exercised our profit share option) and collaboration products. For protected products, we are entitled to receive up to a total of \$35.5 million on a protected product-by-protected product basis based on Beam's development of such protected product and, for collaboration products, up to a total of \$17.8 million on a collaboration product-by-collaboration product basis based on Beam's development of such collaboration product outside of the United States, in each case, with such amounts lowered if such licensed product achieves a given milestone for use in treating an orphan disease. We are also entitled to receive sales-based milestone payments from Beam based on net sales of licensed products. For protected products, we are entitled to receive up to a total of \$84.5 million on a protected product-by-protected product basis based on net sales of such protected product worldwide, and, for collaboration products, up to a total of \$42.3 million on a collaboration product-by-collaboration product basis based on net sales of collaboration products outside of the United States.

Beam is obligated to pay to us tiered royalties ranging from a high-single digit percentage to a low double-digit percentage, but less than teens on net sales of protected products worldwide on a protected product-by-protected product basis and net sales of collaboration products outside of the United States on a collaboration product-by-collaboration product basis. Our royalties are subject to customary offsets and reductions, to a floor that takes into account any royalties we are obligated to pay to our third-party licensors, including Broad Institute. In addition, certain of the rights licensed under the Beam Collaboration Agreement are sublicensed from third parties, and Beam agrees to reimburse us for certain payments we are required to make to our third-party licensors attributable to Beam's exercise of any sublicense we grant to Beam, including payments we make to Broad Institute under the Broad License Agreement.

If we develop a product that is covered by the technology, know-how or patent rights that Beam licenses to us under the Beam Collaboration Agreement, which we refer to as a Prime product, we are obligated to pay to Beam a low single digit percentage royalty on our worldwide net sales of such any product on a Prime product-by-Prime product and country-by-country basis, subject to certain customary reductions, to a floor.

Under the Myeloid Agreement, Myeloid was entitled to receive an upfront payment of \$30.0 million in cash and an aggregate of 3,424,422 shares of our common stock, with a then fair value of \$12.0 million, both of which Myeloid received in January 2022. During the research term, Myeloid is also entitled to receive cash payments of up to \$35.0 million in the aggregate upon the achievement of a research milestone and a patent prosecution milestone.

If we exercise our option, we agree to (i) pay Myeloid an option exercise fee consisting of \$80.0 million in cash and (ii) issue Myeloid shares of our common stock, with a fair value of \$30.0 million. Additionally, if the research collaboration meets its goals, we exercise our option and proceed with the development and commercialization of a product that is covered by (a) the patent rights or know-how subject to our option or (b) the patent rights or know-how developed by one or both of the parties during the research term related to LINE-1 retrotransposon technology, or, collectively, a Prime Product, Myeloid would be eligible to receive, for the first five Prime Products, development and regulatory milestone payments of up to \$120.0 million on a Prime Product-by-Prime Product basis and sales-based milestone payments of up to \$210.0 million on a Prime Product-by-Prime Product basis.

Myeloid is also eligible to receive tiered low to mid single-digit percentage royalties on our annual aggregate global net sales of Prime Products on a Prime Product-by-Prime Product and country-by-country basis, subject to customary offsets and reductions to a floor.

Following the exercise of our option and for a period of two years thereafter, Myeloid will have the right to select up to three targets, subject to certain exclusions, for the development and commercialization of products directed at such targets in all fields and we will be eligible to receive development, regulatory and sales-based milestone payments and royalty payments as set forth above from Myeloid with respect to such products.

To date, no milestone or royalty payments under these agreements have been paid or were due from us. For additional information, see "Business—Our License and Collaboration Agreements— Research Collaboration, Option and License Agreement with Myeloid Therapeutics, Inc" and "Certain Relationships and Related Party Transactions."

In February 2021, we committed to donate \$5.0 million to Broad Institute and Harvard annually for 14 years, commencing in 2021 pursuant to the Pledge. The Pledge is intended to be used for research and development related to new genome editing technologies, for example Prime Editing, improve on existing genome-editing technologies, identify delivery mechanisms for these technologies and apply these technologies to the understanding and treatment of rare genetic diseases. We can terminate the Pledge at our discretion, subject to providing one year of funding from the date of termination. For additional information, see “Business—Our License and Collaboration Agreements—Pledge to Broad Institute and Harvard.”

Critical Accounting Policies and Significant Judgments and Estimates

Our management’s discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosures of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses incurred during the reporting periods. We base our estimates on historical experience, known trends and events, and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities recorded revenues and expenses that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Actual results may differ from these estimates.

While our significant accounting policies are described in more detail in Note 2 to our consolidated financial statements appearing at the end of this prospectus, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Revenue Recognition

We recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services in accordance with ASC 606.

At contract inception, we assessed the goods or services promised within each contract, whether each promised good or service is distinct, and determines those that are performance obligations. In assessing whether promised goods or services are distinct, we consider factors such as the stage of development of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on their own and whether the required expertise is readily available. In addition, we consider whether the collaboration partner can benefit from a promise for its intended purpose without the receipt of the remaining promises, whether the value of the promise is dependent on the unsatisfied promises, whether there are other vendors that could provide the remaining promises, and whether it is separately identifiable from the remaining promises. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when or as the performance obligation is satisfied.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under our arrangements, we performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the assessment of the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations, and (v) recognition of revenue when, or as, we satisfy each performance obligation. As part of the accounting for arrangements under ASC 606, we must use significant judgment to determine: a) the performance obligations based on the determination under step (ii) above; b) the transaction price under step (iii) above; and c) the standalone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above. We also use judgment to determine whether milestones or other variable consideration, except for royalties and sales-based milestones where such payments principally relate to a license of intellectual property, should be included in the transaction price as described below. At the end of each subsequent reporting period, we re-evaluate the estimated variable consideration included in the transaction price and any related constraint, and if

necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment. The transaction price is allocated to each performance obligation based on the relative standalone selling price of each performance obligation in the contract, and we recognize revenue based on those amounts when, or as, the performance obligations under the contract are satisfied. We utilize key assumptions to determine the standalone selling price, which may include other comparable transactions, pricing considered in negotiating the transaction, probabilities of technical and regulatory success and the estimated costs. Certain variable consideration is allocated specifically to one or more performance obligations in a contract when the terms of the variable consideration relate to the satisfaction of the performance obligation and the resulting amounts allocated to each performance obligation are consistent with the amount we would expect to receive for each performance obligation.

During the year ended December 31, 2020, we recognized revenue related to the Beam Collaboration Agreement. We concluded that the Beam Collaboration Agreement and the Beam Mutual Subscription Agreement should be combined and treated as a single arrangement for accounting purposes as the agreements were entered into contemporaneously and in contemplation of one another. We determined that the combined agreements are accounted for under ASC 606 and identified the following performance obligations: (i) exclusive, worldwide license to certain Prime patents, (ii) non-exclusive, worldwide license to CRISPR technology and (iii) joint research committee participation. We also evaluated whether the Beam Option and our right to elect collaboration products in the Beam Collaboration Agreement represented material rights that would give rise to a performance obligation and concluded that neither the Beam Option nor our right to elect collaboration products convey a material right to Beam and therefore are not considered separate performance obligations within the Beam Collaboration Agreement. There have been no protected products or collaborations products to date. Under the Beam Collaboration Agreement, we are eligible to receive certain milestones and royalties regardless of whether any options are exercised, which are considered variable consideration. At each reporting period, we evaluate whether milestones are considered probable of being reached and, to the extent that a significant reversal would not occur in future periods, estimate the amount to be included in the transaction price. During the years ended December 31, 2020 and 2021, we did not receive any milestone payments and all variable consideration related to the Beam Collaboration Agreement remained fully constrained.

We assessed the above promises and determined that the exclusive licenses for certain Prime products and non-exclusive license to CRISPR technology represent performance obligations within the scope of ASC 606. The exclusive licenses for certain Prime products and non-exclusive license to CRISPR technology are considered functional intellectual property and distinct from other promises under the contract. The exclusive licenses for certain Prime products and non-exclusive license to CRISPR technology are considered functional licenses that are distinct in the context of the Beam Collaboration Agreement as Beam can benefit from the licenses on its own or together with other readily available resources. As the exclusive licenses for certain Prime products and non-exclusive license to CRISPR technology are delivered at the same time, they are considered one performance obligation at contract inception. The joint research committee performance promise is immaterial in the context of the contract.

We determined the transaction price under ASC 606 at the inception of the Beam Collaboration Agreement to be \$5.2 million, consisting of the value of the Beam equity investment under the Mutual Subscription Agreement, when measured at fair value, less the fair value of our shares issued to Beam of \$0.2 million. An immediate 10 percent change in the Beam share price would have had a \$0.5 million impact on the collaboration revenue from Beam. The shares we issued to Beam represents a payment to a customer and is therefore a reduction of the transaction price.

We recognized revenue for the license performance obligations at a point in time, that is upon the first anniversary of the effective date when Beam elected to continue its collaboration with us. As control of these licenses was transferred on this date, Beam could begin to use and benefit from the licenses, we recognized \$5.2 million of license revenue during the year ended December 31, 2020 under the Beam Collaboration Agreement. We did not recognize any revenue under the Beam Collaboration Agreement during the year ended December 31, 2021.

Stock-Based Compensation Expense

We measure stock-based awards granted to employees, directors, and non-employees based on their fair value on the date of the grant using the Black-Scholes option-pricing model for stock options or the difference, if any, between the purchase price per share of the award and the fair value of our common stock at the date of grant for restricted stock awards. Compensation expense for those awards is recognized over the requisite service period, which is generally the vesting period of the respective award. Compensation expense for awards to non-employees with service-based vesting conditions is recognized in the same manner as if we had paid cash in exchange for the goods or services, which is generally the over the vesting period of the award. We use the straight-line method to recognize the expense of awards with service-based vesting conditions. We account for forfeitures of stock-based awards as they occur. Compensation expense for awards to employees and non-employees with performance-based vesting conditions is recognized based on the grant-date fair value over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable. As of each reporting date, we estimate the probability that specified performance criteria will be met and does not recognize compensation expense until it is probable that the performance-based vesting condition will be achieved.

Determination of the Fair Value of Common Stock

As there has been no public market for our common stock to date, the estimated fair value of our common stock has been determined by our board of directors as of the date of grant of each option or restricted stock award, with input from management, considering our most recently available third-party valuations of common stock and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Our common stock valuations were prepared using either an option pricing method, or OPM, or a hybrid method, both of which used market approaches to estimate our enterprise value. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceed the value of the preferred stock liquidation preferences at the time of the liquidity event, such as a strategic sale or a merger. The hybrid method is a probability-weighted expected return method, or PWERM, where the equity value in one or more of the scenarios is calculated using an OPM. The PWERM is a scenario-based methodology that estimates the fair value of common stock based upon an analysis of future values for us, assuming various outcomes. The common stock value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of stock. The future value of the common stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock. A discount for lack of marketability, or DLOM, of the common stock is then applied to arrive at an indication of value for the common stock. These third-party valuations were performed at various dates, which resulted in valuation of our common stock of \$1.18 per share as of May 31, 2021, \$3.39 per share as of October 27, 2021 and \$3.51 as of December 24, 2021. In addition to considering the results of these third-party valuations, our board of directors considered various objective and subjective factors to determine the fair value of our common stock as of each grant date, including:

- the prices at which we sold shares of preferred stock and the superior rights and preferences of the preferred stock relative to our common stock at the time of each grant;
- the progress of our research and development programs, including the status of preclinical studies and clinical trials for our product candidates;
- our stage of development and business strategy;
- external market conditions affecting the biotechnology industry and trends within the biotechnology industry;

- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common stock and our preferred stock;
- the likelihood of achieving a liquidity event, such as an initial public offering, or IPO, or sale of our company in light of prevailing market conditions; and
- the analysis of IPOs and subsequent market performance of similar companies in the biotechnology industry.

The assumptions underlying these valuations represented management’s best estimate, which involved inherent uncertainties and the application of management’s judgment. As a result, if we had used significantly different assumptions or estimates, the fair value of our common stock and our stock-based compensation expense could have been materially different.

Once a public trading market for our common stock has been established in connection with the completion of this offering, it will no longer be necessary for our board of directors to estimate the fair value of our common stock in connection with our accounting for granted stock options and other such awards we may grant, as the fair value of our common stock will be determined based on the quoted market price of our common stock.

Share-based Awards Granted

The following table sets forth by grant date the number of shares subject to options granted or number of restricted stock granted since January 1, 2020, the per share exercise price of the options or purchase price of restricted stock, the per share fair value of common stock on each grant date, and the per share estimated fair value of the options or restricted stock:

Grant Date	Type of Award	Number of Shares Subject to Award	Per Share Exercise or Purchase Price of Award	Per Share Fair Value of Common Stock on Grant Date	Per Share Estimated Fair Value of Awards on Grant Date
February 26, 2020	Restricted Stock	2,159,621	\$0.00001	\$0.02 ⁽¹⁾	\$0.02
July 28, 2020	Restricted Stock	12,957,727	\$0.00001	\$0.03 ⁽²⁾	\$0.03
August 13, 2020	Restricted Stock	260,000	\$0.00001	\$0.03 ⁽²⁾	\$0.03
October 27, 2020	Restricted Stock	1,480,000	\$0.00001	\$0.03 ⁽²⁾	\$0.03
January 16, 2021	Restricted Stock	3,000,000	\$0.00001	\$0.11 ⁽²⁾	\$0.11
February 10, 2021	Restricted Stock	298,000	\$0.00001	\$0.11 ⁽²⁾	\$0.11
March 4, 2021	Restricted Stock	1,190,000	\$0.00001	\$0.11 ⁽²⁾	\$0.11
August 4, 2021	Option	3,906,000	\$1.18	\$1.18	\$0.79
August 31, 2021	Option	170,000	\$1.18	\$1.18	\$0.76
October 27, 2021	Option	4,866,720	\$1.18	\$3.39 ⁽³⁾	\$2.76
November 21, 2021	Option	80,500	\$3.39	\$3.39	\$2.21
November 24, 2021	Option	84,000	\$3.39	\$3.39	\$2.29
December 2, 2021	Option	133,000	\$3.39	\$3.39	\$2.21
December 16, 2021	Option	95,000	\$3.39	\$3.39	\$2.21
January 24, 2022	Option	475,500	\$3.51	\$3.51	\$2.30
February 9, 2022	Option	57,000	\$3.51	\$3.51	\$2.30

(1) At the time of the restricted stock grant on February 26, 2020, our board of directors determined that the fair value of our common stock of \$0.04 per share reasonably reflected the fair value of our common stock as of the grant date. However, as described below, the fair value of our common stock as of the date of this grant was adjusted in connection with a retrospective fair value assessment for accounting purposes.

(2) At the time of the restricted stock grants from July 28, 2020 through March 4, 2021, our board of directors determined that the fair value of our common stock of \$0.04 per share reasonably reflected the fair value of our common stock as of the grant date. However, as described

below, the fair value of our common stock as of the dates of these grant was adjusted in connection with a retrospective fair value assessment for accounting purposes.

- (3) At the time of the option grant on October 27, 2021, our board of directors determined that the fair value of our common stock of \$1.18 per share calculated in the third-party valuation as of May 31, 2021 described above reasonably reflected the fair value of our common stock as of the grant date. However, as described below, the fair value of our common stock as of the date of this grant was adjusted in connection with a retrospective fair value assessment for accounting purposes.

The fair value of our common stock of \$0.02 per share as of February 26, 2020 was determined by us, based, in part, on the \$0.02 per share value indicated in the retrospective third-party valuation prepared as of December 31, 2019. In particular, the valuation determined our enterprise value using an OPM market-adjusted backsolve approach that was primarily based on the \$1.00 price per share paid by new and existing investors in the first closing of our Series A preferred stock in September 2019 less the value of the anticipated additional Series A tranche closings, which were treated as call options for the purposes of allocating value to the various equity securities. The market adjustment applied to the equity value considered the performance of guideline public companies and the biotech indices since the most recent sale of our preferred stock through the valuation date. A DLOM of the common stock was then applied to arrive at an indication of value for our common stock.

The fair value of our common stock of \$0.03 per share from July 28, 2020 to October 27, 2020 was determined by us, based, in part, on the \$0.03 per share value indicated in the retrospective third-party valuation prepared as of September 26, 2020. In particular, the retrospective valuation determined our enterprise value using an OPM market-adjusted backsolve approach that was primarily based on the \$1.00 price per share paid by new and existing investors in the first closing of our Series A preferred stock in September 2019 less the value of the anticipated additional Series A tranche closings which were treated as call options for the purposes of allocating value to the various equity securities. The market adjustment applied to the equity value considered the performance of guideline public companies and the biotech indices since the most recent sale of our preferred stock through the valuation date. A DLOM of the common stock was then applied to arrive at an indication of value for our common stock.

The fair value of our common stock of \$0.11 per share from January 16, 2021 to March 4, 2021 was determined by us, based, in part, on the \$0.11 per share value indicated in the retrospective third-party valuation prepared as of December 31, 2020. In particular, the retrospective valuation determined our enterprise value using an OPM market-adjusted backsolve approach that was primarily based on the \$1.00 price per share paid by new and existing investors in the first and second closings of our Series A preferred stock in September 2019 and November 2020, respectively, less the value of the anticipated additional Series A tranche closings, which were treated as call options for the purposes of allocating value to the various equity securities. The market adjustment applied to the equity value considered the performance of guideline public companies and the biotech indices since the most recent sale of our preferred stock through the valuation date. A DLOM of the common stock was then applied to arrive at an indication of value for our common stock.

The fair value of our common stock of \$1.18 per share on August 4 and 31, 2021 was determined by our board of directors, based, in part, on the \$1.18 per share value indicated in the third-party valuation prepared as of May 31, 2021. In particular, the valuation determined our enterprise value using an OPM backsolve approach that was based on the \$4.3803 price per share paid by new and existing investors in the closing of our Series B preferred stock in May 2021. A DLOM of the common stock was then applied to arrive at an indication of value for our common stock.

The fair value of our common stock of \$3.39 per share on October 27, 2021 was determined by us, based, in part, on the \$3.39 per share value indicated in the third-party valuation prepared as of October 27, 2021. In particular, the valuation determined our enterprise value using the hybrid method, which included a PWERM, with an IPO scenario, and a sale scenario. Our enterprise value in the IPO scenario was based on guideline IPO transactions identified within the last one to two years, which was adjusted by a risk-adjusted discount rate. The IPO scenario also assumed an estimated timeline for the IPO to occur. Our enterprise value for the sale scenario was based on an OPM market-adjusted backsolve method based on the \$4.3803 price per share paid by new and existing investors in the closing of our Series B preferred stock in May 2021. The market adjustment applied to the equity value considered the performance of guideline public companies and the biotech indices since the most recent sale of our preferred stock through the valuation date. A DLOM of the common stock was then applied to arrive at an

indication of value for our common stock. In addition, the board determined that the fair value of our common stock remained at \$3.39 per share through December 16, 2021.

The fair value of our common stock of \$3.51 per share on January 24, 2022 and February 9, 2022 was determined by our board of directors, based, in part, on the \$3.51 per share value indicated in the third-party valuation prepared as of December 24, 2021. In particular, the valuation determined our enterprise value using the hybrid method, which included a PWERM, with two IPO scenarios, short-term and long-term, and a sale scenario. Our enterprise value in the IPO scenarios was based on guideline IPO transactions identified within the last one to two years, which was adjusted by a risk-adjusted discount rate. Each IPO scenario also assumed an estimated timeline for the IPO to occur. Our enterprise value for the sale scenario was based on an OPM market-adjusted backsolve method based on the \$4.3803 price per share paid by new and existing investors in the closing of our Series B preferred stock in May 2021. The market adjustment applied to the equity value considered the performance of guideline public companies and the biotech indices since the most recent sale of our preferred stock through the valuation date. A DLOM of the common stock was then applied to arrive at an indication of value for our common stock.

In the course of preparing for this offering, we applied the fair values of our common stock from our retrospective fair value assessments in December 2019, September and December 2020 and October 2021 to determine the fair value of each of the February 2020, July 2020, August 2020, October 2020, January 2021, February 2021, March 2021 and October 2021 awards as of the respective grant date and calculated stock-based compensation expense for accounting purposes based on applicable fair values.

Valuation of Preferred Stock Tranche Right Liability

We classify the preferred stock tranche right as a liability on our consolidated balance sheets as each preferred stock tranche right is a freestanding financial instrument that may require us to transfer assets upon the achievement of certain conditions. Each preferred stock tranche right liability was initially recorded at fair value upon the date of issuance of each preferred stock tranche right and is subsequently remeasured to fair value at each reporting date, and immediately prior to any subsequent Series A preferred stock financing. Changes in the fair value of the preferred stock tranche right liability are recognized as a component of other income (expense), net in the consolidated statement of operations and comprehensive loss. Changes in the fair value of the preferred stock tranche right liability were recognized until the preferred stock tranche right was settled in full upon the satisfaction of certain conditions in April 2021. During the year ended December 31, 2021, we recognized \$74.3 million as a component of other income (expense), net related to the change in fair value of the preferred stock tranche right liability.

We utilize the Black-Scholes option pricing model, which incorporates management's assumptions and estimates, to value the preferred stock tranche right liability. We determine the fair value per share of the underlying convertible preferred stock by taking into consideration the most recent sales of our convertible preferred stock, fair value of the preferred stock at each valuation date as obtained from third-party valuations and additional factors we deem relevant. In November 2020 the second tranche of the Series A preferred stock closed and in April 2021 the third and fourth tranches of the Series A preferred stock closed. Upon the achievement of certain conditions the preferred stock tranche right liability was settled. In November 2020, the fair value of each Series A convertible preferred stock was \$0.73 per share upon the closing of the second tranche. The fair value of each Series A convertible preferred stock was \$2.31 per share upon the closing of the third and fourth tranches.

As of December 31, 2020, the fair value of each Series A convertible preferred stock was \$0.76 per share. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining estimated time period of achievement of the specified milestones underlying the preferred stock tranche right. As of December 31, 2020, an immediate 10 percent increase in the fair value of our Series A preferred stock would have resulted in a \$3.3 million increase, and in the case of a 10 percent decrease, a \$3.1 million decrease to the fair value of the preferred stock tranche right liability.

Valuation of Anti-Dilution Obligation

The fair value of the Anti-Dilution Obligation recognized in connection with the anti-dilution provisions set forth in our license agreement with Broad Institute was determined based on significant inputs not observable in the market, which represented a Level 3 measurement within the fair value hierarchy.

The fair value of the Anti-Dilution Obligation was estimated using a probability-weighted scenario which considered as inputs the probability of occurrence of events that would trigger the issuance of shares, including a (i) the closing of Series A convertible preferred stock, (ii) our initial public offering, and (iii) no future sale of equity securities. The weighted-average fair values of all scenarios were calculated utilizing the fair value per share of the underlying Series A convertible preferred stock and common stock. Changes in the estimated fair value of our common stock and the probability of achieving different financing scenarios can have a significant impact on the fair value of the Anti-Dilution Obligation. An immediate 10 percent change in fair value of our common stock would have had an insignificant impact on the fair value of the Anti-Dilution Obligation as of December 31, 2020. The fair value of our common stock was \$0.11 per share as of December 31, 2020.

The Anti-Dilution Obligation was initially recorded at fair value upon entering into the license agreement with Broad Institute and was subsequently remeasured to fair value at each reporting date. Changes in fair value of the Anti-Dilution Obligation were recognized as a component of other income (expense), net in the consolidated statements of operations and comprehensive loss. Changes in the fair value of the Anti-Dilution Obligation were recognized until the achievement of \$100.0 million in cumulative equity financing was raised by us in connection with the fourth Series A preferred stock closing. As a result, the Anti-Dilution Obligation was settled during the year ended December 31, 2021. During the year ended December 31, 2021, we recognized \$6.7 million as a component of other income (expense), net related to the change in fair value of the Anti-Dilution Obligation.

Internal Control over Financial Reporting

In connection with the audit of our financial statements for the year ended December 31, 2020 and 2019, we identified a material weakness in our internal control over financial reporting that existed as of those periods, which remains unremediated as of December 31, 2021. See “Risk factors—We have identified a material weakness in our internal control over financial reporting. If we fail to remediate this material weakness or identify additional material weaknesses in the future or otherwise fail to maintain effective internal control over financial reporting in the future, we may not be able to accurately report our financial condition or results of operations which may adversely affect investor confidence in us and, as a result, the value of our common stock.”

Recently Issued and Adopted Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our consolidated financial statements appearing at the end of this prospectus.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012 permits an “emerging growth company” such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected not to “opt out” of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we will adopt the new or revised standard at the time private companies adopt the new or revised standard and will do so until such time that we either (i) irrevocably elect to “opt out” of such extended transition period or (ii) no longer qualify as an emerging growth company. As a result of this election, our consolidated financial statements may not be comparable to other public companies that comply with new or revised accounting pronouncements as of public company effective dates. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies.

Quantitative and Qualitative Disclosures About Market Risks

Interest Rate Risk

We are exposed to market risk related to changes in interest rates of our investment portfolio of cash equivalents and short-term investments. As of December 31, 2021, we held cash and cash equivalents and short-term investments of \$269.6 million, which consisted of cash, money market funds, equity securities and U.S. Treasuries. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. The fair value of our cash equivalents, comprised of our money market funds, and U.S. Treasuries are subject to change as a result of potential changes in market interest rates, including changes resulting from the impact of the COVID-19 pandemic. Due to the short-term maturities of our cash equivalents and U.S. Treasuries and the low risk profile of our investments, an immediate 10 percent change in interest rates would not have a material effect on the fair market value of our cash equivalents or U.S. Treasuries.

As of December 31, 2021, we had no debt outstanding and are therefore not exposed to interest rate risk with respect to debt.

BUSINESS

Overview

We are a biotechnology company committed to delivering a new class of differentiated one-time curative genetic therapies to address the widest spectrum of diseases by deploying our Prime Editing technology, which we believe is a versatile, precise, efficient and broad gene editing technology.

Genetic mutations implicated in disease are diverse and can range from errors of a single base, known as point mutations, to errors that extend beyond a single base, such as insertions, deletions, duplications, or combinations thereof. Other mutations can affect regulatory sequences that control the function of genes and can affect the function of larger biochemical and genetic pathways. Furthermore, natural genetic variations, revealed by population-level genomic studies, are known to protect against or to increase risk of disease. To maximize the impact of these genetic insights, we believe the ability to alter the human genome at the foundational level may confer the greatest therapeutic impact on human disease.

Gene editing, including platforms such as Prime Editing, is a novel technology that is not yet clinically validated for human therapeutic use. Over the last decade, the field of genetic medicine has evolved tremendously, with groundbreaking advances in gene therapy, cell therapy, RNA therapy, and, more recently, gene editing. These technologies represent dramatic advancements for genetic therapies, but lack the versatility to precisely and efficiently correct the diverse range of mutations or DNA alterations implicated in disease. Non-targeted gene therapy, which involves introducing a new copy of a gene into a patient's cell, lacks the ability to target a specific, desired genetic location, resulting in the risk of random genomic integration, potentially waning durability and lack of native physiological gene regulation. Nuclease gene editing technologies, such as CRISPR, Zinc Fingers, Arcuses and TAL Nucleases create a targeted double-stranded break in the DNA, and then rely on cellular mechanisms to complete the editing process, thereby limiting their use. While such approaches can be efficient in the disruption of gene expression, they lack control of the editing outcome, have low efficiency of precise gene correction, and can result in unwanted DNA modifications with potentially deleterious implications. The recent emergence of base editing technology has made it possible for more precise gene editing at the single base level without making a double-stranded break in the DNA. Despite this promise, base editing can only edit four out of the twelve types of single point mutations, cannot address errors that extend beyond those single base changes and has the potential to make certain unwanted on-target by-products known as bystander edits.

We believe Prime Editing technology has transformative potential that could change the course of how disease is treated and overcome the challenges associated with current genetic therapies. Although Prime Editing technology is a developing field and is not yet validated in clinical studies, it has been extensively validated *in vitro* and in animal studies, as first described in a Nature publication in December 2019 and replicated in over 50 papers published in the primary scientific literature since then. Our in-licensed Prime Editing technology was described in the Nature publication and further validated in other published papers, although we believe publications have not disclosed or used any of the specific pegRNA, ngRNA or Prime Editor protein sequences that are being used in our current programs.

In addition, in response to the Nature publication, more than 1,500 academic laboratories requested the substances, compounds, or sequences used to carry out the laboratory experiments, or reagents, from Dr. Liu's laboratory to replicate the experiments described in Nature and to perform Prime Editing in their laboratories, demonstrating the impact this new technology has had on the gene editing academic community. We believe that the number of requests for reagents demonstrates the excitement in the academic community about the potential of Prime Editing as most scientific publications tend to generate a much smaller number of requests for reagents.

Prime Editing technology, as developed by Dr. Liu and Dr. Anzalone, has broad theoretical potential therapeutic applications. For example, Prime Editing technology has the ability to repair diverse mutations, including all types of point mutations, deletion mutations, insertion and duplication mutations and insertion-deletion mutations. Our analysis of more than 75,000 pathological, or disease-causing, mutations found in the National Center for Biotechnology Information ClinVar Database shows that those addressable by Prime Editing technology account for approximately 90 percent of genetic variants associated with disease. As such, we believe Prime Editing technology

has the theoretical potential for repairing approximately 90 percent of known disease-causing mutations across many organisms, organs and cell types. Because biotechnology companies can only initiate therapeutic programs for a subset of pathogenic mutations and the associated diseases, we have chosen to strategically focus on disease settings where we believe that Prime Editing technology could offer compelling advantages over both current standard-of-care and novel therapeutic modalities in development. Currently, at Prime Medicine, we are leveraging the breadth of our in-licensed Prime Editing technology to focus on our current portfolio of 18 therapeutic programs.

Our Prime Editors also have the ability to create permanent modifications at their natural genomic location, resulting in durable edits that are passed on to daughter cells, and retain their native physiological control. Our next generation gene editing technology produces a wide variety of precise, predictable and efficient genetic outcomes at the targeted sequence, while minimizing unwanted bystander edits and off-target edits and avoiding double-stranded DNA breaks. Our Prime Editors are designed to make only the right edit at the right position within a gene.

If nuclease gene editing approaches are “scissors” for the genome, and base editors are “pencils,” erasing and rewriting a subset of single letters in the gene, then Prime Editing is a “word processor,” searching for the correct location and replacing or repairing a wide variety of target DNA.

Our novel Prime Editors have two main components that act together to edit DNA: (i) a Prime Editor protein, comprising a fusion between a Cas protein and a reverse transcriptase enzyme, and (ii) a pegRNA, that targets the Prime Editor to a specific genomic location and provides a template for making the desired edit to the target DNA sequence. Prime Editing leverages the established DNA-targeting capabilities of CRISPR-Cas proteins modified to nick, but not cause double-stranded DNA breaks, and combines these with the DNA synthesis capabilities of reverse transcriptase enzymes, which have been engineered to efficiently and precisely copy a pegRNA-encoded edited sequence into target DNA. This proprietary combination enables the precise and targeted editing of any single base pair of DNA to any other desired base pair, the precise insertion or deletion of DNA, and combinations of these edits, which has not been previously possible.

To maximize the potential of our Prime Editing technology to provide one-time curative genetic therapies to the broadest set of diseases possible, we have purposefully built a diversified portfolio organized around four strategic indication categories, each set of indications chosen to deliver a different strategic goal:

- Immediate target indications: Deliberately chosen as potentially the fastest, most direct path to demonstrate technological success of Prime Editing in patients. We are initially focusing on diseases of the blood via *ex vivo* delivery to hematopoietic stem cells and on diseases of the liver, the eye and the ear.
- Differentiation target indications: Aimed to create therapeutics to address the underlying cause of severe genetic diseases with therapeutics that we believe could not have been created before, especially using other gene-editing approaches. These include repeat expansion diseases, or diseases where expansion of pathological DNA repeats results in serious disease.
- “Blue sky” indications: Intended to push new and innovative technological developments in Prime Editing and extend its application beyond rare genetic diseases and towards our goal of more broadly addressing human disease. These programs remain in the early stages of conception and will become an increasing focus over the next few years.
- “March up the chromosome” approaches: Represents opportunities to deliver upon our overarching vision to ultimately treat all patients with a disease and correct the full set of mutations in a particular gene. This category overlaps with other strategic indication categories, where most of our disclosed indications across other categories have a plan that can accommodate expansion opportunities to address additional mutations in that disease.

We believe our Prime Editing programs are well-positioned to leverage the clinical, regulatory, and manufacturing advancements made to date across gene therapy, gene editing, and delivery modalities to accelerate progression to clinical trials and potential approval. To unlock the full potential of our Prime Editing technology across a wide range of therapeutic applications, we are pursuing a comprehensive suite of validated delivery

modalities in parallel. For a given tissue type, we intend to use the delivery modality with the most compelling biodistribution. Our initial, immediate programs rely on three distinct delivery methodologies: (a) electroporation for efficient delivery to blood cells and immune cells *ex vivo*; (b) lipid nanoparticles, or LNPs, for non-viral *in vivo* delivery to the liver and potentially other organs in the future; and (c) adeno-associated virus, or AAV, for viral delivery *in vivo* to the eye and the central nervous system, or CNS.

We have constructed our portfolio of 18 programs, including one partnered program, across our first two strategic indication categories in disease settings where the unique characteristics of Prime Editing could offer compelling advantages over current standard-of-care and novel therapeutic modalities in development.

Our current portfolio includes the following 18 programs:

STRATEGIC CATEGORY	TARGET TISSUE	INDICATION	DELIVERY	DISCOVERY	IND-ENABLING	Phase 1	Phase 2	Phase 3	PARTNER
IMMEDIATE	BLOOD	Sickle Cell Disease	<i>ex vivo</i>						
		Chronic Granulomatous Disease	<i>ex vivo</i>						
		Fanconi Anemia	<i>ex vivo</i>						
	LIVER	Wilson's Disease	LNP						
		Glycogen Storage Disease 1b	LNP						
	EYE	Retinitis Pigmentosa/Rhodopsin	AAV						
		Retinitis Pigmentosa/Usher Syndrome	AAV						
	EAR	Usher's Syndrome Type 3	AAV						
		Non-Syndromic Hearing Loss – GJB2	AAV						
DIFFERENTIATION: REPEAT EXPANSION DISEASES	NEURO-MUSCULAR	Friedreich's Ataxia	viral/non-viral						
		Myotonic Dystrophy Type 1	viral/non-viral						
		Amyotrophic Lateral Sclerosis	viral/non-viral						
		Oculopharyngeal Muscular Dystrophy	LNP						
		Fragile X Syndrome	viral/non-viral						
	Huntington's Disease								
EYE	Fuchs' Endothelial Corneal Dystrophy	viral/non-viral							
DIFFERENTIATION: OTHER	MUSCLE	Duchenne Muscular Dystrophy	AAV						
	LUNG	Cystic Fibrosis	LNP						

* AAV = adeno-associated viral vectors; LNP = lipid nanoparticles

We have established preclinical proof-of-concept *in vivo* with long term engraftment of *ex vivo* Prime Edited human CD34 cells in mice in our partnered Sickle Cell Disease program, where we have precisely corrected the disease-causing mutation. This program is closely followed by Prime Editing for patients with Chronic Granulomatous Disease where we have established Prime Editors with high levels of correction of the disease-causing mutation in the cells that must be targeted. We have demonstrated preclinical Prime Editing of cells *in vitro* at therapeutically relevant levels for all of our remaining named programs. We have designed proprietary high throughput methods to identify highly efficient Prime Editors and have advanced the reach and efficiency of the Prime Editing technology. We have incorporated dual-flap Prime Editing technology enabling us to establish Prime Editors with greater than 77 percent precise removal of pathological expansion repeats in five different repeat expansion diseases.

We have not completed any *in vivo* studies to date. We expect to achieve preclinical proof-of-concept *in vivo*, which would include data from *in vivo* rodent studies in several programs in and non-human primate studies in several programs in through . If successful, this will allow us to initiate investigational new drug, or IND, enabling studies for several of our lead programs beginning in , leading to initial IND filings beginning in . Since we are in early stages of product candidate development, we will provide an update on our timelines in , with the potential to accelerate these programs. We also anticipate continuing to name additional programs as they advance over the next few years.

Team

We began operations at Prime Medicine in the summer of 2020, after being co-founded by a world- renowned leader in the field of gene editing, David Liu, Ph.D. Dr. Liu was joined as co-founder by Andrew Anzalone, M.D.,

Ph.D., who conceived of and developed Prime Editing along with Dr. Liu and others. Dr. Anzalone joined Prime Medicine as Head of Platform Development with years of experience in Prime Editing. This has helped us to rapidly and effectively extend our Prime Editing technology beyond the academic research laboratory and into the company for drug discovery and development.

Drawn by the promise of Prime Editing's ability to transform the field of gene editing, we have assembled a diverse team that has grown to more than 80 as of November 30, 2021. Our research and development team is comprised of experts in gene editing and Prime Editing, computational biology, automation, data sciences, off-target biology, structural biology, RNA chemistry, protein engineering and molecular evolution, genetics, pharmacology, translational medicine and the manufacturing and delivery of genetic medicines.

Our executive leadership team has extensive industry experience in research and development, manufacturing and company building. Keith Gottesdiener, M.D., is our President and Chief Executive Officer and is an experienced executive and company builder with more than 26 years developing new vaccines and medicines, preceded by a 13 year career in academic medicine. Jeremy Duffield, M.D., Ph.D., our Chief Scientific Officer, is a physician scientist executive with over nine years of drug discovery experience in human genetics, innate immunity and regenerative medicine, business development and external innovation, preceded by a 20 year career in academic medicine.

Ann Lee, Ph.D., our Chief Technical Officer, is an accomplished leader with more than three decades of experience in manufacturing and technology innovation, where she contributed to the commercialization of 25 new vaccines and medicines across multiple modalities and has experience building global organizations. Meredith Goldwasser, Sc.D., SVP, Strategy and Corporate Operations, has over 18 years of experience developing new drugs in the biopharmaceutical industry, where she worked across all phases of development and in various leadership roles, including in project leadership, business development and company building. Karen Brown, Ph.D., J.D., is SVP of Intellectual Property and Legal Affairs, with more than 20 years of legal experience and leadership in the biopharmaceutical industry guiding global intellectual property strategy, negotiating complex partnership and collaboration agreements, and overseeing corporate legal matters. Carman Alenson, C.P.A., Chief Accounting Officer and SVP of Finance, has more than 32 years of experience in corporate accounting and finance, with more than 17 in the life sciences industry.

We believe that our team's considerable research and drug development expertise, together with our exclusive and non-exclusive licenses and intellectual property, as well as our depth of expertise in Prime Editing, has positioned us at the forefront of the field of advanced precision genetic medicines.

Relationship with David Liu, Ph.D.

We benefit from a close working relationship with Dr. Liu. In addition to being a co-founder, Dr. Liu is the chair of our Scientific Advisory Board and a Board observer, meets regularly with Company representatives, and provides consulting services to us pursuant to a consulting agreement, or the Liu Consulting Agreement, related to any and all gene editing and related technology for any and all human or prophylactic uses.

Pursuant to the Liu Consulting Agreement, for the term of the Liu Consulting Agreement and six months thereafter, Dr. Liu cannot directly provide material services to any third party in the field of gene editing for therapeutics or become an owner, partner, shareholder, consultant, agent, employee or co-venturer of any third party that has committed, or intends to commit, significant resources to that field, with certain exceptions, including a previous commitment with respect to Beam Therapeutics, Inc., or Beam. Dr. Liu's preexisting commitment to Beam could result in, or may create the appearance of a conflict of interest.

We have also licensed certain improvements to Prime Editing from Dr. Liu's laboratory at Broad Institute and Dr. Liu has entered into an agreement with us pursuant to which he is obligated to assign to us any inventions with respect to the services he performs for us. However, such obligations are subject to limitations and do not extend to his work in other fields or to the intellectual property arising from his employment with Harvard, HHMI and Broad Institute. To obtain such intellectual property rights, we would need to enter into license agreements with such institutions, including negotiations under the Broad Option Agreement, which may expire in November 2022, and such license agreements may not be available on commercially reasonable terms or at all. For more information, see the risk factors entitled "The gene editing field is relatively new and is evolving rapidly. We are focusing our

research and development efforts on gene editing using Prime Editing technology, but other gene editing technologies may be discovered that provide significant advantages over Prime Editing, which could materially harm our business” and “Our rights to develop and commercialize our Prime Editing platform technology and product candidates are subject to the terms and conditions of licenses granted to us by others. If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.”

Dr. Liu, as a member of the faculty of Harvard and Broad Institute, is eligible to apply for use of the funds that we make available pursuant to our Pledge; however, the use of the Pledge is determined by Broad Institute and Harvard, consistent with its purpose. For more information, see “Business—Our License and Collaboration Agreements—Pledge to Broad Institute and Harvard.”

Scientific Advisory Board

In December 2021, we formally assembled our Scientific Advisory Board, a group of prominent and highly accomplished scientists who are leaders in the field of genetic therapies to help us advance the technology and the pipeline. We are continuing to develop rules and procedures for our Scientific Advisory Board.

Focal points include: off-target genome biology, nucleic acid drugs, Prime Editing platform technology, Prime Editing delivery to target tissues and disease indications. The Scientific Advisory Board comprises of the following individuals:

- David R. Liu, PhD (Chair of our Scientific Advisory Board); Richard Merkin Professor, Director of the Merkin Institute of Transformative Technologies in Healthcare, and Vice-Chair of the Faculty at the Broad Institute of Harvard and MIT; Thomas Dudley Cabot Professor of the Natural Sciences and Professor of Chemistry and Chemical Biology at Harvard University; and Howard Hughes Medical Institute Investigator.
- Yvonne Chen PhD; Associate Professor of Microbiology, Immunology, and Molecular Genetics at the University of California.
- Agnieszka Czechowicz; Assistant Professor at Stanford University and Pediatric Hematologist/Oncologist, specializing in pediatric stem cell transplantation for rare genetic diseases.
- Guangping Gao; Co-Director, Li Weibo Institute for Rare Diseases Research, Director, Horae Gene Therapy Center and Viral Vector Core, Professor of Microbiology and Physiological Systems, Penelope Booth Rockwell Professor in Biomedical Research, University of Massachusetts Medical School.
- James Haber, PhD Abraham and Etta Goodman Professor of Biology, and Director, Rosenstiel Basic Medical Sciences Research Center, Brandeis University.
- Ben Kleinstiver; Assistant Professor, Center for Genomic Medicine, Massachusetts General Hospital and Harvard Medical School.
- Muthiah Manoharan; Senior Vice President, Innovation Chemistry & Alnylam Distinguished Scientist, Alnylam Pharmaceuticals.
- Samuel H. Sternberg; Assistant Professor in the Department of Biochemistry and Molecular Biophysics, Columbia University.
- Shengdar Tsai; Assistant Member in the Department of Hematology at St. Jude Children's Research Hospital.

Our Strategy

Our goal is to transform the lives of patients with debilitating diseases through the application of our ground-breaking Prime Editing platform and technology. Our key focus is on patients. We are committed to developing safe and effective therapeutics using Prime Editing approaches to address high unmet need across a broad spectrum of diseases, from rare genetic diseases to severe, chronic and acute diseases, and ultimately to preventing disease. Key components of our strategy are as follows:

- **Deliver the broadest potential of Prime Editing in the service of patients.** We believe our Prime Editing technology and capabilities represent the future of gene editing and could unlock broad applications in medicine and life sciences. As a result of our access to proprietary rights in groundbreaking technology and our continued investment to enhance this gene-editing approach, we have established a clear leadership position in Prime Editing. Our goal is to be the preeminent company to deliver Prime Editing to patients. We have built a cross-disciplinary team comprised of dedicated, scientifically curious individuals and experts in Prime Editing and drug development who are passionate about our common goal of helping patients live longer, healthier lives.
- **Deploy our technology to extend the application of one time potentially curative therapeutics to areas that we believe were not addressable before.** To unlock the full potential of our Prime Editing technology across a wide range of therapeutic applications, we intend to advance multiple therapeutic targets into clinical programs grouped into a series of four strategic indication categories: (1) immediate target indications, (2) differentiation target indications, (3) “blue sky” indications and (4) “march up the chromosome” approaches. Our immediate target indications were deliberately chosen as potentially the fastest, most direct path to demonstrate technological success of Prime Editing in patients. Our differentiation target indication programs aim to create therapeutics that we believe could not have been created before, especially using other gene-editing approaches. Our “blue sky” target indications are intended to push new and innovative technological developments in Prime Editing and extend the range of diseases we can treat. Finally, our “march up the chromosome” category represents opportunities to deliver upon our overarching vision to ultimately treat all patients with a disease and correct the full set of mutations in a particular gene.
- **Advance our pipeline while simultaneously enhancing, validating and enabling our Prime Editing platform.** We have established a diverse pipeline comprised of 18 Prime Editing programs, including one partnered program, with a primary initial focus on the first two of our strategic indication categories. In progressing our current immediate target indication pipeline using validated delivery methods, we believe we will enhance the probability of clinical success for future programs as we achieve early human proof-of-concept with our technology. We intend to advance these immediate programs carefully and quickly into the clinic and through development. We also believe we have the ability to move quickly into similar follow-on programs in each target organ as we achieve therapeutic success. In advancing our current differentiation target indications, we aim to develop programs that build on the advantages of our technology to widen the possibilities for gene editing. Our initial focus on repeat expansion diseases is one of many potential areas of differentiation from other gene therapy and editing approaches, and was chosen to demonstrate where Prime Editing has a unique genetic approach that could be applied to a large set of related diseases with high unmet need: the precise removal of pathogenic repeats at the natural gene location, returning the patient’s genome to wild-type genetics. We believe these longer-term programs will provide a large therapeutic benefit to patients.
- **Continue to push the frontier of innovation in gene editing by optimizing and expanding our Prime Editing technology and capabilities.** We plan to continue investing in our technology, team and intellectual property with a focus on reinforcing our leadership position and making fundamental progress towards better therapies for patients. We believe our relationship with and ability to access certain Prime Editing intellectual property and technology from Dr. David Liu’s laboratory at Broad Institute exclusively in certain fields establishes a clear leadership position in Prime Editing. We aim to continue to supplement this foundational work with in-house generated intellectual property that

supports the translation and advancements to our Prime Editing platform to broaden the scope of applications for Prime Editing. We are also leveraging and investing in a full range of validated, as well as novel delivery modalities in order to retain optionality for our portfolio and select the most appropriate delivery method for each program.

- **Opportunistically evaluate synergistic and value-creating partnerships to maximize the broad potential of our platform.** Our pipeline programs have been internally generated, and we retain worldwide development and commercialization rights to all but one of our programs. Given the broad potential of our technology, we may enter into complementary collaborations with external parties in order to maximize the potential applications of our platform. Examples could include opportunities that expand capabilities in Prime Editor delivery modalities, or collaborations for specific therapeutic areas where we do not currently have specific expertise or resources. We have already established important value- and capability-enhancing collaborations with Beam, a gene editing company that also emerged from the laboratory of Dr. Liu, as well as Broad Institute.
- **Lead with our culture of integrity, ethics, innovation and purpose-driven focus for patients in everything we do.** We believe the potential of Prime Editing can only be achieved through the coordinated effort of our team and the support of our partners across academia and industry. Realizing this promise requires a talented team with a diversity of viewpoints and expertise. We are committed to jointly defining and maintaining a culture that is transparent, develops trust and values integrity and ethics, puts patients first and is science data driven, encourages innovation and relentlessness, to push the boundaries of where gene editing can go.

Prime Editors: A Next Generation Gene Editing Technology

We are developing Prime Editors as a potentially new class of therapeutics with transformative potential to expand the application of curative precision genetic medicines to the broadest spectrum of diseases.

Genetic mutations implicated in disease are diverse and can range from errors of a single base, known as point mutations, to errors that extend beyond a single base, such as insertions, deletions, duplications, or combinations thereof. Other mutations can affect regulatory sequences that control the function of genes and can affect the function of larger biochemical and genetic pathways. Furthermore, natural genetic variations, revealed by population-level genomic studies, are known to protect against or to increase risk of disease. To maximize the impact of these genetic insights, we believe the ability to alter the human genome at the foundational level in a versatile, precise, efficient and broad manner may confer the greatest therapeutic impact on human disease.

Over the last decade, groundbreaking advances in gene therapy, cell therapy and RNA therapeutics have resulted in several approvals for genetic medicines that have transformed the treatment of certain severe genetic diseases and cancers as well as the prevention of infectious diseases, such as COVID-19. More recently, the first generation of CRISPR-Cas based gene editing approaches for gene knockout have demonstrated initial evidence of the ability to correct pathogenic genetic mutations, via either *in vivo* or *ex vivo* delivery to humans. Finally, the first base editing investigational medicine, that enables targeted editing of certain point mutations, has received IND clearance by the U.S. Food and Drug Administration, or the FDA, to begin clinical trials.

Despite this progress, there remain considerable limitations to current genetic medicine approaches that impede their ability to truly deliver on the promise of a curative, one-time therapy to the broadest set of patients. While each gene editing technology differs, the barriers that prohibit one or more of the existing technologies from addressing genetic diseases widely include:

- Limits in the types of edits they can make
- Limits in the types of cells in which they can make edits
- Limits in the precision of gene correction
- Reliance on double-stranded breaks

- Inability to correct the mutated gene at its physiological site

Due to these limitations, we believe that it is critical that new approaches be developed that can edit genes across most therapeutically relevant mutations, precisely at the edited site with minimal off-target, or unwanted, activity elsewhere in the genome, in clinically relevant organs, and at the physiological location to keep an edited gene under native gene control.

We believe our in-licensed and company-owned Prime Editing technology has the potential to address approximately 90 percent of known disease-causing mutations. By overcoming challenges associated with current methods in gene therapy and gene editing, we believe Prime Editing technology has the potential to provide life-long cures after a single treatment. Furthermore, we believe Prime Editing could accelerate progression of product candidates into clinical trials by leveraging the clinical, regulatory, and manufacturing advancements made to date in the field of genetic medicine.

Current Challenges for the Field of Genetic Medicines

Non-Targeted Gene Therapy

Non-targeted gene therapy includes using viral vectors, such as Adeno-Associated Virus, or AAV, or retroviruses such as lentiviruses, to deliver new copies of genes, or transgenes, to cells. It also includes the broad field of mobile gene elements, such as retrotransposons and transposons. These approaches generally do not correct genes but insert new whole genes into cells in a non-targeted manner.

While having some important benefits, non-targeted gene therapy approaches can have many of the following key limitations:

- Lack of programmability, or the ability to target the gene therapy approach to a specific, desired genetic location.
- For transposons and retrotransposons, integration may occur randomly at hundreds or thousands of sites in the human genome.
 - Variable gene expression due to inability to fine tune the vector copy number per cell.
 - Lack of normal endogenous regulation of gene expression.
 - Limited durability for non-integrating viral vectors, such as AAV.
 - Pre-existing immunity to AAV vectors that could limit their use.
 - Inability to re-dose in the context of lack of persistence due to certain immune responses to AAV.
 - Inability to correct the mutated gene which may lead to diminished efficiency of a transgene due to competition with mutated protein.
 - Risk of random genomic integration of the vector, or insertional mutagenesis, for permanent integrating viral vectors, such as lentiviral vectors.
 - Potentially curative only for loss-of-function mutations.

Nuclease Gene Editing

First generation gene editing methods rely on a class of enzymes called nucleases, such as CRISPR, Zinc Fingers, Arcuses and TALENs, to create double-stranded breaks in DNA at a targeted location. The DNA can then be repaired by one of two naturally occurring DNA repair pathways: (1) non-homologous end joining, or NHEJ, which patches the broken ends of the chromosomes back together but can randomly insert indels, or unwanted insertions and deletions; or (2) homologous directed repair, or HDR, which can more precisely replace DNA at the target cut site with the delivery of a template of corrected DNA. However, given NHEJ is typically the dominant

repair pathway in cells and due to the low efficiency of repair and complexity associated with HDR, most nuclease-based editing programs in the clinic have focused on an NHEJ-directed knock out approach to alter or silence gene expression.

Nuclease based gene editing approaches can have the following key limitations:

- Lack of predictability in genetic outcomes at the target site in NHEJ, such as randomly inserting indels (efficient if the goal is to disrupt or knock out a gene).
- Low percentage editing and efficiency with HDR to make correction, replacement or insertions.
- Inability to correct genes in non-dividing cells since currently, HDR DNA repair machinery is only expressed in dividing cells.
- Requirement for DNA template with desired, corrected gene sequence needs to be delivered simultaneously which increases complexity.
- Unwanted DNA modifications associated with double-stranded breaks, including cell death response, genomic instability, off-target editing and the potential for oncogenesis.
- Inability to multiplex edit due to potential for large scale translocations and rearrangements from multiple double-stranded breaks.

Base Editing

Base editing is an emerging gene editing technology that harnesses CRISPR-Cas9 to deliver a deaminase to a target DNA site, which can edit a single base efficiently. Base editing avoids double-stranded breaks and the deleterious effects associated with first generation nuclease editing.

Base editing can have the following key limitations:

- Edits can reliably correct only four out of 12 possible single base mutations, and base editing has no ability to perform or correct insertion or deletions, which limits the number of diseases base editing can address.
- Ability for each base editor to correct or introduce only a single point mutation at a time.
- Potential to make certain types of unwanted on-target by-products, called bystander edits, near the targeted site, e.g. modifying nearby bases which are not being targeted.
- Potential for limited optionality due to its smaller editing window.

Prime Editing: A Next Generation Gene Editing Approach

Prime Editing is a next generation gene editing approach that we believe can address the genetic cause of disease and potentially provide patients with long-lasting cures. Although Prime Editing is a developing technology and is not yet validated in clinical studies, it was first described in a Nature publication in December 2019 and has since been extensively validated *in vitro* and in animal studies, both by our company and in over 50 papers published in the primary scientific literature to date.

In addition, in response to the Nature publication, more than 1,500 academic laboratories requested the reagents, from Dr. Liu's laboratory to replicate the experiments described in Nature and to perform Prime Editing in their laboratories, demonstrating the impact this new technology has had on the gene editing academic community. We believe that the number of requests for reagents demonstrates the excitement in the academic community about the potential of Prime Editing as most scientific publications tend to generate a much smaller number of requests for reagents.

Prime Editors are designed to produce edits across many organisms, organs and types of cells and to work broadly across most types of gene mutations at the natural genomic location, while minimizing unwanted DNA modifications. This approach uses a process designed to produce a wide variety of precise, predictable and efficient genetic outcomes at the targeted sequence, which we believe will dramatically increase the impact of gene editing for a broad range of therapeutic applications.

If nuclease gene editing approaches are “scissors” for the genome, and base editors are “pencils,” erasing and rewriting a subset of single letters in the gene, then Prime Editing is a “word processor,” searching for the correct location and replacing or repairing a wide variety of target DNA.

The below image illustrates the potential of Prime Editing relative to some of the current genetic medicine approaches, using the example of correcting misspellings in a sentence from the Preamble to the U.S. Constitution. In this example, where the sentence represents a target of genetic code, gene therapy is unable to make a precise correction of the misspellings and instead inserts a new corrected sentence either randomly into the paragraph or outside of the paragraph (which is not shown below). In most cases, nuclease editing inserts or deletes letters (indels) within the existing sentence, which results in a sentence that has completely lost its initial meaning. Base editing enables the precise correction of specific letters within the existing sentence, but can only make specific changes like a G to an A, but cannot correct a C to an A. We believe Prime Editing allows for a much broader scope of corrections to the sentence, by either correcting all the misspellings or even modifying the meaning of the sentence by inserting and deleting whole words or groups of words.

<i>“We the People of the United States, in Order to form g more perfeat Union...”</i>	
Gene Therapy	“We the People of the United States, in Order to form g more perfe at Union, establish Justice, insure domestic Tranquility, provide for the common defense, promote the general Welfare, and secure the Blessings of Liberty to ourselves and our Posterity, do ordain and estab We the People of the United States, in Order to form a more perfect Union ish this Constitution for the United States of America. ...”
Nuclease Editing	“We the People of the United States, in Order..... im perfe at Union...”
Base Editing	“We the People of the United States, in Order to form a more perfe at Union...”
Prime Editing	“We the People of the United States, in Order to form a more perfe ct Union...” or “We the People of the United States, in Order to form a more perfe ct and resilient Union...”

Our Prime Editing Platform

Summary of Gene Editing Technologies

The below table describes features of different gene therapy and gene editing methodologies based on our assessment of publicly available data and our own data. It does not represent the results of head-to-head comparison studies and is not intended to represent superiority of any one methodology over any other in any of the displayed categories.

	Prime Editing	Non-Targeted Gene Delivery ¹	Nuclease-Based Gene Editing ²	Base Editing
Versatility				
Can perform and correct insertions and deletions	✓		✓ ³	
Can correct all twelve types of single base pair corrections	✓		✓ ³	✓ ⁴
Direct correction of DNA without delivery of corrective DNA sequence	✓ ⁵		✓ ⁶	✓
Easily programmable target location and type of edit	✓		✓ ⁷	✓
Restores gene function for multiple mutations with a single product	✓	✓		
Precisely targets to insert, delete or invert kilobase-sized DNA	✓		✓ ³	
Precision				
High specificity (low indels rate) and minimal off-target activity	✓			✓
Does not create double stranded breaks	✓	✓ ⁸		✓
Limited potential for “bystander editing” at target site	✓			
Efficiency				
Permanent edits that are passed along to daughter cells	✓	✓ ⁹	✓	✓
Corrects genes <i>in situ</i> , maintaining native gene control	✓		✓ ³	✓
Single-dose, potentially curative correction to wild-type sequence	✓			✓
Breadth				
Corrects mutations in dividing and non-dividing human cells	✓			✓

Note: Yellow checkmarks are explained in the footnotes below.

1. Includes Lentivirus, AAV, mobile gene elements such as retrotransposons/transposon approaches. 2. Includes CRISPR-Cas (most forms), ZFNs, TALENs; most effective at knocking out genes. 3. Inefficient and limited. 4. Reliably corrects 4 of 12 types of single base pair mutations. 5. Except for Prime Editing recombinase approach. 6. Limited correction possible in some approaches. 7. Programmable target but unable to easily program new types of edits. 8. Retrotransposons create double-strand breaks, but not in the same manner as nucleases. 9. Some approaches integrate into the genome, but not as edits/corrections.

This table is based on our assessment of publicly available data, including representative citations listed below, as well as our own data. For Prime Editing references, see: Anzalone, et al. Genome editing with CRISPR–Cas nucleases, base editors, transposases and prime editors. *Nat Biotechnol* 38, 824–844 (2020); and Anzalone, A.V. et al, Programmable deletion, replacement, integration and inversion of large DNA sequences with twin prime editing. *Nat Biotechnol* (2021). For Non-Targeted Gene Delivery, see: Bulcha, J.T. et al, Viral vector platforms within the gene therapy landscape. *Sig Transduct Target Ther* 6, 53 (2021); and Tipanee, J. et al, Transposons: moving forward from preclinical studies to clinical trials. *Hum Gene Ther* 28, 1087-1104 (2017). For Nuclease-Based Gene Editing, see: Anzalone, A.V., et al, *Nat Biotechnol* *Ibid* (2020); Cox, D. et al, Therapeutic genome editing: prospects and challenges. *Nat Med* 21, 121–131 (2015); and Li, H. et al, Applications of genome editing technology in the targeted therapy of human diseases: mechanisms, advances and prospects. *Sig Transduct Target Ther* 5, 1 (2020). For Base Editing, see: Rees, H.A. et al, Base editing: precision chemistry on the genome and transcriptome of living cells. *Nat Rev Genet* 19, 770–788 (2018); and Anzalone, A.V., et al, *Nat Biotechnol* *Ibid* (2020).

Advantages of our Platform

We believe Prime Editing is a versatile, precise, efficient and broad gene editing technology with the following key advantages:

Versatility: Deep and highly differentiated toolbox of editing capabilities to enable a wide variety of therapeutic applications

- Applicable to a wide range of target mutations or alterations of DNA, including all twelve types of single base pair corrections, as well the ability to insert and delete DNA sequences.
- Direct correction of DNA with no requirement for delivery of the corrected DNA sequence in most applications of Prime Editing.
- Greater optionality with respect to editing site availability than other approaches due to a larger editing window.
- Programmable, which means that both the specified target location in the genome and the directed type of edit can be easily modified by replacing the Prime Editing guide RNA, or pegRNA, element of a Prime Editor.
- Multiple potential therapeutic applications, including but not limited to targeted gene correction, gene silencing or activation such as by altering the regulatory regions of genes, inserting or creating premature stop codons, or by modifying splicing sequences, hotspot region replacement, multiplex editing of several genes simultaneously, and wild-type variant modification to protect against or modify risk for a disease.
- Capable of inserting, deleting or inverting kilobase amounts of genomic DNA by combining Prime Editing with proprietary recombinase technology.

Precision: Highly specific and predictable gene editing

- Designed to specifically make only the directed type of Prime Edit at the desired target location.
- Avoidance of the potential negative impacts associated with double-stranded breaks, which results in minimal to potentially no unwanted on-target or off-target by-products and preservation of cell viability.
- Limited potential for bystander editing at the target site, a potential unwanted effect of base editing.

Efficiency: Durable gene edits with potential for superior therapeutic activity

- Single treatment resulting in permanent corrections of disease-causing mutations by restoring the targeted gene back to its wild-type sequence.
- Permanent, durable edits that persist in a cell and are passed along to daughter cells, creating potential for a life-long, “once and done” therapeutic outcome.
- Preservation of natural regulation and a normal number of copies of the gene in the cell by modification of genes in situ, or in their native genomic setting.
- Highly efficient, effecting therapeutically relevant levels of precise gene correction generally unachievable by nuclease-based methods.

Breadth: Able to address a wide range of diseases in multiple tissue types

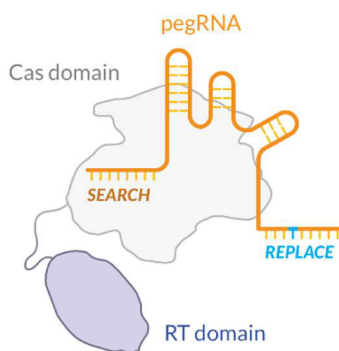
- Applicability in a wide range of human cells, including both dividing and non-dividing human cells, a wide range of organs and cell types, as well as in a wide variety of other organisms, as well as including primary cells such as hepatocytes, hematopoietic stem cells and neurons.
- Potential ability to repair approximately 90 percent of all types of mutations known to cause genetically driven disease.
- Broad therapeutic potential, including rare, genetic diseases as well as severe, chronic, and acute diseases. Beyond correcting disease-causing mutations, potential for gene modification to edit naturally occurring variations within genes known to protect against or modify risk for a disease.

Mechanism

Summary

Our novel Prime Editors have two main components that are designed to act together to edit DNA: (i) a Prime Editor protein, comprising a fusion between a Cas protein and a reverse transcriptase enzyme, and (ii) a pegRNA, that targets the Prime Editor to a specific genomic location and provides a template for making the desired edit to the target DNA sequence. Prime Editing leverages the established DNA-targeting capabilities of CRISPR-Cas proteins, which have been modified so that they do not cause double-stranded DNA breaks, and combines these with the DNA synthesis capabilities of reverse transcriptase enzymes, which have been engineered to efficiently and precisely copy a pegRNA-encoded edited sequence into target DNA. This proprietary combination enables the precise and targeted editing of any single base pair of DNA to any other desired base pair, the precise insertion or deletion of DNA, and combinations of these edits, all of which have not been previously possible with current gene editing technologies.

Illustration of Prime Editor and Two Main Components (Cas domain and RT domain)



Mechanism in Detail

Our Prime Editor proteins contain two protein domains. The first domain is a programmable DNA binding domain, often a CRISPR-Cas domain, or Cas domain. Cas proteins enable targeting of specific DNA sequences, and they have been adapted and engineered to target desired genomic locations in human cells with high specificity, yet modified such that they do not cause a double-stranded break in the DNA. Our Prime Editors most often use Cas9 proteins, though other Cas proteins can also be used to target DNA and we have ongoing efforts to expand our selection of Cas proteins.

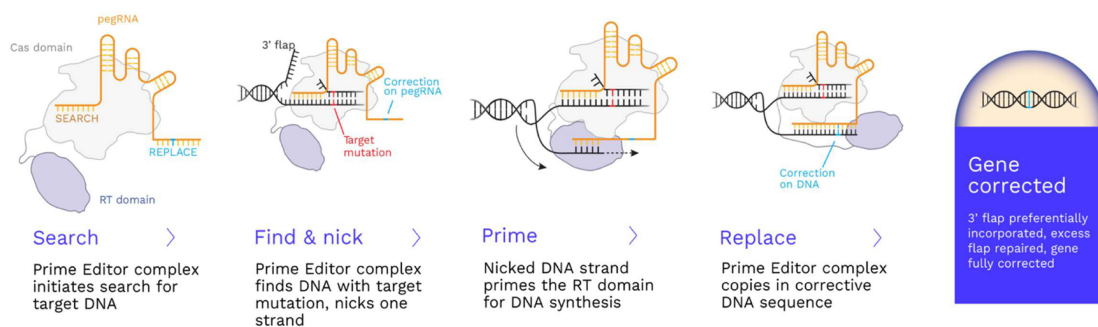
The second protein domain of Prime Editors is a reverse transcriptase enzyme domain, or RT, domain. Reverse transcriptases are DNA polymerase enzymes that write new DNA sequences by copying from an RNA template, provided by the pegRNA. In Prime Editing, the RT copies the edited DNA sequence directly into the target genomic site where the edit is made.

The other main component in Prime Editing is the pegRNA. The pegRNA contains a search sequence, also known as a spacer, which provides a target genomic address for the Prime Editor. This enables the Prime Editor to specifically target a desired gene sequence. The pegRNA also contains a second sequence unique to Prime Editing, a replace sequence, or edit template, which provides a blueprint for the edit that will be made to the target DNA sequence.

As shown in the second panel in the figure below, our Prime Editor and the pegRNA locate the DNA target site using the pegRNA's search sequence. When the correct DNA target is found (referred to as "edit check 1," as described below), the Prime Editor's Cas domain cleaves, or nicks, one of the two DNA strands, creating a single-stranded 3' flap. The other DNA strand remains intact and is not cleaved by the Prime Editor, thus avoiding the formation of double-stranded DNA breaks. Next, the 3' flap binds to a region of the replace sequence in the pegRNA ("edit check 2") and "primes" the DNA synthesis, which is shown in the third panel below. The Prime Editor's reverse transcriptase, or RT, domain copies the pegRNA's replace sequence, directly writing the corrected DNA sequence into the gene, as shown in the fourth panel. After the corrected sequence is fully copied, cellular DNA repair preferentially incorporates the corrective 3' flap ("edit check 3") while removing the excess original DNA sequence. The complementary DNA strand is also corrected, using the Prime-Edited DNA strand as a template. Incorporation of the correction into the complementary DNA strand can be made more efficient by adding a nicking guide RNA, or ngRNA, where the Prime Editor also transiently nicks the complementary strand. The overall result is a target gene sequence that is corrected on both strands of DNA.

As highlighted above, there are three distinct steps in the Prime Editing pathway that require exact matches between the target DNA and pegRNA sequences. Thus, the process of Prime Editing efficiently institutes three "edit checks," or three sequential steps where only if the match is exact does the next step occur. In addition to the lack of double-stranded DNA breaks, we believe that these "edit checks" are also important in helping to ensure that the right sequence in the genome is precisely edited in the desired manner, thereby minimizing both on- target and off-target mis-editing.

Illustration of Editing Mechanism by Prime Editor – No Double-Stranded DNA Breaks



A key feature of Prime Editing is that it is fully programmable, meaning that both (1) the location in the genome and the edit can be chosen specifically, and (2) the location targeted and the edit directed, can both be changed easily, based on simple design rules. By changing the search sequence of a pegRNA, we can quickly and precisely program our Prime Editors to different genomic locations based on their gene sequences. By changing the replace sequence of a pegRNA, we can control which edit is made. Therefore, to make a different correction edit in a new location in the genome, we can readily reprogram the Prime Editor to specifically target a new DNA sequence and to make the precise edit that is required, simply by changing the pegRNA sequence. Most often this will be performed by swapping out one pegRNA and replacing it with another, keeping other parts of the Prime Editor unchanged.

Characteristics of Prime Editing

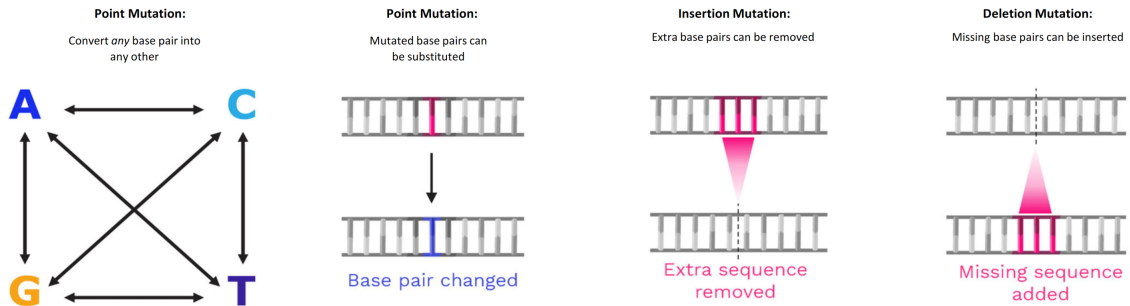
We believe Prime Editing's unique and differentiated mechanism makes it an extremely versatile, precise, efficient and broad gene editing technology. We believe these features, along with its programmable nature, allow

Prime Editors to be rapidly customized for specific diseases, creating a broad array of potential new therapeutic programs.

Versatility

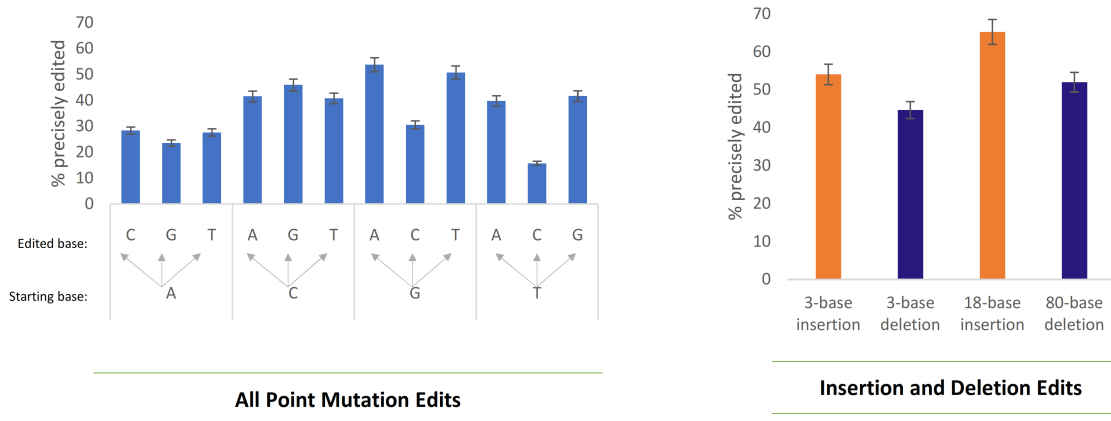
We believe Prime Editing can make diverse sequence edits at nearly any desired location in the human genome, enabling multiple therapeutic applications. Prime Editors are able to change any base pair to any other base pair to correct all twelve types of single base pair point mutations, delete DNA sequences to correct insertion mutations, or insert DNA sequences to correct deletion mutations. We can also make combinations of these types of edits with the same Prime Editor. Notably, Prime Editors also have the ability to make direct corrections of DNA, alter the regulatory regions of genes, insert or create premature stop codons, and modify splicing sequences, differentiating the Prime Editing approach to addressing genetic disease.

Illustration of Versatility of Prime Editors' Ability to Correct All Twelve Potential Base Pair Mutations as well as to Address Sequence Insertions and Deletions



For example, Prime Editing can be used to convert an A to either a C, G or T, to change a C to an A, G or T, to convert a G to an A, C or T, or to change a T to an A, C or G, as shown in the figure below, left. Prime Editing can also make larger insertions or deletions, such as the precise 18-base insertion or 80-base deletion shown in the figure below, right. By combining Prime Editors with proprietary recombinase technology, kilobase amounts of genomic DNA can be inserted, deleted, or inverted. All of these changes can be made with highly efficient and potentially therapeutically relevant levels of precise gene correction, which we believe are generally unachievable by other gene editing approaches.

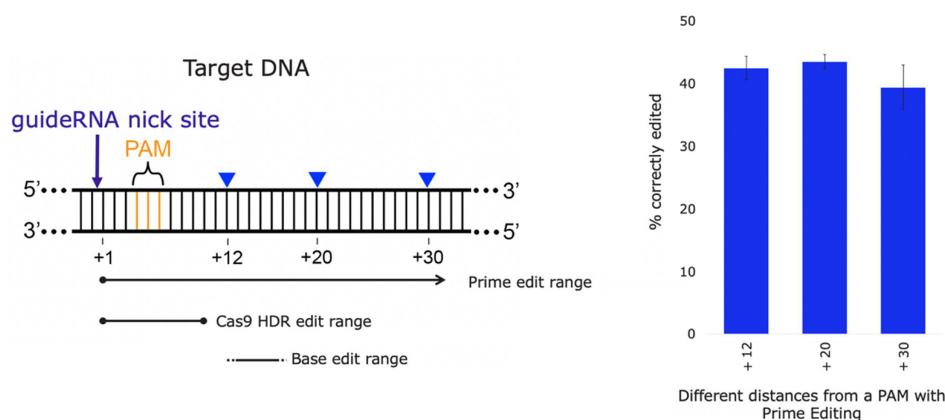
Prime Editors' Have Shown Ability to Address All Twelve Potential Base Pair Mutations (left) as well as Larger Insertions and Deletions (right)



The data displayed represent early demonstrative experiments that established the feasibility of performing each edit type. Prime Editing components were not individually optimized for each edit, and therefore the efficiencies shown are not intended to reflect general or optimal editing efficiencies for the corresponding edit type.

Prime Editing can also target a wide range of mutations throughout the genome that may not be accessible to other technologies. The targeting abilities of Cas proteins, like those used in Prime Editing and other gene editing technologies, to successfully dock onto the target DNA region, requires the presence of an approximately 3-base sequence, known as a PAM, which is adjacent to the target DNA sequence. Other CRISPR gene editing technologies, such as base editing and Cas9-HDR, can generally edit only within a limited sequence window around the location of the PAM. Importantly, Prime Editing is less constrained by PAM availability and can make edits near or far from the PAM sequence. For example, based on *in vitro* experiments, Prime Editing can make gene edits up to about 60 bases and potentially more from the PAM sequence; one supporting *in vitro* experiment is shown below. Because Prime Editing has a larger editing window, the likelihood that a PAM exists in a suitable location nearby a targeted mutation is higher than for other gene editing technologies. The larger Prime Editing window also offers greater flexibility and opportunity for optimization, since there may be multiple PAM options that have Prime Editing windows that cover the location of the targeted mutation. This offers the potential for greater flexibility and optionality for correcting a given target mutation and could broaden the number of mutations that Prime Editing can reach within a gene.

Prime Editing Less Constrained by PAM Availability and Can Correctly Perform Edits Far Removed from PAM Sequence



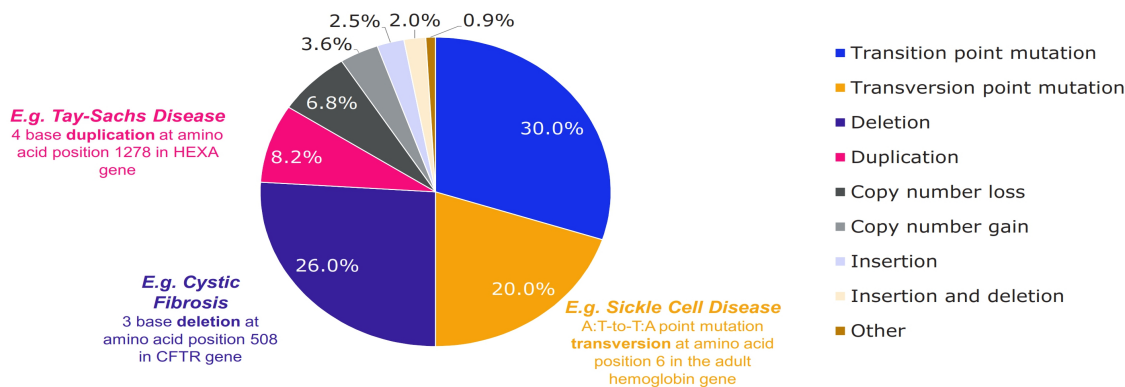
The blue triangles in the left graphic indicate base positions that are within the Prime Editing window, and corresponding examples of Prime Editing at those positions are shown in the bar graph on the right. This experiment was designed to provide initial proof-of-concept of Prime Editing capabilities and was not optimized.

Specifically, we believe that Prime Editing could be extended to additional therapeutic applications, including gene correction, gene modification, gene silencing and activation, multiplex editing, and hotspot editing. While we anticipate pursuing many of these applications as future programs, our current programs do not yet address all of these applications.

Gene Correction: Prime Editing technology has the ability to repair diverse mutations, including all types of point mutations, deletion mutations, insertion and duplication mutations and insertion-deletion mutations. Our analysis of more than 75,000 pathological, or disease-causing, mutations found in the National Center for Biotechnology Information ClinVar Database shows that those addressable by Prime Editing technology account for approximately 90 percent of genetic variants associated with disease. As such, we believe Prime Editing technology has the theoretical potential for repairing approximately 90 percent of known disease-causing mutations across many organisms, organs and cell types. Because biotechnology companies can only initiate therapeutic programs for a subset of pathogenic mutations and the associated diseases, we have chosen to strategically focus on disease settings where we believe that Prime Editing technology could offer compelling advantages over both current standard-of-

care and novel therapeutic modalities in development. Currently, at Prime Medicine, we are leveraging the breadth of our in-licensed Prime Editing technology to focus on our current portfolio of 18 therapeutic programs.

Percentage Distribution of Pathological Genetic Variants Associated with Disease



Gene Modification: We believe that our Prime Editors are also capable of making precise modifications to genes and their controlling elements to mimic natural genetic variations that are known to protect against or modify risk for a disease. For example, the apolipoprotein E4 genotype, or APOE4, is known to confer a higher risk of Alzheimer’s Disease, whereas the “Icelandic” variant of the amyloid precursor protein gene significantly lowers the risk. By converting such variants from the high risk form to the low risk form, we believe Prime Editing could reduce risk of disease in high risk individuals.

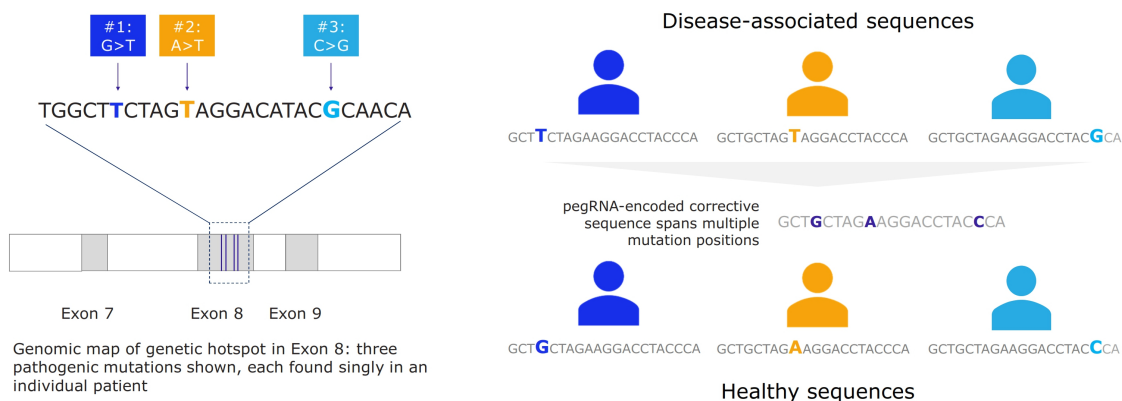
Gene Silencing and Activation: We believe the precision of our Prime Editors is ideally suited for modulation of biochemical pathways that require upregulation, activation, downregulation, or silencing, to prevent or treat disease. Precise editing of regulatory regions of genes at specific bases to achieve the desired effect avoids causing broader disruptions to adjacent regions that may still have important regulatory functions. Our Prime Editors can also be used to silence the expression of genes, without requiring a double-stranded break, either by the conversion of certain short gene sequences, called codons, into STOP codons, by the insertion or deletion of nucleotides that create a STOP codon, or by the disruption of splice donor-acceptor sites.

Multiplex Editing: We believe that our Prime Editors may be particularly advantageous for situations in which multiple sequences in the genome must be simultaneously targeted because they avoid creating double-stranded breaks. The simultaneous creation of multiple double-stranded breaks by nucleases can cause unwanted large-scale genomic rearrangements, such as translocations and deletions. These genomic rearrangements appear to occur more frequently as the number of double-stranded breaks increases. Conversely, Prime Editors do not create double-stranded breaks. The utility of cell therapies is currently limited by the immune recognition of donor cells by the recipient’s immune system. Multiplex editing has the potential to be used to create cell therapies that can evade recipient’s immune system and be given to multiple different individuals. Similarly, xenotransplantation or porcine organs for human disease is currently limited by immune recognition by the recipient’s immune system. We believe that multiplex editing can be used to limit immune detection of porcine organs.

Hotspot Editing: Mutational hotspots are regions within genes where clusters of distinct mutations associated with disease have been found in the human population. By designing the replace sequence of a pegRNA so that it corrects an entire hotspot region, Prime Editing has the potential to correct many mutations within a hotspot using a single pegRNA, making it applicable for correcting multiple distinct but neighboring mutations, each found in different patients. Currently, the replace sequence of a pegRNA is able to target regions approximately 100 bases in length. In the hypothetical graphic shown below, three patients have distinct but neighboring mutations within a gene, representing a hotspot. Each mutation could be corrected by the single pegRNA edit template. By expanding on this approach to target multiple hotspot regions throughout a gene, a larger proportion of mutations could be

addressed by a single Prime Editor, enabling one of our broader goals to treat all patients' mutations in a given disease.

Illustration of How Prime Editors Can Address Hotspots Using a Single pegRNA



Note: G>T = T base pair mutation to be correctly edited to G to return to wild-type sequence; wild-type = normal, non-mutated gene sequence; pegRNA = prime editing guide RNA

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Precision

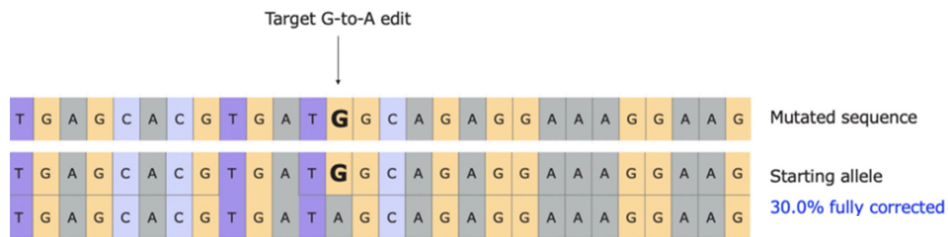
Prime Editing is designed to make only the right edit at the right position within a gene, which greatly minimizes on-target by-products at the site of editing, and results in low, or minimal off-target editing in other places in the genome. Importantly, our Prime Editors do not create double-stranded DNA breaks, which supports the precision of our technology. Prime Editing requires three “edit checks” or places where there must be a match between the editor and the target DNA in order to complete an edit. We believe that these “edit checks” also lead to highly specific and precise edits, as described above for our mechanism.

Precision at the Target Site

Prime Editing is precise in making corrections and edits at the target site in the genome. For example, as shown in the top panel of the graphic below, a specific pegRNA can be designed to edit only the first intended G to an A, and the bases before and after the target G are not edited, even if neighboring G bases are present. In the bottom panel, a different, specific pegRNA can be designed to edit only the second G to an A, again without affecting neighboring bases. With precise editing at the target site, Prime Editing minimizes bystander edits to nearby base sequences. Using the same graphic below, we see that only the intended G is edited, and the nearby G is not edited. This precision contrasts with base editing where it is challenging to selectively edit a single base pair when additional, similar target bases are present in the target window, such as GG in the graphic below, thus leading to bystander edits.

We have demonstrated that, following Prime Editing, more than 99 percent of the time, either a precise edit occurs in a cell or the uncorrected target DNA sequences remain unmodified and fully intact without production of unwanted by-products. Therefore, much of our approach to the optimization of Prime Editing at a target site is focused on increasing the relative percentage of edited cells to unedited, intact cells. We identify that information with “percent precise edits” on our graphs. In addition, we can also readily assess and optimize our choices, by screening and optimizing many pegRNA sequences, to reduce both on-target and off-target edits.

Prime Editing Is Designed to Make the Right Edit While Minimizing Bystander Edits at Neighboring Bases



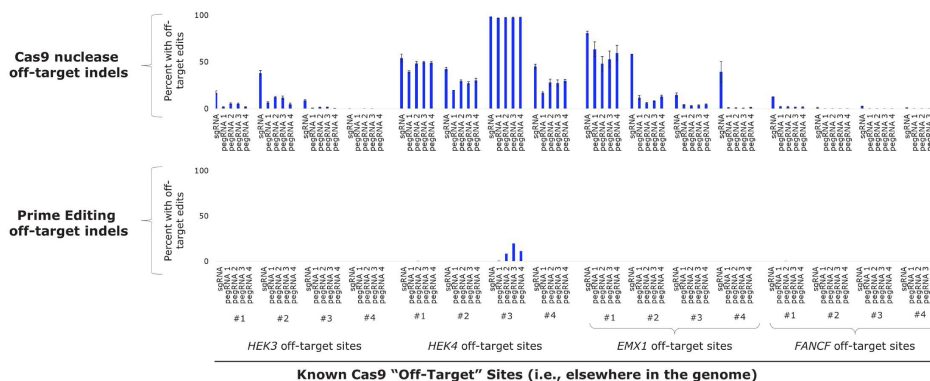
Precision at Off-Target Sites

Prime Editing shows low to no evidence of off-target editing at other locations in the genome. As mentioned above, we believe this is also due to the lack of double-stranded breaks in DNA, as well as our three “edit checks” that are integral parts of our editing mechanism.

An example of the potential for off-target activity is shown in the figure below, which compares Prime Editing to CRISPR-Cas9 editing in a head-to-head comparison. In this figure, the top panel reports percent of off-target editing (from 0 to 100 percent of cells) by CRISPR-Cas9 nuclease editing, and the bottom panel by Prime Editing. The experiment involved four well-known genes that were selected for gene editing (labeled at the bottom of the figure). A single location was edited in each of these genes. For each edit, four different pegRNAs were designed, along with a matched single guide, or sgRNA, for CRISPR-Cas9. CRISPR-Cas9 makes unwanted edits at well-characterized sites elsewhere in the genome, known as “off-target sites.” For each gene that was edited, there are four off-target sites (#1, #2, #3, #4) where off-target gene editing activity was quantified. The sites are well-established sentinel sites, or sites where off-target editing has been demonstrated previously with CRISPR-Cas9 nuclease editing in preclinical studies. The graphic shows the expected, and in some cases quite extensive, resulting off-target edits caused by CRISPR-Cas9. In contrast, the results from Prime Editing using identical conditions generally was very low, minimal or at undetectable levels at all genes and sites. The only exception was off-target site #3 of the HEK4 gene locus, where Prime Editing resulted in some off-target edits. However, as described below, we believe Prime Editing has the ability to optimize guides and other parameters to improve editing. As is shown for pegRNA#1 at the same site and gene, an “optimized” pegRNA was selected with markedly less off target activity.

The actual significance of off-target editing activity is not fully understood, but we believe that the less it occurs, the more likely this will result in a long-term safety advantage to patients. Recent publications have shown that CRISPR-Cas9 editing can be optimized for limited off-target activity, but the ability to do that widely across programs is not clear. We believe that markedly lower levels of off-target activity, along with the greater opportunity to optimize pegRNAs to attain even lower levels, is a major advantage of the Prime Editing technology.

Cas9 Editing Can Result in Significant Off-Target Indels (Top); Prime Editing Has Minimal Off-Target Indels and Use of Different pegRNAs Can Further Mitigate Off-Target Effects (Bottom)

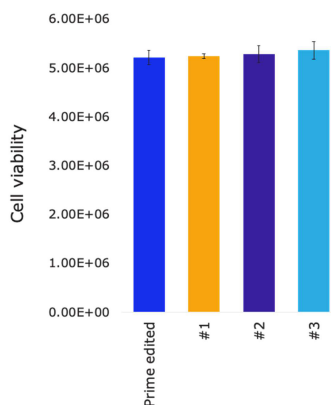


The Importance of Avoiding Double-Stranded DNA Breaks

Unlike first-generation nuclease-based technologies, Prime Editors do not generate double-stranded DNA breaks. Emerging literature supports that double-stranded DNA breaks can result in many disadvantages, including:

- Lack of editing precision at the target site, leading to many indels.
- More likely to cause off-target edits elsewhere in the genome.
- Can lead to large deletions, structural rearrangements, and chromosomal translocations.
- Can activate p53, leading to apoptosis, and may select for somatic cells with p53 inactivation.
- Can reduce cell viability in edited cells.

As shown below in a preclinical experiment, cell viability was observed to be similar with or without Prime Editing, which we believe means that Prime Editing does not affect cell viability.



In this experiment to test cell viability, cells underwent identical procedures with full Prime Editing (left), then with inactive Prime Editing components that prevented Prime Editing correction to occur (#1: inactive reverse transcriptase; #2: inactive Cas9 nuclease; #3 inactive Cas9). The results show similar cell viability in the presence and absence of Prime Editing.

In conclusion, Prime Editing is highly precise and specific, and we believe that these advantageous features of Prime Editing will potentially contribute to better patient outcomes and improved overall safety.

Efficiency

We believe that with a single treatment, Prime Editing could create permanent, positive corrections of disease-causing mutations, resulting in restoration of the gene back to its wild-type healthy sequence. A corrected gene would persist in an edited cell, working naturally and being passed along to daughter cells, resulting in a potentially durable cure or therapeutic outcome. Unlike some other gene editing approaches, Prime Editing occurs in situ, or at the site in a gene where they naturally occur, which preserves a normal number of copies of the gene in the cell, allows for normal physiology, or activity, and gene regulation, normal splice variants and proteins isoforms. All of these benefits have the potential for optimal gene regulation, which we believe could result in long-lasting benefits to patients.

Although Prime Editing is a developing technology and is not yet validated in clinical studies, it has been validated in extensive preclinical testing, both by our company and in over 50 papers published in primary scientific literature to date. Our Prime Editors have demonstrated in preclinical studies the ability to repair mutations with comparable or superior editing efficiency relative to nuclease-based approaches such as Cas9-initiated homology-directed-repair. Continued modifications and optimization aims to further increase the editing efficiency of Prime Editors.

Breadth

Prime Editing is a compelling approach for a wide range of therapeutic applications at the genomic level, and can make precise, targeted edits in an array of cell types, tissues and organs. We believe this breadth in applications and ability to target multiple cell types will enable Prime Editing to bring curative gene editing approaches to a broader set of diseases, beyond genetic disease and towards severe, chronic, and acute diseases.

Further Enhancing the Prime Editing Platform

Over the last two years since Prime Editing was first described, an increase in efficiency as well as an expansion in the scope of applications have been demonstrated and reported in multiple publications and abstracts as well as contributions from our team. The versatile nature of Prime Editing allows for the selection of the right tools for a specific gene edit from up to ten thousand potential choices to optimize for desired effects with high efficiency and precision at the targeted site, while minimizing off-target edits at more distant chromosomal sites.

An important element of our capability is leveraging high-throughput screening and machine learning, coupled with automation of workflow, to build a data-driven model for designing optimized Prime Editing systems that can potentially accelerate our therapeutic candidate development and enhance efficiency. We have also optimized individual subcomponents of our Prime Editors to enhance their capability beyond the first generation of Prime Editors. Some notable developments include engineered pegRNAs and DNA mismatch repair modulation to further enhance efficiency of our Prime Editors where appropriate and expanding the array of gene edits by incorporating recent innovations in Prime Editing, including dual-flap Prime Editing and targeted integration, deletion and inversion of gene-sized DNA.

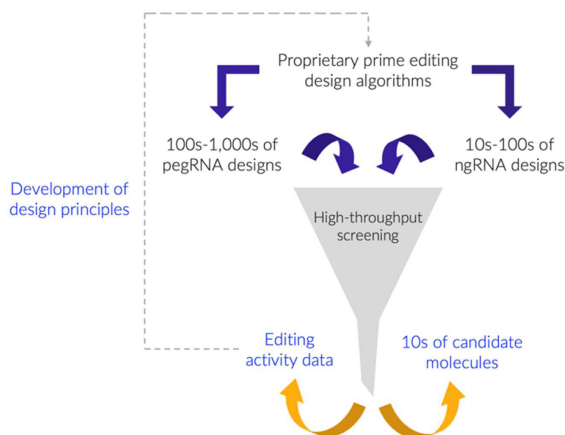
We believe that we have built a leading position in Prime Editing by consolidating technology and intellectual property in the field as well as by establishing extensive internal capabilities to deliver on the promise of this next generation gene editing technology. It is our belief that performing Prime Editing with high efficiency and precision, unlocking its broad applications in different genetic settings, and rapidly progressing towards clinical therapeutics requires great skill, know-how, and knowledge of the intricacies of Prime Editing. We think this expertise differentiates us from the other gene editing platforms, and could allow us to rapidly and efficiently deliver on the promise of Prime Editing.

Enhancements to Improve Efficiency

Automated Screening and Know-How

We are building a high-throughput automated screening engine to rapidly test up to thousands of pegRNAs and hundreds of ngRNAs, for every target edit of interest. Because pegRNA and ngRNA sequences can be chosen from a very large number of possible sequence designs, and since the choice of these designs can meaningfully influence Prime Editing efficiency, identifying the best performing molecules requires both expertise in pegRNA and ngRNA design as well as high-throughput screening capabilities for testing their activities. The figure below depicts the current screening and know-how acquisition engine, which continues to evolve. This process enables identification of optimized Prime Editing systems for a desired target edit, and it provides data that can be used to develop proprietary machine learning algorithms for pegRNA and ngRNA activity prediction, as described below.

We Employ Proprietary High-Throughput Screening and Design Algorithms to Identify Optimal pegRNA and ngRNA Sequences



Machine Learning

PegRNAs contain multiple sequence elements that can be optimized in isolation or together to improve Prime Editing efficiency and specificity. For each target edit, there may be as many as tens of search sequence options, and for each of those, there exist tens to hundreds of possible replace sequences, tens of possible 3' RNA motifs, and tens of additional options for varying other sequence elements. As a result, the combinatorial design space for pegRNAs that target a particular mutation could reach the tens of thousands. One arm of our approach to improving pegRNA design is to assemble our large collection of data derived from our high-throughput screening platform, then use those data to train machine learning algorithms that can accurately predict highly active pegRNA molecules. This allows us to more quickly screen and identify highly active pegRNAs in silico starting from a vast sequence space containing tens of thousands of pegRNA designs. This capability is greatly enhancing our ability to efficiently and rapidly identify pegRNA sequences with the highest activity and specificity.

Other Improvements

We have developed several generalizable proprietary enhancements to our first-generation Prime Editing systems through parallel optimization of our Prime Editor proteins and pegRNAs. By using powerful protein and RNA engineering methods, we are improving the individual subcomponents of our Prime Editors, including the Cas domain, reverse transcriptase domain, and pegRNA constituents.

We believe combining these enhancements and others will enable us to build next-generation Prime Editing that are optimized for efficiency, breadth, precision, and therapeutic delivery. We outline what we believe to be important improvements below.

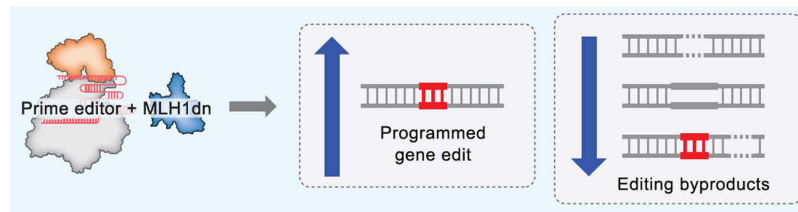
Engineered pegRNAs

Professor David Liu's laboratory at Broad Institute recently developed epegRNAs that can improve Prime Editing efficiency by 3-fold or more in multiple human cell types, an enhancement that is now being incorporated into our research activities. In addition to the elements found in standard pegRNAs, epegRNAs have an extra element called a 3' RNA motif. We believe that 3' RNA motifs stabilize the replace sequence of pegRNA in cells, extending the duration of Prime Editing, and thereby leading to higher editing efficiency. Multiple classes and sequences of 3' RNA motifs can be used in epegRNAs, and therefore represent another lever that we can apply to optimize Prime Editing efficiency. We have exclusively in-licensed and adopted the use of these epegRNAs and are actively developing our own classes of epegRNAs to enhance Prime Editing.

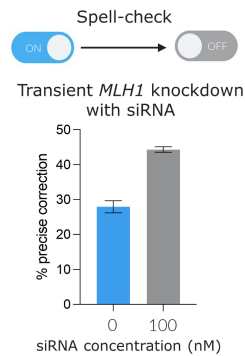
DNA Mismatch Repair Modulation

Recently, it has been shown in *in vitro* experiments that a DNA surveillance system, which is variably active across cells of the body, called mismatch repair pathway, or MMR, can influence Prime Editing outcomes. Transient suppression of MMR, specifically a part of the system called MLH1, in the tissue where Prime Editing is occurring, can moderately boost efficiency, as shown in the figures below. As a result, although many of these approaches require further validation, we are developing approaches to transiently modify MMR so that desired Prime Edits are favored, and any undesired by-products are minimized. We are evaluating several different approaches to modulating the MMR response including active pharmaceutical ingredients, such as siRNA, or small interfering RNA, or other approaches that transiently modulate MMR activity which could be co-administered with a Prime Editor. While inherited mutations in genes encoding the protein factors in the MMR pathway can increase the risk of neoplasms of epithelial tissues including colon and skin appearing in adulthood, we believe short term (days) suppression of MMR is likely to be generally well-tolerated. Safety studies will be required to establish a safety profile of transient MMR suppression.

Suppressing the MMR Pathway, For Example By Inhibiting MLH1, Can Boost Editing Efficiency and Minimize By-Products



Co-Administration of siRNA with our Prime Editors was Observed to Increase Editing Efficiency



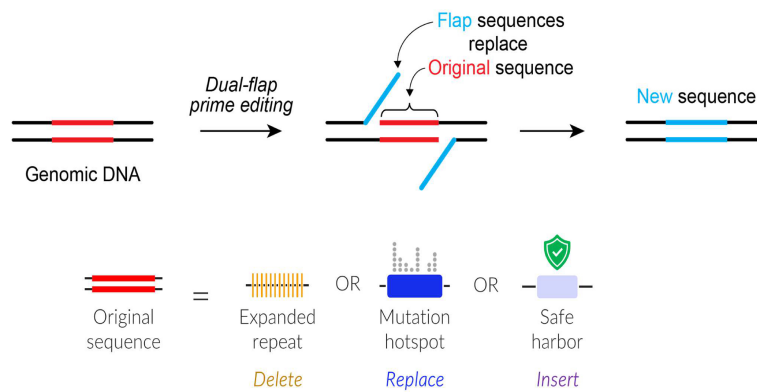
Enhancements to Broaden the Universe of Edits for Prime Editing

Dual-flap Prime Editing

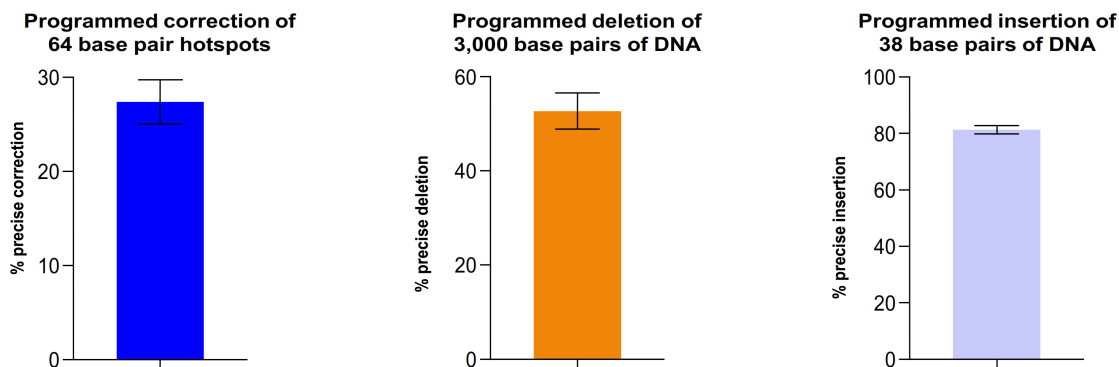
We have in-licensed certain dual-flap Prime Editing technology developed by David Liu’s laboratory at Broad Institute, and expanded and improved on its uses. Compared to traditional Prime Editing, dual-flap Prime Editing uses two Prime Editors instead of one. In different places, each of the Prime Editors creates a nick in the DNA and creates a flap; the two flaps are designed to bind tightly to each other. This results in the looping out of the DNA between the Prime Editors, with replacement of new DNA. Dual-flap Prime Editing is designed to achieve efficient editing of a broader range of edit types, including the precise replacement or insertion of DNA sequences that are a hundred bases or more in length with potentially higher efficiency than standard Prime Editing. In addition, dual-flap Prime Editing can precisely delete up to thousands of bases of DNA, as shown in the data for repeat expansion diseases (see below in Portfolio section). In addition to its high efficiency, it achieves the same level of precision, and we believe it results in minimal off-target editing, as shown in preclinical studies, similar to the more standard forms of Prime Editing.

As illustrated in the figure below, dual-flap Prime Editing could be used to delete expanded repeat sequences like those that occur in repeat expansion diseases, to replace mutation hotspots with corrected sequences, or to insert sequences at safe harbor or other locations in the genome. The figure below depicts examples that use dual-flap Prime Editing to: replace a 64-base mutation hotspot in the gene that causes the metabolic disorder, Phenylketonuria, delete approximately 3,000 bases, or insert 38 bases at a targeted location in the genome.

Dual-Flap Prime Editing Uses Two pegRNAs to Potentially Broaden Applications



Dual-Flap Prime Editing Precisely Corrects a Gene with a Human Mutational Hotspot, Precisely Removes Large Sequence of Pathogenic DNA and Precisely Inserts a 38 Base Pair Sequence into the Human Genome



Note: Error bars represent standard error of N=5 experiments.

Programmable Gene-sized DNA Insertion, Inversion, and Deletion

We are excited about newly developed technology that allows us to expand our gene editing toolbox to include programmable insertion, deletion, or inversion of thousands of bases of DNA. This technology combines the programmability of Prime Editing with another class of genome editing tools called site-specific recombinase enzymes, or SSRs. Although SSRs have long been used as biology research tools to insert large pieces of DNA into the genome, to perform large inversions of DNA, or to make large deletions of DNA, their use in therapeutic applications has been limited by the extremely challenging task of engineering SSRs to be programmable, or to target specific sequences, such as a desired DNA sequence in a gene or genome. While dual-flap can loop out very large pieces of DNA, up to many kilobases in size, currently it can only precisely insert a much smaller number of base pairs of DNA, approximately one hundred base pairs as of today. Therefore, in circumstances where a larger modification is required, this programmable technique is designed to insert or invert multi-kilobase-sized pieces of DNA. In addition, similar to dual-flap, this technique can also delete similarly large pieces of DNA.

Our technology leverages the programmability of Prime Editing to insert recombinase recognition sequences at precisely chosen targeted locations in the genome, as shown in the figure above. Then, an SSR, either fused to the Prime Editor, or transiently delivered as a separate enzyme into target cells, locates the recognition sequence or sequences and carries out DNA recombination at those recognition sequences, resulting in the desired large DNA sequence edit at the desired location in the genome. We believe that such a technology has the potential to precisely insert “gene-sized” pieces of DNA, at a predetermined and specific site in the genome, is a clear differentiator.

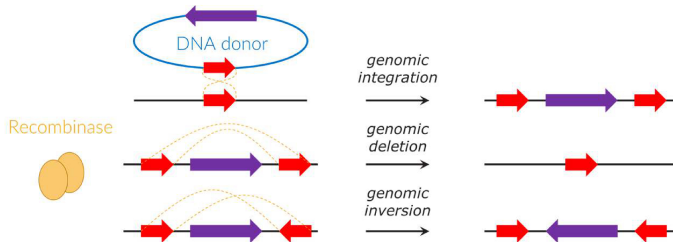
As shown in the figure below, Prime Editing can insert a recombinase recognition sequence at a targeted location in the genome, which can then be used by an SSR to insert DNA that contains a therapeutic gene, potentially such as a chimeric antigen receptor, or CAR. Using multiplex Prime Editing, two recombinase recognition sequences can be inserted so that SSRs can replace, delete, or invert the intervening DNA sequences. Together, these editing capabilities enable therapeutic opportunities to potentially treat genetic variants that are caused by changes to large sequences of DNA sequences, and methods to engineer cell therapies to treat disease.

Combining Site-Specific Recombinase (SSR) Enzymes with Prime Editing Can Effectuate Insertion, Deletion or Inversion of Large DNA Sequences

Step 1: Prime Editing can “write-in” recombinase target sequences at precise locations in the genome

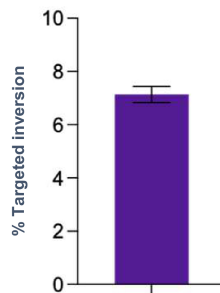


Step 2: Recombinase efficiently inserts, deletes, or inverts **large** pieces of DNA



As shown in the figure below, short recombinase recognition sequences known as attB and attP, used by the site specific recombinase known as Bxb1, were inserted in introns flanking a 40 kilobase inversion mutation in the IDS gene that causes a serious childhood multisystem disorder, called Hunter syndrome. In this early proof-of-concept experiment, delivery of the Bxb1 recombinase to mutated cells resulted in precise correction of the 40 kilobase inversion in 7 percent of cells, with the remainder left unchanged.

40-kilobase inversion in Hunter syndrome¹



This early-stage experiment outlines the potential for programmability and precision

¹ attB and attP recombinase sites were introduced on either side of the inversion by dual-flap Prime Editing, followed by transfection with Bxb1 recombinase, in non-genetically modified human cells.

Multiple enhancements to our Prime Editing platform, including engineered pegRNAs, enhanced Prime Editors, and DNA mismatch repair modulation, provide us with a versatile toolbox for applying Prime Editing to a wide range of diseases. In addition, our focus on high-throughput screening and machine learning are allowing us to grow our internal technical expertise for Prime Editing optimization, and are being used to develop Prime Editors that are both more efficient and more precise. Finally, we are broadening the types of edits that we can make by incorporating recent innovations in Prime Editing, including dual-flap Prime Editing, and programmable insertion, deletion, and inversion of gene-sized DNA sequence.

Translating Prime Editors into Product Candidates

Multi-modality Delivery of Prime Editors

The efficient delivery of our Prime Editors is critical for the development of our therapeutic pipeline indications. The named target indications in our portfolio have been selected to exploit validated delivery methods. We are investing in a broad, multi-modal delivery approach to establish in-house capabilities, tools and partnerships needed to pursue a comprehensive suite of validated delivery modalities, along with evaluation of earlier experimental approaches. On a target-by-target basis, we evaluate the best options for delivery, and select the delivery modality with the most compelling biodistribution for a given tissue type. Our initial, immediate programs rely on three distinct delivery methodologies: (a) electroporation for efficient delivery to blood cells and immune cells *ex vivo*; (b) LNPs for non-viral *in vivo* delivery to the liver and potentially other organs in the future; and (c) AAV for viral delivery *in vivo* to the eye and ear. By leveraging these delivery modalities in parallel, electroporation, non-viral and viral, we believe we will be able to avoid reliance on any one delivery method, mitigate the risks inherent to novel delivery methods, and create optionality by advancing a broad, diversified portfolio.

These delivery approaches will serve as a foundation for us to further optimize to accelerate our work for additional future indications. Nevertheless, we are continuing to evaluate and leverage the many advancements in novel and experimental delivery approaches that are being made in the cell and gene therapy field, and intend to take advantage of complementary collaborations.

Specificity in Prime Editing: On- and-off target unwanted edits

A key element of evaluating safety in gene-editing relates to the specificity of the edits: is the edit precise at the targeted site, and/or are there off-target edits, or unwanted edits, at more distant locations in the genome, that are the result of gene editing? In particular, the ability to demonstrate the absence of low, even minimal, levels of off-target editing is a major differentiator for Prime Editing compared to most other gene editing technologies, and we believe may result in a more benign safety profile for Prime Editing.

A robust and unbiased evaluation of all potential off-target activities is a critical element of our efforts. Our approach to minimizing off-target editing is to start by screening for Prime Editor candidates with very low off-target activity. We then use comprehensive, sensitive, and state-of-the-art methods to identify all putative off-target sites by identifying places where a Prime Editor has a possibility (no matter how small) to nick the DNA. We are developing multiple, complementary, but distinct, methods to measure such possible events. Our approach includes evaluation, among other methods, of: (a) off-target activity in the genome that is specific to the sequence of a particular pegRNA or the ngRNA; (b) similar activity that is independent of the pegRNA or ngRNA sequences; and (c) genomic rearrangements.

To establish a preliminary set of potential off-target sites, we initially evaluate our promising pegRNAs with computer algorithms that identify other sites in the genome with some degree of sequence similarity. In parallel, we identify a comprehensive set of putative sites where the Prime Editor could nick the DNA, as determined by several experiments performed in cell-free conditions with DNA. Combining these sets of sites, we then evaluate each of those locations extensively using sequencing methods to identify the potential for very low frequency off-target edits and perform the evaluation in cells that are relevant to the disease for which the Prime Editor is intended. From these parallel methods, there may be up to thousands of potential sites evaluated for off-target activity for each potential Prime Editor and we are able to quantify the absence or presence of Prime Editing at these sites.

To evaluate off-target effects independent of the pegRNA or ngRNA sequences, we Prime Edit stem cells, and then expand populations of single cell clones, or cells that are genetically identical. From this large pool, we have the ability to evaluate very low frequency events, such as rare off-target edits, using unbiased methods. Each clone undergoes whole genome sequencing and is compared to appropriate controls, which allows evaluation of locations that are not predicted from the pegRNA sequence or genomic location.

Using this same type of approach, we also are employing a combination of methods to look for genomic rearrangements, including targeted or random rearrangements, using whole genome sequencing of clonally expanded Prime Edited stem cells.

Manufacturing Prime Editor Product Candidates

Due to the breadth of potential therapeutic indications that can be served by Prime Editing, we are developing broad manufacturing capabilities and know-how needed to support the rapid advancement of parallel programs into clinical studies. We are investing in building a strong technical development and operations team with diverse experience to develop the manufacturing technologies and process and analytical controls needed to produce the Prime Editor drug product using different delivery modalities. We are leveraging our manufacturing team's extensive late-stage and commercialization experiences in collaboration with our research organization to establish clinical-phase appropriate manufacturing processes and controls with line of sight to our commercialization needs. By developing deep process and product knowledge to support regulatory comparability strategies, we intend to incorporate new manufacturing technologies as they emerge to improve scalability and reliability of the manufacturing process, product quality and cost of goods. We will also use innovative strategies for chemistry, manufacturing and controls, or CMC, automation/machine learning and quality strategies that will be important for achieving product regulatory approvals and commercialization.

The Prime Editor complex is comprised of two main components: i) the Prime Editing protein domain (the Cas nuclease and fused reverse transcriptase), and ii) the pegRNA and, as needed, the ngRNA. The Prime Editor protein domain is generated either from recombinant DNA technology, or can be expressed *in vivo* from mRNA which is made via *in vitro* transcription, or IVT. The guide RNAs are synthetically produced, for example, by solid phase RNA synthesis. For our initial named indications, the Prime Editor complex will initially be delivered to cells via either electroporation (*ex vivo*), LNPs or AAV. We are also assessing additional methods of delivery and those future delivery methodologies may play a greater role in our therapy candidates over the longer-term.

The foundational technologies needed to synthesize, formulate and deliver our Prime Editors are similar to those that are being used for development of nuclease-based gene editing therapeutic products. This allows us to leverage the significant advances and progress that have and are continuing to be made in the field of manufacturing sciences and analytical controls of genetic medicines and therapies, while focusing specifically on the application and optimization of those technologies for Prime Editing. In addition, our collaboration with Beam allows us access to specified know-how, methods and intellectual property in certain fields that we believe will be useful to these activities.

Our overall aim is to design manufacturing platforms to make the Prime Editor product components and associated delivery system with high throughput, high component purity and quality, modularity and scalability. Manufacturing platforms will provide the framework for rapidly developing Prime Editors for subsequent new target indications. Modularity refers to a collection of components which can be rapidly recombined for the construction of a new product candidate. For example, we believe that once a Prime Editor is established, a new drug product candidate will only require the relevant Prime Editing guide and nick guides (or encoded) to be replaced. Similarly, we believe that the Prime Editing guide and nick guides will be able to be produced with modularity.

We are building core capabilities in process and product characterization that we believe will differentiate us from existing genetic medicines. We intend to collaborate seamlessly with various strategic partners to utilize their technologies, capabilities and expertise. We intend to establish strategic partnerships with contract manufacturing organizations with established Good Manufacturing Practice, or GMP, manufacturing capabilities and relevant manufacturing experience in genetic medicines, and where we will bring our Prime Editing process and product knowledge and technical expertise. Over the longer term, we may decide to build our own manufacturing facilities, especially for critical Prime Editing components where we may decide to leverage our core capabilities in process and product characterization.

Our Portfolio

We believe that Prime Editing has transformative potential that could change the course of how disease is treated. To maximize the potential of Prime Editing to provide one-time curative therapies to the broadest set of

diseases possible, we have purposefully built a diversified portfolio organized around four strategic indication categories, each set of indications chosen to deliver a different strategic goal. We have constructed our portfolio of 18 programs, including one partnered program, across our strategic indication categories in disease settings where the unique characteristics of Prime Editing could offer compelling advantages over current standard-of-care and novel therapeutic modalities in development.

Our Four Strategic Indication Categories

1. Immediate Target Indications

Our immediate target indications were chosen as potentially the fastest, most direct paths to demonstrate technological success of Prime Editing in humans. We prioritized and advanced programs in this strategic category based on a number of criteria including high unmet medical need where the underlying genetic pathogenesis, or cause of the disease, is well-understood, and where there were well-characterized delivery methods targeting specific organs or tissues. We also considered the availability of strong clinical and preclinical biomarkers, well-established animal models, a readily accessible patient population, and the regulatory path. In most cases, the correction of the target gene is initially focused on a predominant mutation or set of mutations, and we intend to expand to additional mutations within each indication. We also intend on moving quickly into similar follow-on programs in each target organ as we achieve therapeutic success.

For our initial immediate target indications, we have focused on diseases of the blood via *ex vivo* delivery to hematopoietic stem cells, the liver and the eye. We have initiated six preclinical programs across these organs/tissues, in addition to one program partnered with Beam and other programs in earlier stages of development. In addition, we have initiated two preclinical programs for undisclosed indications in the ear. We believe each of these programs has the potential to deliver rapid preclinical and clinical proof-of-concept for Prime Editing in patients.

2. Differentiation Target Indications

Our differentiation target indications are focused on areas where Prime Editing can potentially overcome limitations of other gene therapies and editing approaches, with the ability to do precise and much more diverse, targeted edits, in a broader array of organs, tissues and types of cells. We also focus on areas where our technology has a special impact on a category of genetic diseases, such as the ability to loop out unwanted repeat sequences. While several potential indications in this category also rely on validated delivery methods, some of our longer-term targets may require novel delivery development.

Programs in this category include:

- repeat expansion diseases, most of which are CNS diseases, or neuro-muscular diseases with pathological, or disease-causing expanded numbers of DNA repeat sequences. These diseases are particularly tailored for Prime Editing approaches, in that Prime Editing can loop out large numbers of unwanted repeats, so pathologic repeats of different lengths can, in principle, be contracted to a single, healthy repeat sequence
- diseases characterized by mutational hotspots
- diseases caused by mutations in extremely large genes, which we refer to as “big gene” diseases
- diseases in difficult to edit cell types
- multiplex editing without the introduction of double-stranded breaks
- edits to regulatory sequences modulating physiological pathways
- diseases requiring precise physiologic control, where too much or too little activity would be a concern
- extremely high-fidelity locations

We have initiated four preclinical programs for repeat expansion diseases, including Friedreich's Ataxia, Myotonic Dystrophy type 1, Amyotrophic Lateral Sclerosis and Fuch's Endothelial Corneal Dystrophy. In addition we have programs in three undisclosed repeat expansion disease indications, and two additional undisclosed differentiation target indication programs in earlier stages of development. We believe these programs have the potential to address difficult and complex diseases of great unmet medical need, which are often not accessible to other forms of gene editing approaches.

3. "Blue Sky" Target Indications

Our "blue sky" target indications category pushes new and innovative technological developments in Prime Editing to extend its application outside of rare genetic diseases and towards our goal of broadly addressing human disease. We have already conducted a process of enhancements, some of which are being implemented in potential new programs, and we are committed to continue to push the frontier of innovation in genomic medicines by optimizing and expanding our Prime Editing technology and capabilities further. We believe these advancements to our technology should allow us to proceed more rapidly into opportunities beyond rare genetic diseases, including:

- transforming chronic therapies into a single-dose, one-time permanent therapeutic correction
- preventing serious diseases by targeting the causes before the onset
- treating the genetic basis of common diseases
- inserting or replacing whole exons or genes
- treating infectious diseases
- treating cancers by correcting underlying germline or other mutations or by broadening the reach of immunological approaches to cancers
- using multiplex editing to treat immunological diseases
- treating diseases that require insertion, replacement or inversion of large sequences, enabling novel cell therapies
- enabling other important technologies such as xenotransplantation

While these programs remain in the early stages of conception, we expect this category to become an increasing focus for our company over the next few years.

4. "March Up the Chromosome" Approaches

As part of our commitment to patients, we envision a truly personalized medicine approach in which we can treat every individual patient with a given disease by "marching up a chromosome," correcting each individual mutation in a gene. Because Prime Editing can search and replace, by simply swapping out the pegRNA while keeping other elements of a program the same, such as clinical trial design and manufacturing, we believe we will be able to march from mutation to mutation, or from hotspot to hotspot, along a single gene, and eventually treat every individual patient with a specific disease, not just the few with the most prevalent mutations.

This effort will require a multi-year, multi-step strategic approach to identify a limited set of data to support registration across the set of mutations within a gene. This category can overlap with other strategic indication categories, where we are designing each of our previously-described strategic indications with this approach in mind. As such, most of our disclosed indications have a plan that can accommodate expansion opportunities to address additional mutations in that disease.

Our Pipeline

Our current portfolio is focused primarily on the first two strategic indication categories, and includes the following 18 programs, including the Sickle Cell Disease program which is partnered with Beam.

STRATEGIC CATEGORY	TARGET TISSUE	INDICATION	DELIVERY	DISCOVERY	IND-ENABLING	Phase 1	Phase 2	Phase 3	PARTNER
IMMEDIATE	BLOOD	Sickle Cell Disease	<i>ex vivo</i>						
		Chronic Granulomatous Disease	<i>ex vivo</i>						
		Fanconi Anemia	<i>ex vivo</i>						
	LIVER	Wilson's Disease	LNP						
		Glycogen Storage Disease 1b	LNP						
	EYE	Retinitis Pigmentosa/Rhodopsin	AAV						
		Retinitis Pigmentosa/Usher Syndrome	AAV						
	EAR	Usher's Syndrome Type 3	AAV						
Non-Syndromic Hearing Loss – GJB2		AAV							
DIFFERENTIATION: REPEAT EXPANSION DISEASES	NEURO-MUSCULAR	Friedreich's Ataxia	viral/non-viral						
		Myotonic Dystrophy Type 1	viral/non-viral						
		Amyotrophic Lateral Sclerosis	viral/non-viral						
		Oculopharyngeal Muscular Dystrophy	LNP						
		Fragile X Syndrome	viral/non-viral						
	Huntington's Disease								
EYE	Fuchs' Endothelial Corneal Dystrophy	viral/non-viral							
DIFFERENTIATION: OTHER	MUSCLE	Duchenne Muscular Dystrophy	AAV						
	LUNG	Cystic Fibrosis	LNP						

• AAV = adeno-associated viral vectors; LNP = lipid nanoparticles

Prime Milestones

We have not completed any *in vivo* studies to date. We expect to achieve preclinical proof-of-concept *in vivo*, which would include data from *in vivo* rodent studies in several programs in [redacted] and non-human primate studies in several programs in [redacted] through [redacted]. If successful, this will allow us to initiate investigational new drug, or IND, enabling studies for several of our lead programs beginning in [redacted], leading to initial IND submissions beginning in [redacted]. Since we are in early stages of product candidate development, we will provide an update on our timelines in [redacted], with the potential to accelerate these programs. We also anticipate continuing to name additional programs as they advance over the next few years.

In the near-term, we plan to define the early-stage manufacturing processes and controls to produce representative drug product using our multi-modal delivery approaches consisting of electroporation for our *ex vivo* programs, LNP, as well as AAV. Key steps in our company growth include announcing shortly our permanent site in Cambridge that will enable us to grow beyond 200 people, anticipated in [redacted]. We are also investing in a dedicated chemistry facility for medicinal chemistry, process development, and analytical chemistry groups, including a non-GMP piloting lab for making guide RNA, mRNA and synthesizing lipids to support our research activities.

Immediate Target Indications

OUR BLOOD PROGRAMS

Chronic Granulomatous Disease – Our program using *ex vivo* electroporation of hematopoietic stem cells

The Disease

Chronic granulomatous disease, or CGD, is a rare inherited hematologic disorder that results in a failure of immune defense against extracellular pathogens. In CGD patients, myeloid cells lack a functional NADPH oxidase, or NOX2, complex, which renders patients susceptible to prolonged and recurrent bacterial and fungal infections and inflammatory complications. NOX2 is only produced by certain types of bone marrow-derived myeloid cells. CGD causative mutations occur in approximately one in 200,000 births in the United States, and most children are

diagnosed within the first three years of life. Approximately 60 percent of patients with CGD reach age 30 and Aspergillus infection is the leading cause of mortality.

The NOX2 protein complex has five domains encoded by five separate genes. Loss-of-function mutations in any of these genes can present as CGD. The most common form, which represents approximately 65 percent of cases, is caused by mutations in the CYBB gene encoding the gp91^{phox} protein. We have identified hotspots in exons 7 and 9 that are amenable to Prime Editing. The second most common form, which represents approximately 25 percent of cases, is caused by biallelic loss-of-function mutations, in both copies of the *NCF1* gene encoding the p47^{phox} protein. More than 78 percent of p47^{phox} CGD patients have a specific, 2-nucleotide deletion, or Δ GT, in the *NCF1* gene. The *NCF1* gene location is complex, and also contains pseudogenes, or non-functioning copies of the *NCF1* gene. Preclinical studies have demonstrated that correcting just one copy of the Δ GT mutation restores protein expression and full NOX2 activity.

Limitations of Current Approaches

For individuals with an HLA-matched donor, an allogeneic CD34+ hematopoietic stem cell transplant, or HSCT, may provide a possible cure, but the three-year event-free survival rate for patients that receive HSCT may be as low as 70 percent and patients often experience many frequent, debilitating complications, such as graft versus host disease. Many patients are not able to find a suitable donor for the hematopoietic stem cells and, without transplantation, 50 percent of patients will die by the fourth decade of life. Antibiotics also provide important supportive care.

Our Approach and Results: Direct correction of prevalent CGD mutations or hotspots

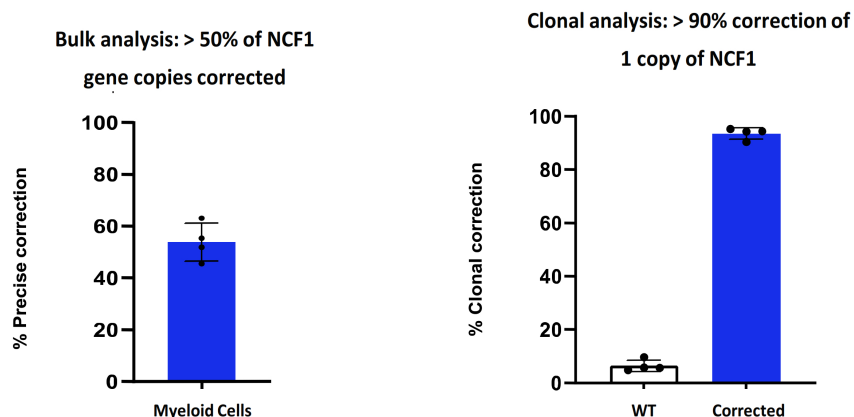
We are using Prime Editing in *in vitro* studies to precisely correct the Δ GT mutation in one copy of the *NCF1* gene to restore p47^{phox} protein expression and NOX2 activity. Our approach is to mobilize a patient's CD34+ cells into the blood stream followed by apheresis, and separation of these cells by *ex vivo* enrichment. Prime Editing components will then be delivered to these CD34+ cells *ex vivo* via electroporation. These Prime Edited cells are cryopreserved, quality control tested, and the thawed cells are injected intravenously back to the patient for engraftment. A critical element of assessing this approach is the presence of long-term engraftment, which is discussed below under Sickle Cell Disease. Using the programmable features of our Prime Editing technology and ability to address hotspots, our plan is to expand our targets to include key mutations of the more common CYBB gene.

We have screened pegRNA and ngRNA to identify Prime Editing guides and guide pairs that have high activity and perform precise editing at the *NCF1* locus. Initial experiments have utilized healthy donor mobilized CD34+ hematopoietic stem cells, or HSCs, which are readily available, and we measure precise editing of Δ GT as a surrogate for editing in patient CD34+ HSCs. We have performed a series of optimizations to tailor activity for editing at this locus, and several different, high activity Prime Editor proteins remain under evaluation.

The Prime Editor complex is delivered to CD34+ HSCs using electroporation by an established method. The Prime Editor mRNA is generated by *in vitro* transcription, and the pegRNA and ngRNA are generated by solid phase RNA synthesis. The Prime Editor complex is delivered by simultaneously electroporating mRNA encoding the Prime Editor protein along with pegRNA and ngRNA. The mRNA is translated into the Prime Editor protein during a period of incubation, then the Prime Editor protein assembles with pegRNA or ngRNA, and the complex enters the nucleus with Prime Editing commencing at the target site in the genome.

We have identified a series of Prime Editor complexes that demonstrate approximately 55 percent precise correction at the NCF gene in the target cells, or human primary HSCs, as shown in the figure on the left side. Following cloning of myeloid-differentiated clones after 14 days, clonal analysis showed that nearly 90 percent of clones had received at least one precise corrective edit to Δ GT, as shown in the figure on the right side below. This

greatly exceeds the approximately 15 percent precise editing target threshold that is predicted to provide a clinical benefit.



Note that each data point represents the result from a different, individual Prime Editor, with the average percent precise correction of cells shown in the bar graph.

We have also demonstrated in a different model system of Prime Editing to correct the Δ GT mutation in NCF1 in patient-derived lymphocytes, that the level of precise editing of NCF1 results in at least an equivalent level of restoration of the missing p47phox protein, which supports that the genetic correction of the gene has the desired effect of restoring production of the missing protein.

Next Steps

We intend to demonstrate that we have restored NOX2 protein function in patient-derived myeloid cells as a result of Prime Editing. We will also begin *in vivo* engraftment experiments in rodent models, as already demonstrated in Sickle Cell Disease, as described in the section that follows. We will also evaluate alternative approaches to delivery, and we will begin developing Prime Editors targeted to CYBB mutational hotspots.

Sickle Cell Disease (partnered with Beam)

We are partnering with Beam on the preclinical efforts related to the Prime-Edited Sickle Cell Disease, a program which they have licensed from us. Some of the results from these efforts provide important proof-of-concept for key aspects of our Prime Editing technology, which is the focus of the description below.

The Disease

Sickle cell disease, or SCD, is a serious inherited autosomal recessive blood disorder caused by a single point mutation in the beta globin gene HBB at the sixth amino acid. The mutant protein is also known as hemoglobin S, or HbS. The mutation causes the beta globin protein to aggregate in long rigid biomolecules that bend red blood cells into a sickle shape when oxygen concentrations are low. The sickled red blood cells obstruct small blood vessels and have a shortened life span. This results in anemia, severe pain crises, tissue infarctions, local and systemic infections, stroke, and premature death. SCD is the most common inherited blood disorder in the United States affecting approximately 100,000 individuals. Current therapeutics are very limited.

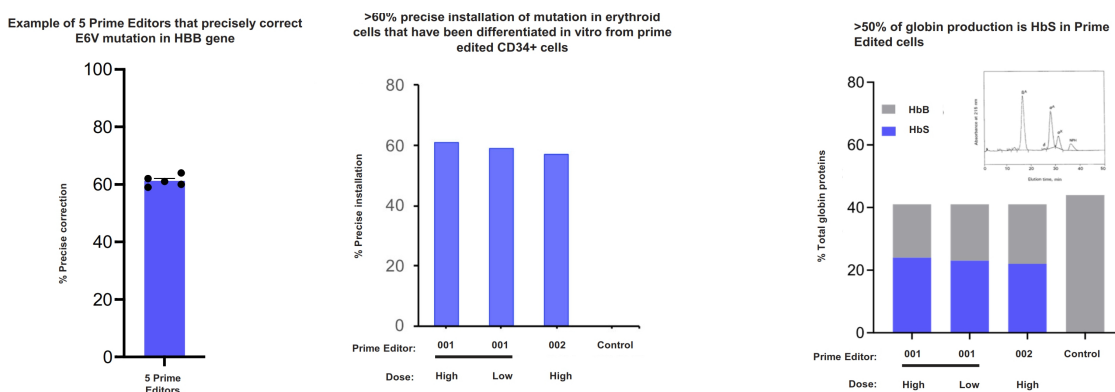
The Prime Editing Approach and Results: Direct correction of the actual disease-causing point mutation in Sickle Cell Disease

We and our partner, Beam, which has conducted all studies described in this section, are using Prime Editing in *in vitro* studies to precisely correct the disease-causing HbS mutation back to the normal genomic sequence, resulting in wild type hemoglobin. The approach is similar to that described above for CGD. Published studies

suggest that a 20 percent correction may be sufficient to cure the disease. Prime Editing is differentiated from other genetic approaches in that it can precisely correct the HbS mutation, restoring normal hemoglobin and directly addressing the underlying cause of SCD, without causing double-stranded breaks. Double-stranded breaks may result in detrimental insertions or deletions of sequence at this gene location. In addition, correction of the HBB gene at its natural site leads to permanent, physiological production of normal hemoglobin directly.

To achieve proof-of-concept and demonstrate precision editing and safety in primary HSCs, we have screened pegRNAs and ngRNAs to identify guides and guide pairs that have high activity and perform precise editing at the HBB locus. To move rapidly, we have created an SCD model using readily available healthy donor mobilized CD34+ HSCs to install the HBB E6V mutation, thereby creating the SCD mutation and phenotype and acting as a surrogate for Prime Editing at that unique location in the gene. As noted in the below, these Prime Editors have demonstrated approximately 60 percent precise edits at the HBB locus (left), and when differentiated into red blood cells, under various conditions, they retain the approximately 60 percent editing (middle), and contain more than 50 percent of hemoglobin as HbS, showing we have created the phenotype of SCD.

Active Prime Editors That Correct E6V HBB Mutation Identified. Prime Editing to Install the E6V Mutation in Erythroid Cells Resulted in HbS Production

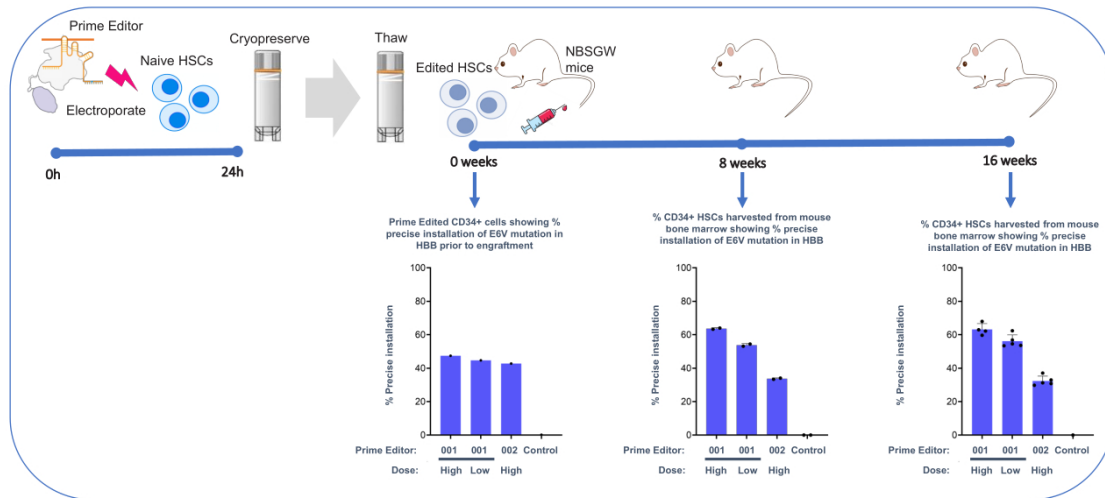


Note: 001 and 002 represent the two Prime Editors that were screened and install the E6V mutation.

Importantly, the Prime-Edited SCD program demonstrated long-term and high-level engraftment of the edited HSCs in bone marrow. The figure below outlines an experiment in rodents that represents the approach planned for humans:

- In this experiment, HSC cells are Prime Edited via *ex vivo* electroporation to introduce the disease-causing sickle mutation, and then cryopreserved.
- After thawing, the edited cells are introduced back in mice, and allowed to engraft in the bone marrow.
- The proportion of precisely edited cells is evaluated at the beginning of the experiment, after eight weeks, and then again after 16 weeks, looking for evidence that edited cells have long-term durability.

Ex Vivo Prime Editing of Mobilized Peripheral Blood Human CD34+ Cells to Install the E6V HBB Resulted in Long Term (16 Week) Engraftment of Precisely Edited Hematopoietic Stem Cells In Vivo



Note: In this experiment, each data point represents the results from a single mouse. 001 and 002 represent the two Prime Editors that were screened.

As shown in the figure, edited cells were shown to have long term duration with no decrease in the percent of precisely edited cells. This is a critical proof-of-concept that Prime Edited HSC cells successfully engraft, and once engrafted, permanently populate the bone marrow. We believe these results greatly increase the probability of success of any HSC-based Prime Editing clinical indication, such as CGD described above.

Fanconi Anemia: Another indication using *ex vivo* electroporation of HSC cells

The Disease

Fanconi anemia, or FA, is a rare and life-threatening DNA repair disorder that arises from loss-of-function mutations in any of 23 genes whose protein products are involved in the Fanconi Anemia/Breast Cancer DNA repair pathway. The FA core complex comprises 10 individual proteins. Almost all cases of FA result from inactivation of FA genes on both chromosomes. The protein products of FA genes form the Fanconi complex, which responds to and repairs DNA breaks that occur naturally during cellular replication or in response to radiation or DNA crosslinking agents. Clinical presentation includes congenital anomalies, loss of many types of blood cells and progressive bone marrow failure, as well as a predisposition to cancers such as leukemia and head and neck cancers. The majority of FA patients show serious disease within the first decade of life.

Limitations of Current Approaches

Allogeneic hematopoietic stem cell transplant, or allo-HSCT, is currently considered the standard of care for FA and can result in hematologic correction of the disorder. However, HSCT is associated with both acute and long-term risks, including transplant-related mortality, graft versus host disease as well as increased risk of subsequent cancers. Additionally, the sensitivity of FA patient cells to DNA damage complicates allo-HSCT because of the reliance on alkylating agents and radiation for pre-transplant conditioning. Median survival for all FA patients, despite standard of care, is 24 years.

Our Approach and Results

Inherited pathogenic variants in FANCA, FANCC or FANCG genes, all members of the FA core complex, account for approximately 90 percent of FA cases. Among these, mutations in FANCA account for more than 60

percent of patients, FANCC for 15 percent of patients and FANCG for 10 percent of patients. We are initially focusing on the two predominant FANCC mutations and our initial approach is to design Prime Editors to correct each predominant FANCC mutation independently. We are targeting 50 percent correction as heterozygotes have no disease, but evidence suggests moderately lower rates of correction have the potential to be therapeutic due to a survival advantage of corrected cells. Unlike most *ex vivo* HSC indications, there is strong clinical evidence that engraftment of HSC can occur without the need for strong bone marrow conditioning.

Our preliminary screening process has identified Prime Editors that achieve approximately 40 percent precise editing in preclinical studies.

Next Steps

Our initial Prime Editors have not yet been optimized for FA, nor have they been tested with enhancements such as ngRNAs. We intend to continue to optimize these Prime Editors to improve the efficiency of the edits. In addition, Prime Editors targeted at the second predominant mutation within the FANCC gene are currently under evaluation. Ultimately, we intend to develop Prime Editors to address all known mutations in FA across the three genes.

Expansion Opportunities in Hematology Pipeline

We plan to add additional hematology-related indications to our pipeline. In addition to establishing the indications above, the experience and methods developed with Prime Editing should enable our ability to advance other hematology programs. This highlights the versatility and modularity of our platform that potentially enables the rapid creation of new product candidates by merely replacing the pegRNA and ngRNA components.

OUR LIVER PROGRAMS

Wilson's Disease: Our lead Prime Editing liver program using LNP delivery technology

The Disease

Wilson's disease, or WD, is a devastating rare disease of the liver, with manifestations throughout the body, that is caused by copper accumulation. Most people are diagnosed with WD between ages five and 35 years and with reported prevalence rates ranging between 1/10000 and 1/30000, it is expected to affect upwards of 35,000 to 100,000 patients in the United States and Europe. It is also understood that there may be significant under-diagnosis of WD, which could increase the prevalence substantially.

Normally, excessive copper is excreted through the liver as bile. For patients with WD, copper is not eliminated correctly and accumulates to toxic levels. While the key site of pathology is the liver, and many patients present with liver disease, patients often show persistent neurological problems including involuntary movements, tremor, gait disturbance, and kidney, hematological or psychiatric problems.

WD is caused by mutations in both genomic copies of the ATP7B gene, which encodes a copper transporter that removes excess copper. Two predominant mutations have been described in WD:

- (1) H1069Q, found in approximately 40 percent of all patients in the United States and 18 to 72 percent in Europe; and
- (2) R778L, frequently found in Asian patients and those of Asian ancestry, reported in 46 percent of Chinese, 38 percent of Korean, and 25 percent of Japanese WD patients.

Both of these mutations lie adjacent to hotspots or areas with other pathogenic mutations, for which we are currently designing Prime Editors.

Genotyping of ATP7B is not routinely performed during diagnosis and is used to confirm the symptomatic diagnosis when necessary.

Limitations of Current Approaches

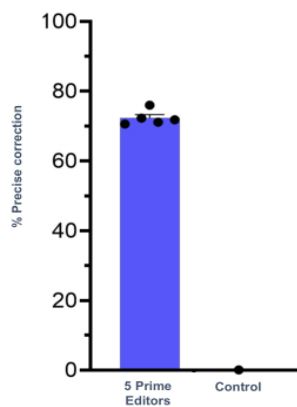
There are no therapies that target the underlying cause of WD. Current therapy includes removal of copper from the body using copper chelators d-penicillamine and Trientine and prevention of dietary absorption of copper in the intestine using zinc. In five to 10 percent of the patients that present with severe or sudden onset, or fulminant, WD, liver transplantation is the primary treatment option. The disease is fatal if undiagnosed and/or untreated. Most patients improve on chelator therapies; nevertheless, a lack of compliance is associated with rapid progression to death, and treatments can include significant and intolerable side effects. Patients are eligible for liver transplant if they have fulminant liver failure or severe progressive liver cirrhosis. Successful transplant has a good response with many patients but requires life-long immunosuppression, and five-year patient survival after transplant has been reported to be 65 percent.

Our Approach and Results: Direct correction of prevalent ATP7B mutations

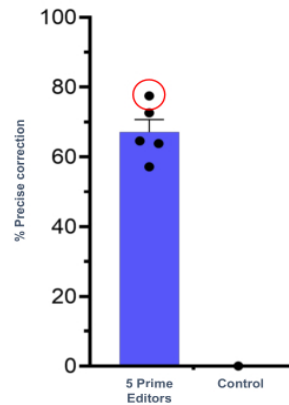
Our initial approach to Wilson's disease is to correct the prevalent mutations ATP7B H1069Q and R778L in hepatocytes of the liver at their genomic location. A Prime Editor that corrects R778L will also correct R778W and R778G mutations, rarer mutations that are seen in the U.S. and Europe. We have performed pegRNA and ngRNA screens and identified guide combinations that correct the disease-causing point mutations. Correction of the gene in the liver should address all aspects of the disease by normalizing the process in which the body removes copper in the liver.

In a hepatocyte cell line with the human Wilson's disease mutation, we have identified Prime Editors that demonstrate precise correction of H1069Q ATP7B in 77 percent of cells as shown in the figure below on the left. We have observed similar results in primary human hepatocytes with the R778L mutation, which is shown in the figure below on the right.

Example of 5 Prime Editors that precisely correct H1069Q mutation in ATP7B gene



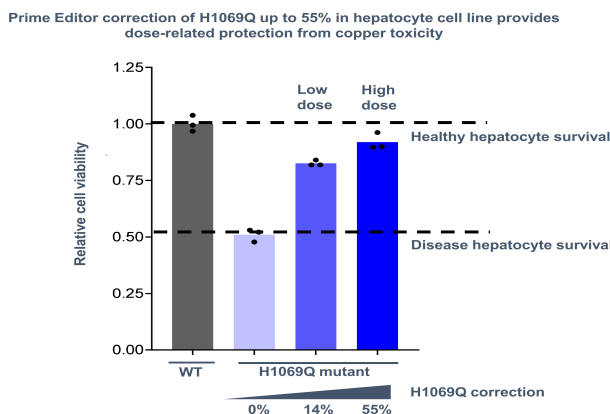
Example of 5 Prime Editors that precisely correct at the R778L locus in ATP7B gene



Note that each data point represents the result from a different, individual Prime Editor, with the average percent precise correction of cells shown in the bar graph and the red circle highlights the best performing Prime Editor from the 5 demonstrated.

This high level of precise editing in primary hepatocytes meets our threshold of 25-50 percent for predicted clinically relevant effects. To support this, we performed a copper toxicity challenge in liver cells that are normal and liver cells with a pathogenic H1069Q mutation with varying degrees of precise editing correction. As shown in the figure below, we observed a marked difference in cell survival in the presence of high levels of copper between healthy cells (WT; left bar) and liver cells with a pathogenic mutation that are unedited (0 percent; 2nd bar). The third and fourth bars show that with different degrees of precise correction, such as 14 percent and 55 percent, the

ability of Prime Edited cells to survive copper toxicity returns towards normal levels the greater the level of correction.



Next Steps

We are currently conducting preclinical studies to confirm the ability to correct the human R778L sequence and the human H1069Q sequence in mouse models, using LNP technology. We are also currently optimizing LNP formulations for validation of Prime Editing experiments in non-human primates.

Glycogen Storage Disease 1b: Another Prime Edited liver indication using LNP delivery technology.

The Disease

Glycogen Storage Disease 1b, or GSD1b, is a rare, serious progressive disease affecting approximately 1,500 patients and caused by impaired glycogen metabolism. This autosomal recessive disease is caused by mutations in the glucose-6-phosphate transporter, G6PT also known as SLC37A4. Deficiencies in this transporter result in hypoglycemia or low blood glucose levels which can be fatal if patients do not adhere to a strict regimen of slow-release glucose including overnight feeding. Most patients experience symptoms within the first six months of life presenting with hypoglycemia, lactic acidosis or with a large liver. They also can manifest seizures and low white blood cell levels, resulting in recurrent bacterial infections and oral and intestinal mucosa ulceration. Many patients have liver tumors, which can progress to liver carcinoma. Multiple other serious manifestations can occur.

Limitations of Current Approaches

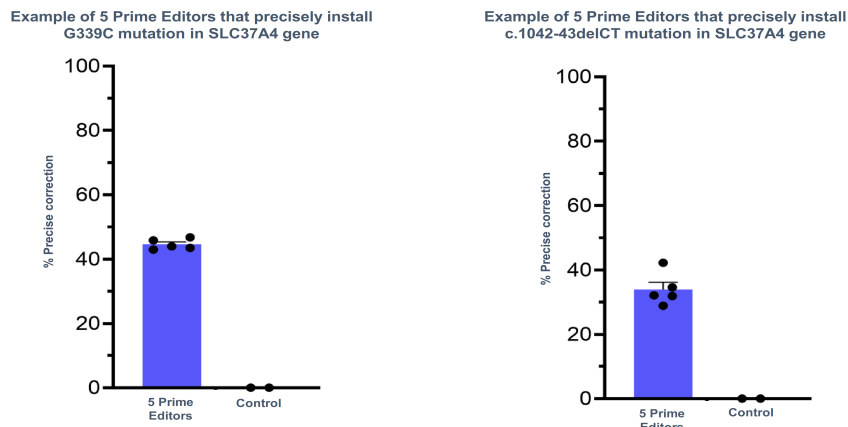
Current care focuses on nutritional therapy to avoid fasting hypoglycemia with small, frequent feedings high in complex carbohydrates, and limitation of fructose, sucrose, and lactose. There are no disease modifying therapies for patients with GSD1b. Others are developing genetic therapies for patients with a similar disease, GSD1a.

Our Approach and Results: Direct correction of prevalent mutations in SLC37A4

Our initial approach to treating patients with GSD1b is to apply Prime Editing via LNP delivery to hepatocytes in the liver to correct the two most prevalent mutations that cause the disease, which are located very close to each other in the gene. In Caucasian populations, these two predominant mutations together are found in 45 percent of patients. Based on prevalence data we estimate there are approximately 650 patients in the United States and 1,450 patients in Europe with GSD1b, and we estimate there are approximately 950 patients with these mutations. Heterozygote carriers have no disease and animal studies of GSD1b suggest that little as 11 percent of normal activity has the potential to restore normoglycemia.

As shown in the figure below, in our initial screening studies, we have identified Prime Editors that demonstrate editing of the first mutation with 40 percent efficiency (left), before any optimization. Similarly, initial screening

studies have identified Prime Editors that demonstrate editing of the second mutation with 45 percent efficiency (right), also prior to optimization.



Next Steps

We are currently evaluating whether a single Prime Editor could correct both prevalent mutations (hotspot editing) since the mutations are only 26 base pairs separated in the gene. We are establishing patient-derived hepatocyte cultures to establish a genotype-phenotype biomarker response, and are establishing novel mouse models harboring the human gene. We also plan to capitalize on the learnings from the Wilson’s disease program to formulate Prime Editors within LNPs for delivery to the liver.

Expansion Opportunities in the Liver Pipeline

Once we have established the ability to deliver Prime Editors via LNPs to hepatocytes, we could potentially advance other Prime Editing liver programs to the clinic quickly. This highlights the versatility and modularity of our platform, which potentially enables the rapid creation of new product candidates by merely changing Prime Editing guide RNAs. In addition, in each of our liver indications, our “march up the chromosome” personalized medicine approach allows expansion opportunities into the larger set of pathological mutations that exist in patients with these debilitating diseases.

OUR EYE PROGRAMS

Retinitis Pigmentosa Caused by Rhodopsin Mutations: Our lead eye indication using AAV delivery technology

The Disease

Retinitis pigmentosa, or RP, is a subset of related inherited retinal diseases, or IRDs, where disease progression is characterized by loss of night vision in childhood or early adulthood, followed by loss of peripheral vision in adulthood characterized by constricting visual field and eventual loss of central vision leading to blindness later in life. One of the most common IRDs is autosomal dominant RP, or adRP, caused by mutations in RHO which encodes the light sensitive Rhodopsin protein, or RhoP, expressed by rod photoreceptors of the retina. The disease is dominant, or manifests even with mutations to just one of the two gene copies in the genome, because mutant RhoP is toxic to rod photoreceptors, resulting in loss of function followed by rod death. Approximately six to seven thousand patients have adRP in the United States caused by RHO mutations. We are initially focused on one predominant mutation, P23H, which is highly prevalent in the United States and has been identified as causing disease in approximately 30 percent of all patients (approximately 2,000-2,500 patients). As we advance our portfolio, we believe that hotspots and other frequent mutations may also be suitable targets for Prime Editing.

Limitations of Current Approaches

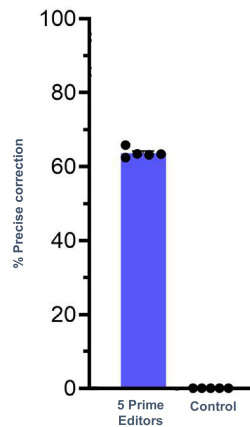
There are currently no disease modifying therapies for the P23H form of RHO, and patients are currently managed by supportive care.

Our Approach and Results: Directly correct prevalent mutations in the RHO gene in photoreceptors of the retina

Our initial approach to adRP is to correct the RHO P23H mutation in rod photoreceptors of the retina at their natural genomic location. We believe a Prime Editor that corrects P23H will also correct rarer, nearby P23L and P23A mutations. We have performed pegRNA and ngRNA screens and identified guide combinations that correct the disease-causing P23H point mutation. Natural history studies suggest that correction of only 25 percent of rod photoreceptors would have an important clinical impact, because when 25 percent or more of rods are preserved, there is full preservation of cone photoreceptors that are critical to central vision.

We have identified Prime Editors that demonstrate approximately 65 percent precise correction of the RHO P23H mutant locus.

Example of 5 Prime Editors that precisely correct P23H mutation in RHO gene



Next Steps

To deliver our Prime Editors to the eye, we are initially leveraging the tropism of AAV capsids that efficiently transfect the retina to deliver our Prime Editor as a transgene along with our pegRNA (and ngRNA, if necessary) to rod photoreceptors. Given our lead Prime Editor is larger than AAV packaging capacity, we are using a split AAV system that delivers the Prime Editor with two AAV vectors. Once inside the rod photoreceptor, the two halves of the Prime Editor protein are recombined to create a functional Prime Editor protein.

We are currently conducting preclinical studies to confirm that Prime Editing of P23H will correct healthy donor human retinal explants. We also plan to evaluate our approach in non-human primate studies where the Prime Editors will be delivered by subretinal injections to mimic the anticipated route of administration in the clinic. In parallel, we are generating patient-stem cell derived human retinal organoids to evaluate Prime Editor potency in addressing the phenotypic changes in Rhodopsin localization and rod photoreceptor function. Finally, we have also generated new mouse models that have introduced the human RHO gene, replacing the mouse RHO gene.

While we are advancing the RHO P23H program, we are also identifying Prime Editors that can correct other prevalent mutations and hotspots in the RHO adRP gene as part of our “march up the chromosome” approach.

Retinitis Pigmentosa and Usher Syndrome: Our second eye indication using AAV delivery technology.

The Disease

RP can also be caused by mutations in other genes different from RHO. Mutations in USH2A encoding the very large Usherin protein account for approximately 20 percent of autosomal recessive RP cases and can result in Usher syndrome. Approximately 14,300 patients in the United States have RP due to mutations in USH2A. While patients with various forms of RP present generally as described for RHO above, each type of RP has differences. In the case of Usher syndrome, patients present with ocular disease given normal usherin is involved in the regulation of protein transport in photoreceptors. Patients also present with severe hearing loss and potential vestibular defects, given normal usherin is involved in the maintenance of hair bundle formation during inner ear development in the inner ear.

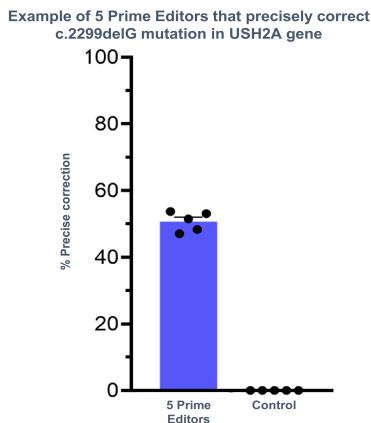
In photoreceptors, usherin is involved in the regulation of protein transport, and in the inner ear, usherin is involved in the maintenance of hair bundle formation during inner ear development. The USH2A 2299delG mutation is the most prevalent mutation in the USH2A gene, accounting for approximately 16 to 44 percent of all USH2A mutant alleles. A second predominant mutation USH2A C759F accounts for approximately 15 percent of all pathogenic USH2A alleles. These two mutations occur within a mutation hotspot. The precise number of rod and cone photoreceptors that need to be corrected is not known. Individuals with a single mutant copy of USH2A have no disease, therefore correcting 50 percent of all gene copies would restore patients to healthy gene function. Based on natural history studies from other genetic forms of RP and macular degeneration, correction of one gene copy in 10 percent and 25 percent of cone and rod photoreceptors respectively is sufficient to preserve vision. Therefore correcting mutations in 25 percent of rods and cones may be sufficient to halt disease.

Limitations of Current Approaches

There are currently no treatments available for USH2A RP, or Usher syndrome. However, hearing aids or cochlear impanation can be used to support hearing loss.

Our Approach and Results: Directly correct prevalent mutations in the USH2A gene in photoreceptors of the retina.

Our initial approach to USH2A RP is to correct the USH2A 2299delG mutation in rod and cone photoreceptors of the retina at their genomic location. We have performed pegRNA and ngRNA screens and identified guide combinations that correct the disease-causing nucleotide deletion. As shown in the figure below, through our initial screening approach, we have identified Prime Editors that demonstrate approximately 54 percent precise correction of the USH2A 2299delG mutation. Like with adRP, many of the selected pegRNAs are able to install a silent mutation (which does not affect the amino acid code) to disrupt the target site, which prevents further editing once successful corrective editing has occurred.



Next Steps

Our approach for USH2A is similar to our approach for adRP. While we are advancing the USH2A 2299delG project, as part of our “march up the chromosome” effort, we are identifying Prime Editors designed to correct other prevalent mutations and hotspots in the USH2A gene.

Expansion Opportunities in the Ophthalmic Pipeline

We plan to add additional eye-related indications to our pipeline. Once we have established delivery to the retina of a Prime Editor through AAV delivery, there are numerous other retinal diseases where our editing technologies could be applied. By merely changing the pegRNA and ngRNA sequences, we may be able to rapidly create new product candidates using the same AAV production and delivery approaches pioneered in these retinitis pigmentosa programs.

OUR EAR PROGRAMS

Our Approach to Genetic Hearing Loss

Genetic hearing loss consists of a group of diseases with high unmet need, despite the availability of current therapies. These diseases result in learning difficulties, behavioral problems and social isolation. We estimate that there are approximately 6,000 new cases each year in the United States alone, and approximately 470,000 individuals in the United States with genetic deafness. These diseases are all caused by mutations in proteins that are expressed by specialized cells of the inner ear or cochlea. Although mutations in many different genes have been identified, mutations in a small number of genes cause hearing loss in the majority of patients. Many of these mutated genes have prevalent or closely-clustered mutations. Similar to our other immediate indications, well-characterized delivery methods are established for delivery of genetic therapies to the inner ear and can be applied to Prime Editing. Methods to objectively measure changes in appreciation of sound may facilitate early detection of benefit for patients. Our initial approach is to correct prevalent mutations in genes causing progressive hearing loss, targeting delivery to the cells of the inner ear where those proteins are expressed. We are currently performing screens to identify Prime Editors that precisely correct prevalent mutations in several genes that cause hearing loss.

We have two initial hearing loss programs.

Usher’s Syndrome Type III: Our First Hearing Loss Program

The Disease

Usher’s syndrome type III, or USH3, is characterized by progressive post-lingual hearing loss, variable vestibular dysfunction, as well as adolescent-onset progressive vision loss due to retinitis pigmentosa. The hearing loss is progressive during childhood years, resulting in complete deafness in adolescents or early adults, learning difficulties, behavioral difficulties, and social isolation. Usher syndrome is found in 4 to 17 per 100,000 children.

USH3 is inherited recessively and caused by mutations in the Clarin 1 protein encoded by the CLRN1 gene. Clarin 1 is produced in inner and outer hair cells of the inner ear and, to a lesser extent, by the spiral ganglion cells, where it plays an important function in the maintenance of structures of the hair cells. In certain populations USH3 accounts for 40 to 50 percent of all Usher patients. N48K is a mutation commonly found in patients of Ashkenazi Jewish descent, whereas S50fs is commonly found in those descended from Northern Europeans and Y176X is commonly found in individuals of Finnish descent.

Limitations of Current Approaches

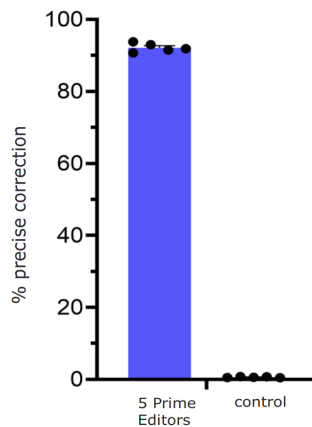
There are no disease modifying therapies for these patients. Hearing aids and speech therapy provide support. Cochlear implants have offered limited benefit to patients, likely because the disease usually manifests post-lingually.

Our Approach and Results: Correct prevalent mutations in the CLRN1 gene to restore normal Clarin 1 and hair cell function in the cochlea

Our initial approach to treating patients with USH3 is to apply Prime Editing via dual AAV delivery to hair cells in the organ of Corti in the cochlea or the inner ear to correct the most prevalent mutations that cause the disease, N48K and S50fs.

As shown in the figure below, following optimization from our initial screening studies, we have identified Prime Editors that demonstrate precise correction of the N48K mutation with more than 90% efficiency. We are currently exploring similar Prime Editors to correct the neighboring S50fs mutation.

Example of 5 Prime Editors that precisely correct N48K mutation in CLRN1 gene



Next Steps

To deliver our Prime Editors directly to the cochlea by local injection, we are initially leveraging the tropism of AAV capsids that effectively transduce the supporting cells and hair cells to deliver our Prime Editor as a transgene along with our pegRNA. Similar to the retinal programs, we will initially use a dual AAV approach to deliver both the Prime Editor protein and pegRNA.

We are currently building preclinical assays using patient stem cells differentiated into hair cells to confirm that Prime Editing of N48K will correct Clarin 1 expression and hair cell function. In parallel we are developing assays to optimize delivery of Prime Editors to the cochlea.

Non-Syndromic Hearing Loss – GJB2: A Follow-On Hearing Loss Program

The Disease

Two thirds of genetic hearing loss is non-syndromic and is inherited recessively. The GJB2 gene, which encodes the connexin 26 protein, is expressed by supporting cells of the cochlea and contributes to the normal production of endolymph in the cochlea. GJB2 is the most commonly-mutated gene in non-syndromic hearing loss, found in 1:2,000 live births and accounting for approximately 1,875 newly diagnosed patients each year in the United States and similar number in Europe, with a very common mutation, c.35delG, found on average in 57% of these patients. Additional mutations are found in patients of Asian (c.235delC, V37I), Indian/European (W24X) and Ashkenazi Jewish descent (c.167delG). Since the widespread adoption of newborn and pre-school hearing screening for early diagnosis, many patients are diagnosed with abnormal but preserved hearing and show progressive disease. Because the disease can lead to profound hearing loss (complete deafness) in the first few years of life, patients suffer learning difficulties, speech difficulties, social isolation and behavioral problems.

Limitations of Current Approaches

There are no disease modifying therapies. Current therapies include hearing aids, cochlear implants and speech and language therapies. These approaches do not treat the cause of disease, with limited but important benefits. In particular, cochlear implants provide a partial restoration of sound but require extensive speech and language retraining with variable outcomes. Moreover, implants require permanent wearing of large external devices.

Our Approach: Correct prevalent mutations in the GJB2 gene to restore normal connexin 26 function in the cochlea and prevent hearing loss progression

Our initial screens are to find Prime Editors to precisely correct c.35delG. After identifying preliminary Prime Editors that show installation of the c.35delG mutation with good levels of efficiency, we are currently screening for Prime Editors to precisely correct this mutation.

Next Steps

We will leverage the work on the USH3 program to deliver Prime Editors to the cochlea with a focus on targeting support cells.

We are currently building preclinical assays using patient stem cells differentiated into inner ear cells to confirm that Prime Editing of c.35delG will correct GJB2 expression and connexin 26 function.

Expansion Opportunities in the Hearing Loss Pipeline

We plan to add additional hearing loss-related indications to our pipeline. Once we have established delivery to the cochlea of a Prime Editor through AAV delivery, we believe there are many other hearing loss diseases where our editing technologies could be applied. By merely changing the pegRNA and ngRNA sequences, we may be able to rapidly create new product candidates using the same AAV production and delivery approaches pioneered in these initial hearing loss indications.

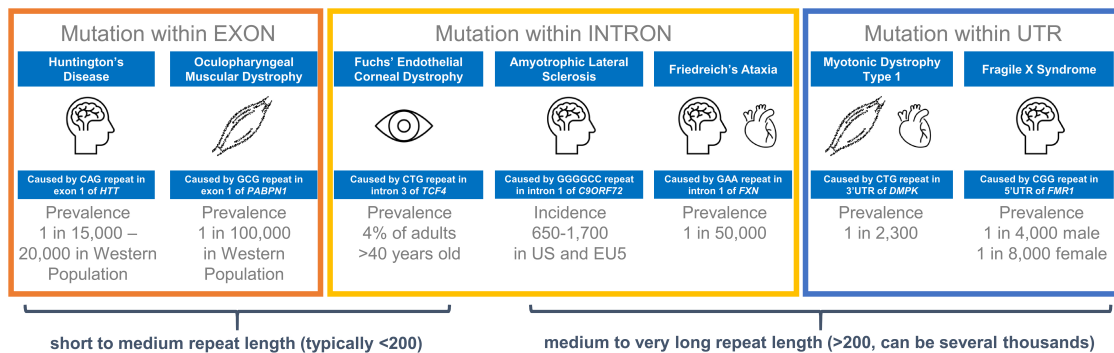
Differentiation Target Indications

OUR REPEAT EXPANSION DISEASE PROGRAMS

Our Approach to Repeat Expansion Diseases

Repeat Expansion Diseases, or REDs, are a collection of more than 50 progressive diseases, mainly affecting the CNS and musculoskeletal system. These diseases are all caused by mutations that are an expansion of repeat DNA sequences, often triplets of nucleotides, found in the normal genome. We believe these repeats can potentially be exponentially expanded from typically approximately five to 15 repeats in normal tissues to up to many thousands of repeats in diseased tissues. The repeats are found within parts of the coding region of genes, called exons; in non-coding regions of a gene between exons, called introns; and in non-coding regions of the gene, either at the beginning or end of a gene, that are not translated in RNA, called untranslated regions, or UTRs. In addition, sometimes REDs are described by the size of the expansion, ranging from short and medium repeats (often less than

200 extra repeats) to medium to long repeats (often more than 200 extra repeats to several thousand extra repeats), as described in the figure below.



The above figure exemplifies our initial approach to repeat expansion diseases, showing disease names, primary organs affected by disease, approximate estimates of prevalence or incidence, type of expansion mutation, gene where expansion mutation occurs, location and approximate length of expansion mutation within the gene.

In certain repeat expansion diseases, the repeats often cause a pathological gain-of-function, or a new deleterious impact, and are inherited dominantly. In other settings, the disease is inherited recessively. Prime Editing enables us to fix the underlying and fundamental causes of these diseases by precisely and completely removing the repeat expansion copies from the DNA, potentially replacing them with the normal, usually small number of healthy repeats, or possibly removing any repeats from the gene.

Our initial approach is to establish the utility and breadth of Prime Editing technology by precisely removing repeat sequences in the pathological target tissues. In settings where the repeats are in an exon, Prime Editing may be applied to remove the repeat and replace the repeat with the healthy coding sequence precisely. In other settings, such as repeats in introns, we have more flexibility to our approach.

To build the foundation for the potential correction of all 50 or more repeat expansion diseases, which would address a huge unmet medical need, we are evaluating many different types of these diseases to understand where Prime Editing can be efficient. For our initial studies, we broadly selected diseases of high unmet need with a path to deliver the Prime Editor to target tissues. We are studying repeats within exons, introns and the UTR regions, as well as diseases with small-to-medium and medium-to-very large numbers of expansion repeats. In each individual indication, beyond exploring the potential for Prime Editing to perform these precise corrections or completely remove the pathological repeats, we are also evaluating whether genetic correction will result in phenotypic or biochemical results consistent with a clinical improvement.

We have focused on REDs since inception of our initial preclinical program efforts. Independently published proof-of-concept of this idea was demonstrated in a repeat expansion disease called Fragile X syndrome, providing corroboration of the potential of this approach. More than 50 repeat expansion diseases are known to be pathogenic, and we believe our broad approach supports that most, if not all, of the diseases may be amenable to Prime Editing corrections of the target DNA, thereby potentially halting, preventing, or even curing such diseases.

Friedreich's Ataxia: Our lead repeat expansion disease indication

The Disease

Friedreich's Ataxia, or FRDA, is a multisystem, autosomal recessive neurodegenerative disorder affecting the central and peripheral nervous system as well as the heart and other organs. FRDA significantly reduces survival for patients, with the mean age of death being 39 years. FRDA is characterized by progressive ataxia, or lack of muscle control or coordination of voluntary movements, with mean age at onset of approximately five to 16 years. A vast majority of patients progress to loss of unsupported sitting within two years and loss of ambulation on average 10 to 15 years from diagnosis. In addition, patients develop cardiomyopathy, or heart failure or dysfunction, which is the

most common cause of premature death. In the United States, it is estimated that around 4,000 individuals are affected by FRDA, while there are estimated to be 15,000 to 94,000 patients globally.

FRDA is caused by GAA-repeat nucleotide sequence expansions in the 1st intron of the FXN gene encoding the frataxin protein, which plays important roles in mitochondria. The expanded repeats occur early in the gene, and cause disruptions in transcribing the FXN gene into RNA resulting in low levels of the frataxin protein, the pathogenesis of the clinical disease. Published literature shows that removal of expanded repeats can restore frataxin expression *in vitro*.

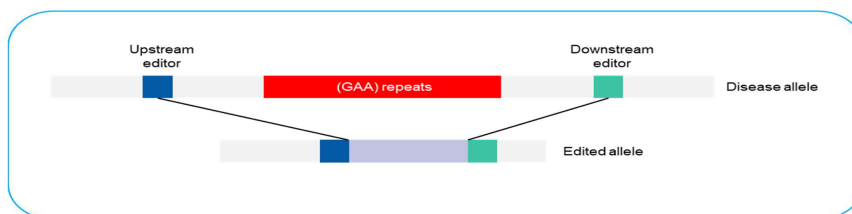
Limitations of Current Approaches

There is no approved disease-modifying therapy, and current clinical management guidelines mainly focus on symptom management.

Our Approach and Results: Directly and precisely remove the pathogenic GAA repeats in the FXN gene

Our Prime Editing technology enables us to precisely remove the expanded repeat sequences that cause FRDA. Using the dual-flap technology with a Prime Editor targeted both upstream, or before the GAA pathological repeats, and downstream, or after the repeats, our goal is to precisely remove the repeat sequence from intron 1 of the FXN gene to restore normal FXN regulation and normal expression of frataxin; the approach is shown in the figure below. Removal of repeats from FXN in the myocardium is also highly desirable to prevent cardiomyopathy and reduce mortality. The primary target tissues are for areas of the brain and spinal cord, but we plan to address cardiomyocytes as well.

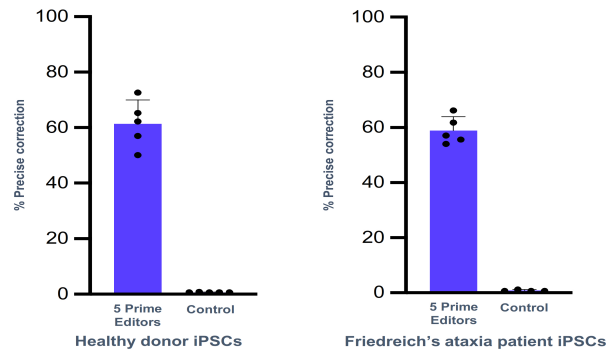
Our Approach to Restore Normal FXN Regulation and Normal Expression of Frataxin



We have performed screens to identify the pegRNA pairs that achieve highly efficient and precise removal of the expanded repeats. We have demonstrated removal of pathological repeats from healthy donors, who have only a short length of repeats. We show up to 77 percent precise editing which results in the total removal of the pathogenic repeat region, without errors, as shown in the figure below on the left, where each dot represents an individual candidate Prime Editor. In addition, the figure on the right shows approximately 60 percent precise editing in FRDA patient-derived induced Pluripotent Stem Cells, or iPSCs, which contain larger numbers of pathological repeats, numbering from 420 to 541 nucleotide triplet repeats. In later, preliminary experiments, some of our Prime Editors have achieved greater than 80 percent precise editing out of the pathogenic repeat region. Remarkably, the total

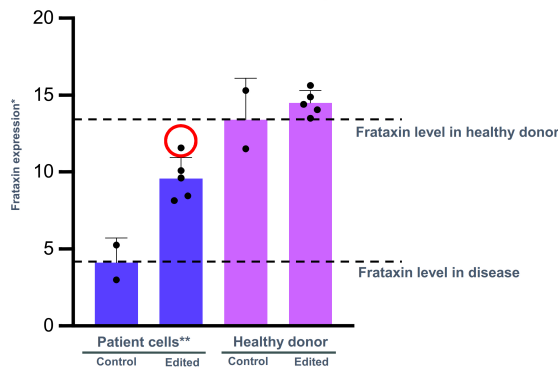
length of sequence precisely removed can be more than 7,000 nucleotides, or seven kilobase, using dual-flap Prime Editing.

Example of 5 different dual-flap Prime Editors in precise correction of FXN gene in healthy donor and patient-derived iPSCs

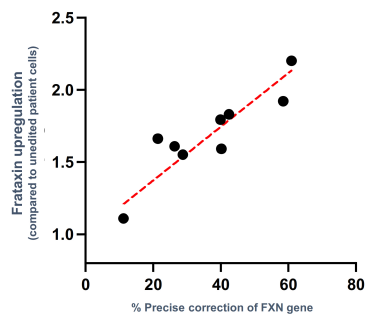


Our initial experiments are encouraging. In our models in donor- and patient-derived iPSCs we measure the amount of frataxin expression in both FRDA patient cells, as well as cells derived from healthy donors. As expected, and as shown in first panel of the figure below, we show that patient cells have low levels of frataxin (control; left bar), and healthy donor cells (both control and edited; right bars) have high levels of frataxin. When we Prime Edit the FRDA patient cells in this model, as indicated by the arrow, each of five individual Prime Editors, in association with high levels of precise correction, restore levels of frataxin towards that seen in healthy donor cells. As each data point, or dot, represents a different Prime Editor, our best candidate can restore frataxin levels to approximately 80 percent of normal levels, which exceeds the 30 percent-of-normal threshold predicted to provide a potential clinical benefit to patients. To corroborate that the precise editing is causative of the increase in frataxin levels, in the right panel of the figure below, a tight correlation is shown among the results of nine different Prime Editors, where the percentage of precise FXN gene correction shows a strong relationship with the effect on increase in frataxin levels.

5 different dual-flap Prime Editors all restore frataxin expression levels in patient cells toward levels in healthy donor cells



Percentage precise FXN gene correction in patient cells correlates with level of frataxin expression



*Quantitative polymerase chain reaction data for FXN transcripts normalized to housekeeping control.
 **Patient iPSCs contain 541 and 420 GAA repeats.

We have also developed patient-derived stem cell models of disease. As a first step, we have generated patient derived cardiomyocytes to evaluate the effect of dual-flap Prime Editing on frataxin levels, the decreased levels of which are causative of the disease. In addition, we are developing models of mitochondrial function and other functional assays.

Next Steps

We have established preliminary methods to deliver Prime Editors to terminally differentiated cardiomyocytes and plan to establish editing and functional recovery of frataxin expression in this cell system. Then, to ultimately deliver Prime Editors to heart and other tissues, we expect initially to rely on the tropism of AAV capsids, each optimized to deliver our Prime Editors to the central nervous system or heart. We are currently optimizing the AAVs for expression in neurons and glial cells as our first focus. We are also planning to evaluate our Prime Editors in a disease model in mice which contain the human frataxin gene with pathological repeats. While AAV delivery is our primary route of delivery for early programs such as this, we will be actively determining whether a non-viral delivery system could be used to efficiently deliver the Prime Editor to one or more of our key target organs.

Myotonic Dystrophy Type 1: Another repeat expansion disease indication

The Disease

Myotonic Dystrophy type 1, or DM1, is a common autosomal dominant muscular dystrophy among people of European ancestry and is principally a muscle disease affecting skeletal and cardiac muscle with multisystem manifestations. Patients often initially present with muscle weakness. Recent newborn screening studies indicate that the true prevalence of DM1 is 1:2,100 (approximately 140,000 patients in the United States). Patients can be clinically divided into three groups: congenital DM1; childhood/juvenile DM1, and adult-onset DM1. Congenital DM1, where patients typically have more than 800 repeats, often occurs from asymptomatic parents and presents at birth with severe weakness, hyporeflexia, or lack of reflexes, and respiratory insufficiency, and has a 40 percent mortality, with cardiac conduction abnormalities accounting for approximately 70 percent of that mortality. Survivors have distal weakness, cognitive impairment, and neuropsychological disorders. Childhood/juvenile DM1 is more similar to adult disease presenting at ages of five to 15 years with developmental delays and speech and learning difficulties. In adolescent patients, muscle weakness, myotonia, or the inability for muscles to relax, and GI symptoms are most prominent.

DM1 is caused by expanded CTG repeats in the 3' UTR of one copy of the DMPK gene. When transcribed into RNA, the expanded repeat nucleotides in the case of DM1 sequester critical splicing factors, thereby preventing the correct function of many genes that regulate cell function.

Limitations of Current Approaches

Current therapy includes supportive care to manage symptoms, though many experimental approaches are under consideration.

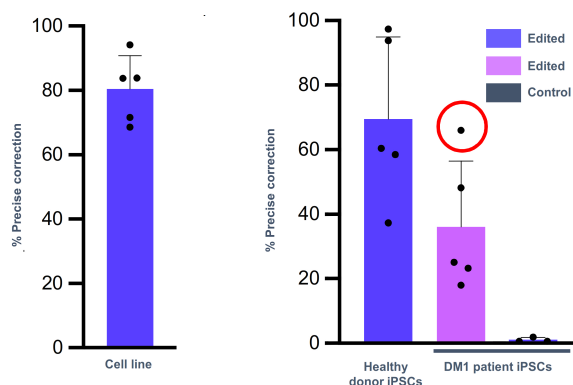
Our Approach and Results: Directly and precisely remove the pathological repeats in the DMPK gene

Our dual-flap Prime Editing technology enables the removal of the expanded repeat sequences that cause disease. Our goal in DM1 is to leverage our Prime Editing technology to precisely remove the repeat sequence from the UTR region of the DMPK gene, to restore DMPK regulation and expression of DMPK protein back to normal levels. The primary target tissues are cardiac and skeletal muscle, which we believe could have a transformative effect on patients; CNS is an important secondary target tissue.

We have performed screens to identify pegRNA pairs that achieve highly efficient and precise removal of the expanded repeats and have demonstrated precise removal of pathological repeats from the DMPK gene. In the example provided in the figure on the left below, we have established precise removal of the smaller number of repeats in healthy cell lines with more than 80 percent efficiency. In a second set of experiments as shown in the figure on the right, we again demonstrated up to 90 percent precise editing in healthy donor cells. In patient derived iPSCs, which contain approximately 1,600 pathological repeats, we have demonstrated precise removal of repeats, with our best Prime Editors achieving up to approximately 66 percent precise editing and removal of the pathological repeats. These data are also shown in the figure on the right, with each dot representing the data of a

different individual Prime Editor, both in healthy- and patient-derived cells; one potential lead candidate is circled in red.

Example of 5 different dual-flap Prime Editors in precise correction of DMPK gene in cell line, healthy and patient-derived iPSCs



Next Steps

We are developing patient-derived stem cell-derived models of disease. As a first step, we have generated patient-derived cardiomyocytes and patient fibroblasts in which to evaluate dual-flap Prime Editing. We have established preclinical methods to deliver Prime Editors to terminally differentiated cardiomyocytes and will establish editing and functional recovery in this cell system. In parallel, we will perform similar experiments in patient-derived skeletal muscle cells. The progression of this program will broadly follow the general path described above for FRDA.

Amyotrophic Lateral Sclerosis: Another repeat expansion disease indication

The Disease

Amyotrophic lateral sclerosis, or ALS, is a rapidly progressive neurodegenerative disease characterized by progressive motor neuron loss. Mean age of onset for ALS is 58 to 60 years, with mean survival of three to four years after onset. The disease selectively results in dysfunction of upper and lower motor neurons, which later degenerate and die. Degeneration of these cells primarily causes impairment of motor function, and leads to muscle weakness, changes in speech, and difficulty breathing and swallowing, with death caused by paralysis and respiratory failure. Overall ALS prevalence in the United States and Europe is approximately 40,000 patients.

Approximately 11 percent of ALS cases have pathological expansions of the hexa repeat GGGGCC in intron 1 of the ALS C9orf72 gene. The same repeat expansions have been found in a study to cause as high as 53 percent of frontal temporal dementia and an overlap syndrome known as ALS/FTD; in addition, C9orf72 is thought to be causative in a proportion of Parkinson's disease, Huntington's disease, Corticobulbar syndrome and Olivopontocerebellar degeneration.

Eleven or fewer repeats are normal, but the disease is associated with expansion to hundreds or even thousands of repeats. Longer repeats are associated with earlier onset and more severe disease. The primary pathology is thought to be a toxic RNA gain-of-function by which the mRNA sequesters nuclear factors in a different but analogous way to the repeats in DM1.

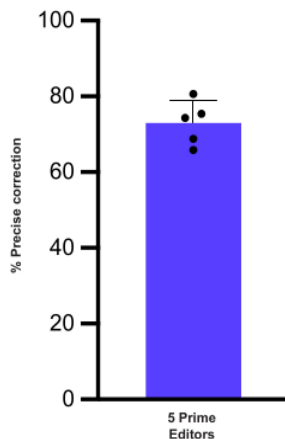
Limitations of Current Approaches

Currently resveratrol is the only approved therapy for ALS which modestly slows disease and may function as an anti-oxidant. All other therapies are supportive.

Our Approach and Results: Directly and precisely remove the pathological repeats in the C9orf72 gene

Our initial approach is the correction of the C9orf72 mutation by removing the GGGGCC repeat expansion tract using dual-flap Prime Editing, thereby restoring normal C9orf72 regulation and expression. We have performed screens to identify pegRNAs pairs that achieve highly efficient and precise removal of the repeats in the 1st intron of C9orf72. As shown in the example provided in the figure below, we have established precise removal of repeats in healthy cell lines with more than 80 percent efficiency. We are currently assessing precise editing efficiency in patient-derived stem cell-derived models of disease.

Example of 5 Prime Editors that precisely remove the GGGGCC repeats in intron 1 of the C9ORF72 gene



Next Steps

Our approach to delivery is similar to that of other repeat expansion diseases, such as FRDA described above. Similarly, we will continue our work in patient-derived models of ALS, as well as assess editing efficiency in mouse models, eventually progressing to non-human primate studies.

Fuch's Endothelial Corneal Dystrophy: Another repeat expansion disease indication

The Disease

Fuch's Endothelial Corneal Dystrophy, or FECD, is a common disease of the cornea of the eye leading to progressive corneal opacification and blindness. FECD patients present with blurred vision, visual acuity loss, bright light sensitivity and presence of extracellular matrix excrescences called guttae, which can cause pain. The disease starts with degeneration of the corneal endothelial cells which supply nutrients to the inner layer of the cornea and maintain transparency.

FECD is estimated to affect over 600,000 patients in the United States, usually presenting in patients over 40 years of age. We estimate that between 14,000 and 14,500 cases annually progress to visual deterioration in the United States sufficient to require corneal transplantation.

Approximately 79 percent of FECD patients have a mutation in the TCF4 gene, with expanded nucleotide triplet repeats; the repeats result in aggregates that sequester cell splicing factors, such as in patients with Myotonic Dystrophy.

Limitations of Current Approaches

Early treatment is localized, but as the disease progresses, surgical management becomes necessary.

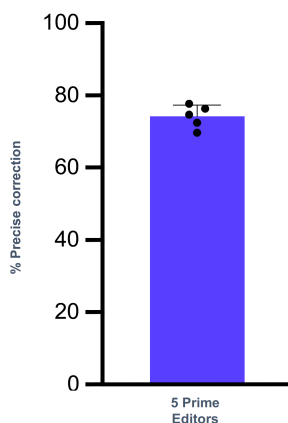
Current approaches are surgical and require corneal grafts, which are sourced from cadavers and are in scarce supply. Surgery is also complicated by graft loss; there is only approximately 64 percent graft survival at 10 years following surgery. The procedure requires general anesthesia, may require immunosuppression, long periods off work, may be complicated by infections, glaucoma, cataract, astigmatism, and it can still take up to one year following the procedure for full sight restoration.

Our Approach and Results: Correct the TCF4 mutation in corneal endothelial cells

Our initial approach is to deliver Prime Editors to the anterior chamber of the eye to correct the TCF4 mutation in corneal endothelial cells by looping out the pathological repeats. The advantages include avoiding surgery and the lack of requirement for cadaveric tissue, among others, as well as the potential to achieve a permanent correction.

We have performed screens to identify dual-flap Prime Editors that can achieve highly efficient and precise removal of the repeats in the TCF4 gene, achieving precise removal of repeats from healthy cell lines with more than 70 percent efficiency, as shown in the figure below.

Example of 5 Prime Editors that precisely remove the CTG repeats in intron 3 of the TCF4 gene



Next Steps

Our next steps include validating the activity of these Prime Editors in patient-derived endothelial cells. Our goal is to deliver Prime Editors to the corneal endothelial cells before degeneration of the capillary network. Our initial approach will be to encapsulate Prime Editors, to be delivered as either ribonucleoprotein or RNA, and deliver to the endothelium by anterior chamber microinjection.

Oculopharyngeal Muscular Dystrophy: Another Repeat Expansion Disease Indication

The Disease

Oculopharyngeal muscular dystrophy, or OPMD, is a rare autosomal dominant disease, characterized by progressive weakness in the muscles around the eyelids as well as in the tongue and pharynx. This weakness manifests as difficulties with vision, swallowing and speaking. As the disease progresses it affects the neck, shoulders and the limbs, resulting in difficulty in walking. The disease is often first diagnosed in adults in their 40's with a small minority ultimately requiring a wheelchair. Major manifestations include eyelid drooping, dysphagia (difficulty swallowing) and facial muscle weakness. Dysphagia can result in malnutrition, aspiration and pneumonia.

OPMD is often identified in individuals of French Canadian descent, Ashkenazi Jewish, and Latino populations from central and northern America where prevalence may be high (e.g. in French Canadian populations it is 1 in 1,000). Overall prevalence estimates in Europe are approximately 1 in 100,000.

OPMD is caused by expansion of a GCG repeat sequence in the 1st exon of the PABPN1 gene which encodes the poly-A binding nuclear protein-1. The GCG repeat encodes a short track of alanine residues with 7 CGC repeats. Short expansions of 11 to 18 repeats are sufficient to cause disease. OPMD affects all voluntary muscles but appears to spare smooth and cardiac muscle. The disease is characterized histologically by intranuclear inclusions in muscle comprising aggregated PABPN1 protein. Aggregation of the mutant PABPN1 protein is thought to be an important part of the pathological mechanism, due to sequestration of normal PABPN1 or a toxic gain-of-function to the formation of poly-Alanine protein.

Limitations of Current Approaches

Current therapies are supportive and may involve surgical procedures to the eyelids and esophagus including local botulinum toxin injections. There are currently no disease modifying agents.

Our Approach: Precisely remove the repeats from the mutant PABPN1 gene and replace with healthy sequence to restore normal PABPN1 function in the eyelid and pharyngeal muscles.

Our initial approach is the correction of the *PABPN1* mutation by removing the GCG repeat expansion tract using Prime Editing and replacing with a sequence encoding 7 alanine amino acids, thereby restoring normal function to the *PABPN1* gene. This is an early-stage program, where we are performing initial screens and identifying Prime Editors that achieve efficient and precise removal of the repeats while simultaneously recoding the normal alanine repeat.

Next Steps

We plan to perform additional screens and to optimize currently identified Prime Editors to increase efficiency, then validate Prime Editors in patient-derived cells and demonstrate correction of the *PABPN1* localization protein function. We are currently evaluating whether a local therapeutic approach to inject muscles of the eyelid, pharynx and tongue using a LNP encapsulating Prime Editor cargo of an mRNA and pegRNAs would provide a strong therapeutic benefit to patients.

Fragile X Syndrome: Another Repeat Expansion Disease Indication

The Disease

Fragile X syndrome, or FXS, is an X-linked dominant rare disease, which is the most common monogenic cause of childhood intellectual disability and autism. Patients have cognitive, behavioral, and sensory deficits, and may have cardiac and skeletal manifestations. FXS is found globally, and is estimated to affect 40,000 to 60,000 in the United States, with a similar number in Europe.

FXS is caused by expansion of a CGG repeat tract in the 5' untranslated region of the *FMR1* gene, leading to aberrant gene silencing and loss of the Fragile X mental retardation protein (FMRP), a protein important for brain development. Loss of FMRP leads to abnormal protein synthesis from many genes involved in synaptic function leading to abnormal synaptic signaling and abnormal morphology of neurons.

CGG is repeated more than 200 times in FXS patients, whereas 5-40 repeats regularly occur in healthy people. More than 200 repeats usually leads to aberrant hypermethylation of both the promoter region and the expanded repeat itself, and this results in transcriptional silencing of *FMR1*. Some FXS patients with a full mutation but unmethylated *FMR1* gene may only have anxiety and/or behavioral issues without intellectual disability. Individuals carrying a premutation (between 55 to 200 repeats) are associated with increased risk for Fragile X associated tremor/ataxia syndrome which has later onset.

Limitations of Current Approaches

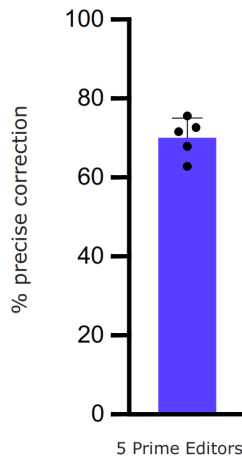
Current approaches are aimed at reducing symptoms. Several therapies are in development including small molecules targeting symptoms and gene therapies.

Our Approach and Results: Correct the FMR1 mutation in neurons

Our initial approach is to deliver Prime Editors to neurons of the CNS to correct the mutation in the FMR1 gene, restoring normal expression of the FMRP protein and synaptic function. The Prime Editor will loop out the pathological repeats in the FMR1 gene. This approach aims to correct the underlying cause of disease and has the potential to achieve a permanent correction. We are focusing on particular regions to deliver editors including caudate nucleus, hippocampus and various areas of the cortex. Guided by human genetics, we believe restoration of FMRP to 15 to 20 percent of normal FMRP may be sufficient to restore normal function to patients.

We have performed screens to identify dual-flap Prime Editors that can achieve highly efficient and precise removal of repeats in the FMR1 gene, achieving precise removal of repeats from healthy cell lines with more than 80 percent efficiency, as shown in the figure below.

Example of 5 Prime Editors that precisely remove the CGG repeats in 5' untranslated region of the FMR1 gene



Next Steps

We are validating the activity of these Prime Editors in patient-derived neurons to demonstrate restoration of normal FMRP protein expression and normal synaptic function. Our goal is to deliver Prime Editors to the cortical and deep brain structures. Similar to our delivery approach for Friedreich's ataxia, we will initially employ a dual AAV system to deliver the Prime Editor.

Huntington's Disease: Another Repeat Expansion Disease Indication

The Disease

Huntington's disease, or HD, is an autosomal dominant progressive neurodegenerative disease affecting teenagers through middle aged adults. Most individuals are diagnosed by age 45, with approximately 15 percent of patients diagnosed as teenagers. Prevalence estimates are 1 in 10,000, suggesting between 20,000 to 40,000 individuals in the United States have the disease. It is characterized by progressive loss of motor and cognitive function often with involuntary limb movements and fine motor impairments which progress steadily. Natural history studies indicate substantial preservation of brain parenchyma (functional tissue) at the time of diagnosis, and in those with prodromal disease suggest cellular dysfunction precedes loss of neurons. The first tissues to degenerate in the CNS are the striatum, followed by the cortex. More than 95 percent of neurons in the striatum are medium spiny neurons which control muscle movement of limbs, body, eyes, as well as reward reinforcement and aversion responses. These specialized neurons are the first to degenerate. Typical progression to end-stage disease occurs over 10 years.

HD is caused by an expansion of a CAG repeat sequence in the 1st exon of the HTT gene which encodes the huntingtin protein. The repeat encodes a run of glutamate amino acids. Whereas 5 to 35 repeats are found in healthy individuals, having more than 40 repeats is considered pathological, with repeats often expanding well beyond 120 and with as many as 700 repeats observed in individual disease-affected cells. Many distinct toxic or pathological consequences of the expanded repeat sequence occurring in the HTT mRNA or huntingtin protein have been documented. These include toxic protein fragments and protein aggregation, transcriptional dysregulation, disrupted protein homeostasis, mitochondrial dysfunction, altered synaptic plasticity and defects in axonal transport. These findings suggest mutant huntingtin has widespread pathological effects on neurons.

Limitations of Current Approaches

There are supportive measures and therapies to modify symptoms, but there are currently no disease modifying agents.

Our Approach: Precisely remove the repeats from the mutant HTT gene and replace with healthy sequence to restore normal huntingtin function in the CNS

Our initial approach is the correction of the *HTT* mutation by removing the CAG repeat expansion tract using dual-flap Prime Editing or single long flap Prime Editing, and replacing with a sequence encoding 5 glutamate amino acids, thereby restoring normal function to the *HTT* gene. We are evaluating the best method to deliver Prime Editing to deep brain structures including the striatum (caudate nucleus, putamen, nucleus accumbens), as well as the hippocampus, thalamus and cerebral cortex. This is an early-stage program, where we are performing initial screens and identifying Prime Editors that achieve efficient and precise removal of the repeats while simultaneously recoding the normal glutamate repeat. We are currently performing optimizations to the Prime Editors to increase efficiency above 50%.

Next Steps

Similar to our other programs, we will evaluate promising Prime Editors in patient cells and differentiate patient-derived stem cells into medium spiny neurons in order to evaluate the impact of correction of *HTT* on normal huntingtin protein function. Such assays include the restoration of normal huntingtin protein, as well as detection and quantification of inclusion bodies.

Expansion Opportunities in Repeat Expansion Diseases

In five of our repeat expansion diseases, including the four described in detail above, we have identified in our preliminary experiments at least one candidate Prime Editor that can achieve greater than 77 percent precise editing at each gene locus.

In particular for repeat expansion diseases, our approach has been to pick important surrogate examples, so that progress in the pipeline would considerably increase the probability of success for others of the approximately 50 repeat expansion diseases. We plan to use our knowledge from existing programs to expand our pipeline of preclinical candidates, based on rapid progress in looping out pathological repeats.

OUR OTHER INITIAL DIFFERENTIATION TARGETS

Duchenne Muscular Dystrophy: “Differentiation” Disease Indication

The Disease

Duchenne muscular dystrophy, or DMD, is an X-linked recessive disease affecting boys that is characterized by early onset progressive muscle weakness affecting limbs. It is frequently diagnosed between 2 to 3 years of age, and progresses to most patients being wheelchair bound by age 10. In teenage years patients develop progressive cardiomyopathy and respiratory weakness, and patients die in their early 20's from related complications. It is estimated to affect 1 in 3,500 live births with diagnosed prevalent cases in the United States of 16,000 to 17,000.

The disease is caused by loss-of-function mutations in the *DMD* gene, which is one of the largest genes in humans. The *DMD* gene encodes the dystrophin protein which is a critical protein component in the membrane of muscle fibers. Dystrophin stabilizes the membrane of muscle fibers and connects the actin-myosin muscle machinery to the cell membrane. In the absence of dystrophin, myofibers are susceptible to use injury. Use injury causes damage and inflammation of the myofibers resulting in myofiber degeneration, inflammation, fibrosis and fatty replacement.

Many of the mutations causing DMD are large deletions in the *DMD* gene resulting in out-of-frame gene sequence, complete loss-of-function, and the absence of any dystrophin protein. A smaller number of mutations are large duplications, and a small number of mutations are substitutions or small insertions/deletions.

A milder form of DMD, called Becker muscular dystrophy is caused by in-frame mutations in the *DMD* gene which produce shortened forms of the dystrophin protein. The Becker disease ranges from a milder form of DMD with teenage or adult onset, through to asymptomatic individuals with a normal lifespan. Asymptomatic individuals often have large deletions in the central region of the dystrophin protein, indicating that production of a truncated protein is compatible with normal or near normal muscle function. Because muscle is a syncytium (a single muscle fiber may be several feet in length containing several hundred nuclei), correction of the gene defect in a limited number of nuclei may be sufficient to completely restore protein expression in the muscle fiber. Studies of DMD in dogs suggest gene correction in as few as 11 percent of nuclei restores dystrophin to within 90 percent of normal levels.

Limitations of Current Approaches

In addition to supportive care, patients benefit from steroid therapy which reduces inflammation and has a modest impact slowing progression of disease. An oligonucleotide delivered by regular IV infusions, which promotes exon skipping of the 51st exon during mRNA splicing and can result in reframing of the *DMD* gene to result in a functional *DMD* protein, has offered minimal to modest benefits to some patients. Gene therapies in development that are delivering an engineered “microdystrophin” protein to patients have demonstrated effective protein delivery to muscle, but to date have resulted in limited or no functional benefit.

Our Approach: Precisely reframe the DMD gene to restore functional dystrophin protein in muscle

Prime Editing can precisely introduce or remove nucleotides from the *DMD* gene at pre-specified positions to reframe the gene so that a shortened but highly functioning protein is produced instead of no protein. Guided by human biology of patients with Becker muscular dystrophy, we have initially designed Prime Editors to reframe the *DMD* gene in positions such that many individuals with different mutations, particularly large deletions in the central region of the *DMD* gene, will achieve functional dystrophin protein restoration from a single Prime Editor. This is an early program, where we are performing screening to identify Prime Editors that demonstrate efficient and precise nucleotide insertion or deletion to reframe the gene. Based on known *DMD* mutations, a small number of different Prime Editors could reframe the *DMD* gene and restore functional protein for more than half of the *DMD* patients.

Next Steps

Following optimization of the Prime Editors we will use patient-derived cardiomyocytes to evaluate the efficacy of selected editors to restore dystrophin protein. Using similar delivery methods to those we are establishing for delivery of Prime Editors to skeletal and cardiac muscle for Myotonic Dystrophy type I, such as a dual AAV delivery approach, we will deliver lead Prime Editors to a humanized animal model and establish their pharmacokinetic and pharmacodynamic properties.

Cystic Fibrosis: “Differentiation” Disease Indication

The Disease

Cystic fibrosis, or CF, is a progressive lung disease characterized by production of thick mucus lung secretions which lead to blockage of airways, inflammation, lung infection, progressing ultimately to lung failure. It also

affects the pancreas gland and biliary system of the liver in a similar way, leading to exocrine pancreatic failure and mild to moderate cholestatic liver disease in some patients. Most patients are diagnosed before 2 years of age through newborn screening or because of symptoms of lung disease, combined by salty skin which can be confirmed using a sweat test. Through supportive care and antibiotic therapies patient median survival has increased to early 30's before lung failure necessitates lung transplantation if available. Overall CF prevalence in the United States and Europe is approximately 70,000 to 90,000 patients.

The disease is inherited recessively and caused by loss of function mutations in a chloride protein transporter called cystic fibrosis transmembrane conductance regulator, or CFTR. Approximately 65 to 75 percent of CF patients have a three-nucleotide deletion in the CFTR gene known as F508del. The vast majority of remaining patients have one of several prevalent mutations in a small number of genetic hotspots in the CFTR gene, including mutations such as N1303K, W1282X, G542X, or G551D. F508del and several other mutations result in misfolding of the CFTR protein which fails to reach the plasma membrane, whereas other mutations lead to complete absence of protein or a protein which does not function even though it is localized at the correct site in the cell. The failure of CFTR to function at the cell surface leads to cell secretions that lack sufficient salt and water, resulting in high viscosity and inability to clear secretions from lung and pancreas.

Limitations of Current Approaches

In addition to supportive care, antibiotics and lung transplantation, patients also receive pancreatic enzyme supplements daily. Recently, a combination medicine containing 3 small molecules, known as Trikaftor has proven highly effective at correcting the folding of the CFTR protein which harbors either the F508del mutation or one of a few other mutations. Trikaftor has improved lung function and survival for those patients. For 15 to 30 percent of patients (those with CF caused by other mutations) there is currently no disease modifying therapy. In addition, adverse events and discontinuations reported for individuals taking Trikaftor (or one or more of the constituent active pharmaceutical ingredients), indicates patients with F508del also continue to have unmet need.

Our Approach: Correct prevalent mutations and mutational hotspots in the CFTR gene

We are using either classical Prime Editing or dual-flap Prime Editing to correct different CFTR mutations to restore CFTR protein regulation, expression and function. This is an early program, where we are performing screens to identify pegRNAs or pegRNA pairs that achieve efficient and precise correction of CFTR at multiple sites in the gene, including hotspots. Our goal is to identify Prime Editors to target mutations initially in 8 hotspots in the CFTR gene.

Next Steps

Initially we will perform optimizations of the Prime Editors from the first screens to increase efficiency. We will deliver Prime Editors to patient-derived cells, such as iPSCs differentiated in intestinal organoids, and establish that mutation correction will restore CFTR function. Our initial approach to delivery of Prime Editors to the lung epithelium includes the use of lipid nanoparticles with tropism to basal cells of the lung airways.

Our Future Opportunities in Expanding the Prime Editing Pipeline

To maximize the potential of Prime Editing, we have purposefully built a diversified portfolio organized around four strategic indication categories: (1) immediate target indications, (2) differentiation target indications, (3) "blue sky" indications and (4) "march up the chromosome" approaches, with each set of indications chosen to deliver a different strategic goal.

We constructed our current portfolio of 18 programs, including one partnered program, across our first two strategic indication categories in disease settings where the unique characteristics of Prime Editing could offer compelling advantages over current standard-of-care and novel therapeutic modalities in development. We expect to achieve preclinical proof-of-concept *in vivo*, which would include data from *in vivo* rodent studies in several programs in _____ and non-human primate studies in several programs in _____ through _____. If successful, this will allow us to initiate investigational new drug, or IND, enabling studies for several of our lead programs beginning in _____, leading to initial IND filings beginning in _____. Since we are in early stages of product

candidate development, we will provide an update on our timelines in _____, with the potential to accelerate these programs.

Beyond these current 18 programs, we believe we have the ability to advance quickly into similar follow-on programs in blood, liver, eye and ear as we achieve therapeutic success. We also will continue to invest in research around our “blue sky” target indications, which are intended to push new and innovative technological developments in Prime Editing and delivery and extend its application beyond rare genetic diseases and towards our goal of more broadly addressing human disease. These programs remain in the early stages of conception and will become an increasing focus over the next few years. Finally, our “march up the chromosome” approaches represent opportunities to deliver upon our overarching vision to ultimately treat all patients with a disease and correct the full set of mutations in a particular gene. Many of our disclosed indications across our other strategic categories have a plan that can accommodate expansion opportunities to address additional mutations in that disease.

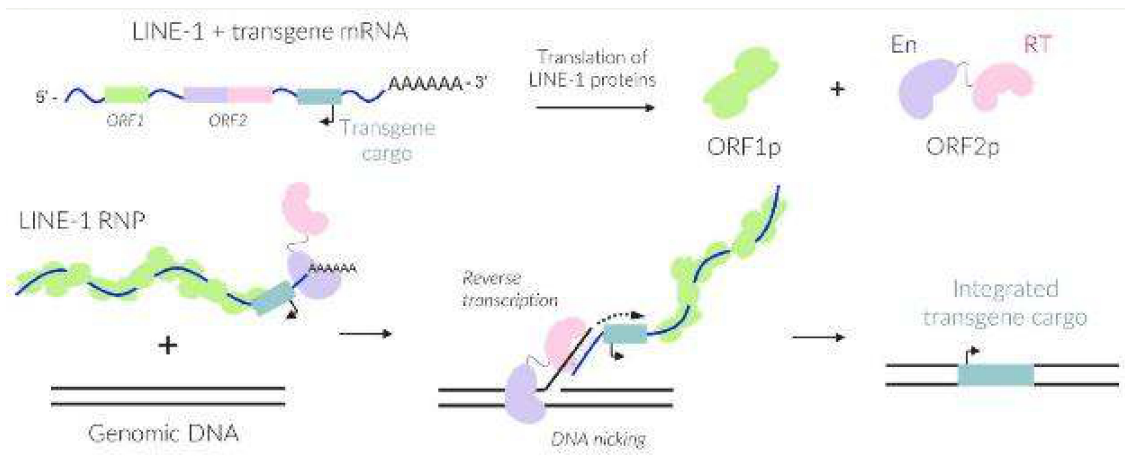
Complementary retrotransposon mediated gene-insertion technology to enable an all-RNA approach to insert gene-sized DNA into the genome

We are continuing to evaluate opportunities that we see as potentially uniquely-positioned to advance our gene editing toolbox, including new technologies to help us to fulfil our strategic goals across both our “blue sky indications” and “march up the chromosome” approaches. For these efforts to be successful, we believe it is important to pursue and to develop technologies that enable the targeted insertion of gene-sized pieces of DNA into the genome. In December 2021, we entered into the Myeloid Agreement with Myeloid, a company primarily focused on harnessing and reprogramming myeloid cells for treating cancers. Through this research collaboration, we received an exclusive option to obtain ownership of certain patent rights and know-how that relate to a new retrotransposon-based technology to enable the insertion of gene-sized DNA sequences into the genome that, if successful, we believe this could open new opportunities for programmable gene editing. See “Our License and Collaboration Agreements—Research Collaboration, Option and License Agreement with Myeloid”

We believe this retrotransposon-based approach is complementary to Prime Editing and, if successfully deployed alongside Prime Editing, could expand the applicability of our Prime Editing technologies towards our goal of more broadly addressing human diseases. The Myeloid team includes experts in retrotransposon biology, complementing our deep in-house gene editing expertise. In addition, Myeloid maintains an intellectual property position in retrotransposon-based editing, which, if we exercise our option, can be transferred to us.

This emerging approach uses human LINE-1 retrotransposase, which has been engineered by Myeloid to insert transgenes into the genome when delivered as an RNA, without the need for co-administration of DNA. We believe this approach may be complementary to the combined Prime Editor with the SSR recombinase approach outlined above.

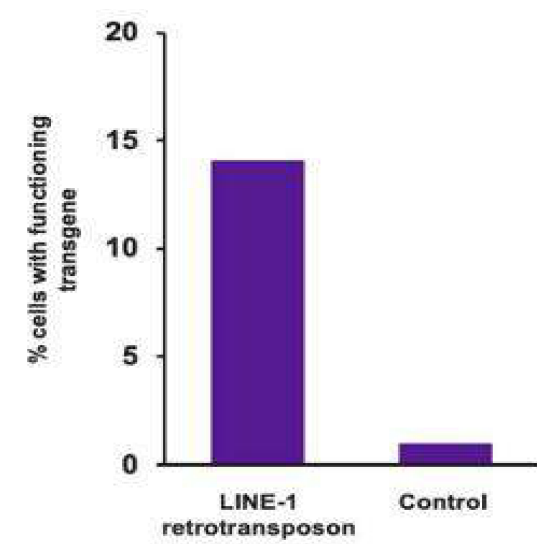
Genomic Integration of Transgenes (>3kb) Using LINE-1 mRNA (No Donor DNA Required)



Note: An mRNA carrying the LINE-1 genes (ORF1 and ORF2) and transgene cargo (teal) is delivered to the cell. Inside the cell, the LINE-1 mRNA is translated, producing ORF1p (green) and ORF2p (purple and pink) proteins. The ORF2p protein contains an endonuclease domain (En, purple) and a reverse transcriptase domain (RT, pink). The ORF1p and ORF2p proteins bind to the LINE-1 mRNA to form a ribonucleoprotein complex (LINE-1 RNP). At permissive sites in the genome, the LINE-1 RNP binds and nicks the DNA using the En domain, and then reverse transcribes the mRNA into the genome using the RT domain, thereby integrating the transgene sequence into the genome. En = endonuclease domain; RT = reverse transcriptase domain; RNP = ribonucleoprotein complex.

This retrotransposase technology is still at an early-stage of development and has not yet been optimized to operate with the same efficiency or programmability as Prime Editing (See Figure below). Using our protein engineering capabilities, we plan to adapt the LINE-1 retrotransposase technology to increase its programmability so that it can be directed to pre-specified, targeted site(s) in the genome, similar to a Prime Editor. Protein engineering and other methods, like those employed to increase the efficiency of Prime Editing, will also be used to increase the efficiency of transgene integration by the LINE-1 retrotransposon. If this research collaboration with Myeloid is successful, we intend to utilize this technology initially in *ex vivo* cell therapies, with the potential to expand and deliver *in vivo* to enable precise gene insertion.

Insertion of a Functioning Transgene using human LINE-1 Retrotransposon Technology



Note: Example of human LINE-1 retrotransposon inserting a green fluorescent protein transgene into primary human monocytes following electroporation of LINE-1 mRNA carrying the sequence for the transgene (Source: Myeloid)

Our License and Collaboration Agreements

Strategic relationship with Beam Therapeutics

In September 2019, we established a strategic, collaborative relationship with Beam Therapeutics Inc., or Beam, a biotechnology company developing precision genetic medicines. One of our founders, David Liu, is also a founder of Beam. Through our relationship, we collaborate with Beam on the research, development, manufacture and commercialization of certain prime editing products within a specified field and provide each other with access and licenses to certain proprietary technology to advance the other's progress.

Mutual access and licenses under the Beam Collaboration Agreement

We entered into a collaboration and license agreement with Beam, which we refer to as the Beam Collaboration Agreement, under which we agree to provide each other with access to, and licenses under, certain technology, know-how and patent rights controlled by each of us for a limited number of years after the effective date, known as the initial term, and certain improvements thereto. Certain licenses we grant to Beam are limited to exploiting licensed products in the Beam field, as further described below, and certain licenses Beam grants to us are limited to exploiting products in the Prime field, as further described below.

Under the Beam Collaboration Agreement, we grant to Beam an exclusive (even as to us and our affiliates), worldwide license under (i) certain prime editing technology, know-how and patent rights that we control during the initial term, and improvements thereto that we control for a specified number of years following the initial term, and (ii) our interest in certain jointly-owned collaboration technology, in each case, solely to develop, make, have made, use, offer for sale, sell, import and commercialize licensed products only in the Beam field, which is limited to (a) the prevention, modification, improvement, amelioration or treatment of human disease, including cell-based therapies and the creation of one or more protective mutations, through administration of a licensed product that incorporates or contains a qualifying prime editing agent, which is a macromolecule or macromolecular complex that uses prime editing to make one or more transition point mutations (that is, C to T, T to C, A to G or G to A) in the sequence of one or more DNA targets, without intentionally making any non-transition mutations or other changes, including insertions, deletions, duplications, indels, transversions or combinations thereof, and does not incorporate or contain any other prime editing agent or other gene editing approach that is not a qualifying prime editing agent or (b) the prevention, modification, improvement, amelioration or treatment of sickle cell disease through administration of a licensed product that incorporates or contains a more broadly defined prime editing agent. We refer to each of clause (a) and clause (b) of the Beam field as subfields. We also grant to Beam a non-exclusive, worldwide license under certain CRISPR or delivery-related technology, know-how and patent rights that we control during the initial term, and improvements thereto that we control for a specified number of years following the initial term, solely to develop, make, have made, use, offer for sale, sell, import and commercialize licensed products only in the Beam field.

Under the Beam Collaboration Agreement, Beam grants to us certain non-exclusive, worldwide licenses under certain technology, know-how and patent rights, including under certain CRISPR or delivery-related technology, know-how and patent rights, that it controls during the initial term, and improvements thereto that Beam controls for a specified number of years following the initial term, solely to develop, make, have made, use, offer for sale, sell, import and commercialize products only in the Prime field, which is limited to the prevention, modification, improvement, amelioration or treatment of human disease (excluding sickle cell disease), including cell-based therapies and the creation of one or more protective mutations, through administration of a product or service containing or incorporating a prime editing agent that is not a qualifying prime editing agent, but excluding (a) the Beam field, (b) the administration of any product or service containing or incorporating a base editor and (c) a field related to microbial cells in the human flora in certain Asia territories and the development of products targeting four named gene targets. For clarity, the Prime field includes products or services that contain or incorporate (x) at least one prime editing agent that is not a qualifying prime editing agent and (y) any other gene-editing approach, including other prime editing agents, which may include one or more qualifying prime editing agents, subject to the

aforementioned exclusions. The licenses granted to us by Beam under the Beam Collaboration Agreement are subject to the terms of certain third party agreements and certain rights retained by third parties.

In addition to the ongoing licenses, under the Beam Collaboration Agreement, we are both obligated to adhere to a technology transfer plan, under which each of us agrees to disclose or otherwise share the technology, know-how and patent rights licensed to the other and to provide the other party with reasonable assistance in the exercise of its licenses.

The licenses granted to each party under the Beam Collaboration Agreement are sublicensable to affiliates and third parties, subject to certain requirements, including providing the other party a copy of each executed sublicense agreement, and ensuring any sublicensee comply with the terms of the Beam Collaboration Agreement.

Beam's development and commercialization of licensed products in the Beam field

Unless we exercise our profit sharing option for a licensed product, as described below, Beam is solely responsible for the development and commercialization of licensed products in the Beam field under the Beam Collaboration Agreement. Beam is required to use commercially reasonable efforts to develop and seek marketing approval for at least one licensed product in each subfield of the Beam field in each of (a) the United States and (b) one other specified major market country, and to commercialize any such licensed product that achieves marketing approval. As described further below, we are entitled to receive ongoing milestone and royalty payments from Beam based on Beam's development and commercialization of each licensed product.

Our profit sharing option

Subject to the provisions in the next paragraph, on a licensed product-by-licensed product basis, we have the right to elect to share equally with Beam in the profits and losses in the United States for Beam's licensed products. We may exercise such right for each licensed product within a specified period of time. Any such licensed product for which we exercise such right we refer to as a collaboration product. If we exercise such right, we agree to share equally in the costs, profits and losses of each such collaboration product in the United States, rather than receiving milestones and royalties based on development and sales thereof by Beam in the United States. For clarity, we are still entitled to receive milestones and royalties on the development and sales of each such collaboration product outside of the United States. We also have the right to elect, within a specified time period, to co-promote with Beam each collaboration product in the United States, in addition to sharing in the profits and losses. To the extent we exercise our co-promote option with respect to a given collaboration product, we and Beam must use commercially reasonable efforts to commercialize such collaboration product, in each case, in the Beam field in the major markets in which marketing authorization has been obtained. After we have exercised our right to profit share on a collaboration product, we are able to, at any time during the term of the Beam Collaboration Agreement, on a collaboration product-by-collaboration product basis, opt-out of the profit and loss share and co-promotion activities with respect to any collaboration product with prior written notice to Beam within a certain time period.

Notwithstanding the rights described above, at any time prior to or within 30 days of the filing of an IND for a licensed product, Beam may designate up to a mid-single digit number of licensed products for which (i) we are not permitted to exercise our profit sharing right, and (ii) Beam assumes sole control and decision-making authority and bears all costs and expenses, with respect to the development and commercialization of such products. Under the Beam Collaboration Agreement, a "protected product" is a licensed product for which either (a) we have not exercised our profit share option or (b) Beam has designated as a protected product pursuant to the foregoing sentence. For clarity, we are entitled to ongoing milestones and royalties from Beam based on its development and commercialization of protected products worldwide. Upon Beam's designation of a licensed product as a protected product, Beam is required to pay us \$5.0 million if the product is developed for non-sickle cell disease or \$10.0 million if the product is developed for sickle cell disease.

Consideration

As partial consideration for the licenses and rights granted to each other under the Beam Collaboration Agreement, Beam issued to us \$5.0 million in shares of its common stock and we issued to Beam an aggregate of 5,000,000 shares of our common stock. Beam is also entitled to appoint a representative to our board of directors, which right expires after a certain period of time or upon the occurrence of various events, including upon our initial public offering. Beam initially appointed its CEO, John Evans, to our board of directors.

We are entitled to receive development milestone payments from Beam on Beam's development of protected products (which, for clarity, includes any licensed product for which we have not exercised our profit share option) and collaboration products. For protected products, we are entitled to receive up to a total of \$35.5 million on a protected product-by-protected product basis based on Beam's development of such protected product and, for collaboration products, up to a total of approximately \$17.8 million on a collaboration product-by-collaboration product basis based on Beam's development of such collaboration product outside of the United States, in each case, with such amounts lowered if such licensed product achieves a given milestone for use in treating an orphan disease. We are also entitled to receive sales-based milestone payments from Beam based on net sales of licensed products. For protected products, we are entitled to receive up to a total of \$84.5 million on a protected product-by-protected product basis based on net sales of such protected product worldwide, and, for collaboration products, up to a total of approximately \$42.3 million on a collaboration product-by-collaboration product basis based on net sales of collaboration products outside of the United States.

The sickle cell disease product partnered with Beam is a licensed product under the Beam Collaboration Agreement. Beam has not designated this product as a protected product and we have not received any development or sales-based milestones with respect to Beam's exploitation thereof.

Beam is obligated to pay to us tiered royalties ranging from a high-single digit percentage to a low double-digit percentage, but less than teens on net sales of protected products worldwide on a protected product-by-protected product basis and net sales of collaboration products outside of the United States on a collaboration product-by-collaboration product basis. Our royalties are subject to customary offsets and reductions, to a floor that takes into account any royalties we are obligated to pay to our third party licensors, including Broad Institute. In addition, certain of the rights licensed under the Beam Collaboration Agreement are sublicensed from third parties, and Beam agrees to reimburse us for certain payments we are required to make to our third party licensors attributable to Beam's exercise of any sublicense we grant to Beam, including payments we make to Broad Institute under the Broad License Agreement.

If we develop a product that is covered by the technology, know-how or patent rights that Beam licenses to us under the Beam Collaboration Agreement, which we refer to as a Prime product, we are obligated to pay to Beam a low single digit percentage royalty on our worldwide net sales of such any product on a Prime product-by-Prime product and country-by-country basis, subject to certain customary reductions, to a floor.

Each party's obligation to pay the other royalties expires on a country-by-country and product-by-product basis on the latest of (a) the expiration of the last to expire valid claim of an issued patent or pending patent application within the applicable licensed patent rights that cover such product in such country, (b) the expiration of regulatory exclusivity for such product in such country or (c) ten (10) years after the first commercial sale of such product in such country.

If we exercise our option to profit share on collaboration products, we share equally in the profits and losses of any such collaboration product in the United States and share in a lower portion of any development or commercialization costs attributable to such collaboration product outside of the United States.

Intellectual property ownership and patent prosecution

Under the Beam Collaboration Agreement, Beam assigns ownership to us of certain improvements Beam makes, itself or jointly with us or others, to certain technology, know-how and patent rights we license to Beam, and we assign to Beam ownership of all improvements we make, ourselves or jointly with Beam or others, certain technology, know-how and patent rights Beam licenses to us. Each party grants back to the other certain exclusive

and non-exclusive licenses to such improvements. Except for any such improvements, each party owns any other inventions that it developed under the Beam Collaboration Agreement and an equal, undivided interest with the other party in any inventions jointly developed.

We are responsible for prosecution and maintenance of the patent rights we license to Beam, while keeping Beam reasonably informed and providing Beam the opportunity to provide comments and make requests of us, in each case regarding the patent rights that we exclusively license to Beam in the field of the exclusive license. Beam has a step-in right to the extent we decline or fail to prosecute any patent rights that are exclusively licensed to Beam and applicable to the Beam field. Beam is responsible for prosecution and maintenance of the patent rights it licenses to us, while keeping us reasonably informed and providing us the opportunity to provide comments and make requests of us, in each case with respect to any patent rights that Beam exclusively licenses to us in the field of the exclusive license.

Beam has the first right to enforce any patent rights we exclusively license to Beam in the Beam field against any third party developing a product in the Beam field that is competitive with a licensed product Beam is developing under the Beam Collaboration Agreement. We have a step-in right on any such enforcement to the extent Beam declines or fails to initiate such enforcement action.

Term and termination

Unless earlier terminated in accordance with its terms, the Beam Collaboration Agreement will expire on the later of (a) expiration of the last royalty term for a product on which a party is obligated to pay royalties to the other party or (b) with respect to any collaboration product, the date on which neither party is developing or commercializing any such collaboration product in the United States.

After expiration of the initial term, Beam can terminate the Beam Collaboration Agreement for convenience in its entirety, or on a licensed product-by-licensed product or subfield-by-subfield basis, with ninety (90) days' prior written notice to Prime. Each party may terminate the Beam Collaboration Agreement for (a) the other party's uncured material breach within ninety (90) days of notice of such breach, (b) upon the insolvency or bankruptcy of the other party if such proceeding is not dismissed within ninety (90) days after the filing thereof or (c) immediately to the extent the other party (or its affiliates or sublicensees) challenges a patent right licensed to such party.

License agreement with Broad Institute

In September 2019, we entered into a license agreement with Broad Institute, and in May 2020 and February 2021, we entered into amendments to the license agreement. We refer to the amended license agreement as the Broad License Agreement. Under the Broad License Agreement, Broad Institute grants to us certain rights and licenses under certain patent rights it owns or controls related to editing of deoxyribonucleic acid (DNA) sequences using a prime editor. Certain of the licensed patent rights are co-owned by Broad Institute with MIT and Harvard.

License rights under the Broad License Agreement

The licenses Broad Institute grants to us under the Broad License Agreement are limited to the field of prevention or treatment of human disease, and most licenses granted to us under the Broad License are further limited to the prevention or treatment of human disease by editing (including modifying or converting) or targeting DNA *ex vivo*, *in vivo*, or through xeno-transplantation methods. We refer to this field as the Prime Broad Field. The Prime Broad Field specifically excludes the prevention or treatment of human disease using small or large molecules that are not otherwise "prime editor products" and other specified agricultural and livestock applications of the technology covered by the licensed patent rights. Under the Broad License Agreement, "prime editors" are macromolecules or macromolecule complexes intended to insert DNA sequence into, delete DNA sequence from, or replace one or more bases of a target DNA sequence, using a combination of (i) natural or engineered reverse transcriptase(s) or any other nucleic acid polymerase enzyme and (ii) a nucleic acid binding protein that can be programmed to bind to a DNA sequence to be so changed. "Prime editor products" are products that combine prime editors and nucleic acid molecules that bind to and direct the prime editors to specified DNA sequences and that contain template sequences for introducing the intended alteration into the specified DNA sequences.

Under the Broad License Agreement, Broad Institute grants to us (i) an exclusive, worldwide license under the licensed patent rights solely to offer for sale, sell, have sold and import products covered by such licensed patent rights, or licensed products, solely for use within the Prime Broad Field (subject to certain specified limitations and exclusions with respect to certain applications), (ii) a non-exclusive, worldwide license under the licensed patent rights solely to make, have made, offer for sale, sell, have sold, and import licensed products solely for use in the Prime Broad Field, (iii) a non-exclusive, worldwide license under the licensed patent rights solely to make, have made, offer for sale, sell, have sold and import other products that are enabled by (a) the licensed patent rights or (b) the use of certain materials transferred to us by Broad Institute, solely for the prevention or treatment of human diseases and (iv) a non-exclusive, worldwide license solely for internal research. Further, with respect to DNA delivery or targeting applications covered by the licensed patent rights, the exclusive license granted to us by Broad Institute is limited only to “prime editor” products and specifically excludes applications relating to the production or processing of small or large molecules, including for the prevention or treatment of human disease.

All of the above license grants (i) specifically exclude (a) human germline modification, (b) the stimulation of biased inheritance of particular genes or traits within a plant or animal population and (c) certain modifications of the tobacco plant, and (ii) are subject to certain retained rights of Broad Institute, MIT and Harvard and the U.S. federal government. Broad Institute also retains certain rights for itself, MIT and Harvard and for other non-for-profit research organizations and government agencies to practice the licensed patent rights for research, teaching, educational and scholarly purposes. In addition, because an employee of HHMI was an inventor on certain of the licensed patent rights, the licenses granted to us with respect to such patent rights are subject to a non-exclusive, irrevocable, worldwide license to HHMI to exercise any such patent rights for research purposes.

We are permitted to sublicense the licensed patent rights to our affiliates and third parties, subject to certain requirements, including that any such sublicense agreement be in compliance with and be consistent with the terms of the Broad License Agreement. In addition, any such sublicense agreement must include certain customary provisions to ensure our ability to comply with the Broad License Agreement. We are also responsible for any breaches of a sublicense agreement by the applicable sublicensee and for all payments due to Broad Institute under the Broad License Agreement by operation of any such sublicense.

Our licenses are subject to Broad Institute’s inclusive innovation model, pursuant to which Broad Institute retains the right, under specified circumstances, to grant to third parties (other than specified competitors of ours) licenses under the licensed patent rights that would otherwise fall within the scope of the exclusive license granted to us. If a third party provides Broad Institute with a bona fide proposal to develop a product covered by the licensed patents and directed to a particular gene target, Broad Institute may notify us of the proposal, including the identity of such gene target and the proposing third party. Broad Institute is not required to share any other information provided by the requester with us in connection with the inclusive innovation model. Within a specified time period following such notification, we may provide Broad Institute with evidence that either (i) we (ourselves, or through our affiliates or sublicensees) are currently developing one or more licensed products directed to the applicable gene target or (ii) we have a good faith interest in developing licensed products directed to such gene target (ourselves, or through our affiliates or sublicensees) or sublicensing our rights to such gene target directly to such third party or another third party. If we notify Broad Institute that we are currently developing licensed products directed to such gene target or that we have a good faith interest in developing licensed products directed to such gene target, we have a specified period of time to evidence such activities or interest by providing Broad Institute with a development plan and either continuing or commencing, respectively, such activities under such development plan. We must continue to use commercially reasonable efforts to continue to progress such activities. If we notify Broad Institute that we have a good faith interest in sublicensing our rights to such third party or another third party, we have a specified period of time to negotiate and enter into a sublicense agreement with a third party. If we (i) notify Broad Institute that we are not interested in developing such product (internally or with another third party) or do not respond to the proposed product notice, or (ii) notify Broad Institute of our interest as outlined above and do not complete or, for an internal program, commence, those activities within the specified time periods, Broad Institute has the right, subject to certain conditions, to terminate our rights to such gene target and may grant to such proposing third party an exclusive or non-exclusive license under the patent rights to exploit products covered by the licensed patent rights and directed to such gene target, which we refer to as a march-in license.

In addition to the inclusive innovation model, our licenses are also subject to Broad Institute's right to designate a single-digit number of gene targets per year in which it has a good faith interest in reserving for its own development of products covered by the patent rights directed to such gene targets. Such reserved gene targets are referred to as a reserved Broad Institute targets. If Broad Institute notifies us that it desires to exercise such right for a given gene target, and we do not, within a specified time period, evidence that we (ourselves or through an affiliate or sublicensee) have an on-going program or good faith interest in pursuing a program for prime editor products for such gene target, Broad Institute may terminate our license with respect to such gene target, with such gene target becoming a reserved Broad Institute target. We have a right to negotiate a sublicense with a third party for-profit company interested in licensing the rights to such reserved Broad Institute targets, which we must complete within a specified period of time, after which Broad Institute may grant such rights to such third party. Broad Institute has not yet exercised its right to designate any reserved gene targets.

Under the Broad License Agreement, we are required to use commercially reasonable efforts to develop licensed products in the Prime Broad Field in accordance with a development plan that we prepared and submitted to Broad Institute. This includes several developmental milestones that we are required to meet with respect to licensed products within a specified number of years. We may update the development plan from time to time if we believe, in our good faith judgment, that such update is needed to improve our ability to meet such development milestones. Broad Institute has the right to terminate the Broad License Agreement if we fail to use commercially reasonable efforts or to achieve a development milestone, subject to our right to extend or amend such milestone in accordance with certain procedures. If, despite using commercially reasonable efforts, we will not achieve a development milestone, we may request an extension of the development milestone timelines by providing a reasonable explanation for the extension and a reasonable, detailed, written plan for promptly achieving such reasonable extended or amended milestone to Broad Institute, and following Broad Institute's approval of the request to delay, the applicable milestone deadline will be automatically amended (to the extent we request an extension of less than a specified number of years). We have not yet requested any such extension and have met the deadlines for diligence milestones that have already occurred. In addition to the diligence obligations to achieve the milestones in the development plan, for any products that attain regulatory approval, we are required to use commercially reasonable efforts to introduce any such licensed product into the commercial market and to commercialize and make such licensed products reasonably available to the public.

Consideration under the Broad License Agreement

As partial consideration for the rights granted to us under the Broad License Agreement, we paid Broad Institute an upfront fee of \$0.5 million, and issued Broad Institute an aggregate of 1,938,429 shares of our common stock.

We also are obligated to pay to Broad Institute an annual license maintenance fee ranging from the low- to mid-five figures to the low six-figures, depending on the particular calendar year, for the term of the Agreement. Broad Institute is also entitled to receive clinical and regulatory milestone payments up to a total of \$20.0 million per licensed product, depending on the patient population to be treated by the licensed product achieving the applicable milestone. If we undergo a change of control at any time during the term of the Broad License Agreement, certain of the clinical and regulatory milestone payments will increase by a specified percentage. Broad Institute is also entitled to sales-based milestone payments up to a total of \$54.0 million per licensed product, depending on the patient population to be treated by the licensed product achieving the applicable milestone. Broad Institute is entitled to lower payments to the extent the clinical and regulatory milestones or sales-based milestones are achieved by enabled products, rather than licensed products.

Broad Institute is entitled to receive mid-single digit percentage royalties on net sales of licensed products, and low single-digit percentage royalties of enabled products. Royalties payable to Broad Institute are subject to customary offsets and reductions with respect to a product in a given country, to a floor. On a country-by-country and product-by-product basis, the royalty term for a product in a country will terminate on the latest of: (i) the expiration of the last to expire valid claim of an issued patent or pending patent application within the licensed patent rights covering such product in such country, (ii) the period of regulatory exclusivity for such product in such country or (iii) ten (10) years after the first commercial sale of such product in such country. As of January 2022, we estimate the last patent right licensed under the Broad License Agreement will expire in 2041, without giving effect to any potential patent term extensions or patent term adjustments. Broad Institute is also entitled to a percentage of

consideration that we receive from our sublicensees, with such percentage at low double-digits and decreasing to high single digits, dependent on the development stage of products under the Broad License Agreement at the time of sublicense execution. If we (or one of our affiliates or sublicensees) initiate a patent challenge of the licensed patent rights, among other things, our payment obligations could be doubled and we could lose exclusivity of our license.

Prosecution and enforcement of licensed patent rights under the Broad License Agreement

Broad Institute is responsible for the prosecution and maintenance of all licensed patent rights, although we are entitled to certain consultation, comment and review rights with respect to such prosecution and maintenance activities of the exclusively licensed patent rights. We are obligated to reimburse Broad Institute for its documented, out-of-pocket costs incurred while prosecuting and maintaining such licensed patent rights.

So long as we remain the exclusive licensee of licensed patent rights in the Prime Broad Field, we have the first right to enforce the licensed patent rights in the Prime Broad Field, where we reasonably determine that a third party is marketing or has specific plans and is preparing to market an infringing product in any country that competes with one of our licensed products in the Prime Broad Field. Broad Institute has a step in right to the extent we decline to exercise such first right to enforce.

Term and termination of the Broad License Agreement

Unless earlier terminated, the Broad License Agreement will remain in effect until the later of (i) the last to expire valid claim of an issued patent or pending patent application within the licensed patent rights covering our licensed products or (ii) the expiration of the last royalty term for a licensed product in a country.

We can terminate the Broad License Agreement for our convenience following prior written notice to Broad Institute. Each party may terminate the Broad License Agreement for the other party's uncured material breach. Broad Institute may also immediately terminate the Broad License Agreement (i) to the extent we (or our affiliates or sublicensees) challenge a licensed patent right, (ii) upon our bankruptcy or insolvency or (iii) if we fail to procure and maintain insurance.

Amendments to the Broad License Agreement

We amended the Broad License Agreement in May 2020 to correct an error to an exhibit to the Broad License Agreement and amended the Broad License Agreement in February 2021 to include additional licensed patent rights. Under the February 2021 amendment, as partial consideration for the addition of licensed patent rights relating to prime editing improvements, we paid Broad Institute an amendment fee of approximately \$0.1 million.

Option Agreement with Broad Institute

In May 2021, we executed an exclusive option agreement with Broad Institute, pursuant to which Broad Institute granted to us an exclusive option to negotiate an amendment to the Broad License Agreement to include certain additional patent rights relating to prime editing improvements to our license thereunder (subject to certain specified limitations and exclusions with respect to certain applications). In connection with the option agreement, Broad Institute also granted to us, during the option period, a limited, non-exclusive license under the new patent rights solely for research purposes to evaluate whether to exercise our option (subject to certain specified exceptions). Our option expires in November 2022, unless we mutually agree in writing with Broad Institute to extend such expiration date. Our option is subject to certain reserved rights by (i) Broad Institute, Harvard, other not-for-profit research organizations and government agencies and certain other third parties, (ii) the US government and (iii) HHMI. Under the option agreement, we own any research data we generate while exercising our evaluation license. If we conceive of any inventions other than research data, Broad Institute (and institutional co-owners of these patent rights) owns such inventions and we assign all of our right, title and interest in such other inventions to Broad Institute. Broad Institute is responsible for the prosecution and maintenance of the patent rights and we agreed to reimburse Broad Institute up to an aggregate of a mid-five figure amount for the out-of-pocket costs it incurs, or has incurred, in prosecuting the applicable patent rights. We also paid Broad Institute an upfront payment of \$50,000 upon execution of the option agreement. We can terminate the option agreement for convenience by providing prior

written notice to Broad Institute, while Broad Institute can terminate if we (i) fail to make a payment to Broad Institute under the option agreement and fail to cure such non-payment within a certain time period, (ii) are otherwise in material breach of the option agreement and fail to cure within a certain time period, or (iii) become insolvent.

Pledge to Broad Institute and Harvard

In February 2021, we committed to donate \$5.0 million to Broad Institute and Harvard annually for 14 years, commencing in 2021, or the Pledge. The Pledge is intended to be used for research and development related to new genome editing technologies, for example Prime Editing, improve on existing genome-editing technologies, identify delivery mechanisms for these technologies and apply these technologies to the understanding and treatment of rare genetic diseases. Initially, one half of the Pledge made to Broad Institute is allocated to Broad Institute and the other half is transferred to Harvard. The division of the Pledge may change at our discretion. The Pledge is not directed to any particular lab or group and, once granted, funds may be used at the sole discretion of Broad Institute and Harvard, consistent with the purpose of the Pledge.

We can terminate the Pledge at our discretion, subject to providing one year of funding from the date of termination. We will evaluate and approve the Pledge annually, and will consider in our annual granting decisions, if the previous year's grant was used for the intended purpose, and if David Liu has continued in good standing on his active agreements with Prime Medicine.

Research Collaboration, Option and License Agreement with Myeloid

In December 2021, we entered into a research collaboration and exclusive option agreement with Myeloid Therapeutics Inc., or Myeloid, and such agreement, the Myeloid Agreement. Under the Myeloid Agreement, we collaborate with Myeloid, a related party, on the research and development of LINE-1 retrotransposon technology. This retrotransposon-based approach is complementary to Prime Editing and, if successfully deployed alongside Prime Editing, could expand the applicability of our technologies towards our goal of more broadly addressing human diseases. In connection with the Myeloid Agreement, we also entered into a subscription agreement with Myeloid under which we were obligated to issue an aggregate of 3,424,422 shares of our common stock as additional consideration for the license.

Myeloid grants to us an exclusive option, exercisable during the research term and for 60 days thereafter, to obtain ownership of certain patent rights and know-how owned by Myeloid that relate to LINE-1 retrotransposon technology. If we exercise our option, in addition to assigning us ownership of the applicable patent rights and know-how, Myeloid also agrees to grant us certain exclusive and non-exclusive licenses, including to certain improvements and other enabling technology.

Following the exercise of our option, we agree to grant Myeloid, in addition to certain other licenses, an exclusive, worldwide license under the assigned patent rights and know-how to develop and commercialize products in the field of myeloid cells and myeloid cell engineering, or the Myeloid Field. As of December 31, 2021, we have not exercised our option.

Upon entering into the Myeloid Agreement, Myeloid was entitled to receive an upfront payment of \$30.0 million in cash and an aggregate of 3,424,422 shares of our common stock, with a then fair value of \$12.0 million, both of which Myeloid received in January 2022. If the research agreement meets its goals, then (i) during the research term, Myeloid is entitled to cash payments of up to \$35.0 million in the aggregate upon the achievement of certain milestones reflecting the technology's development; and (ii) if we exercise our option, we agree to pay to Myeloid an option exercise fee of \$80.0 million in cash, and shares of our common stock with a then fair value of \$30.0 million. Additionally, if the research collaboration meets its goal and we exercise our option, and we are able to proceed with the development and commercialization of a product that is covered by (a) the patent rights or know-how subject to our option or (b) the patent rights or know-how developed by one or both of the parties during the research term related to LINE-1 retrotransposon technology, or, collectively, a Prime Product, Myeloid would be eligible to receive, for the first five Prime Products, development and regulatory milestone payments of up to \$120.0 million on a Prime Product-by-Prime Product basis and sales-based milestone payments of up to \$210.0 million on a Prime Product-by-Prime Product basis.

Myeloid is also eligible to receive tiered low to mid single-digit percentage royalties on our annual aggregate global net sales of Prime Products on a Prime Product-by-Prime Product and country-by-country basis, subject to customary offsets and reductions to a floor. On a country-by-country and Prime Product-by-Prime Product basis, the period during which royalties will be paid will continue until the latest of (i) the expiration date of the last to expire valid claim of an issued patent or pending patent application within the patent rights subject to our option or the patent rights developed by one or both of the parties during the research term related to LINE-1 retrotransposon technology, in each case, covering the applicable Prime Product, (ii) loss of regulatory exclusivity for such Prime Product in such country, or (iii) ten (10) years after the first commercial sale of such Prime Product in such country.

Following the exercise of our option and for a period of two years thereafter, Myeloid will have the right to select up to three targets, subject to certain exclusions, for the development and commercialization of products directed at such targets in all fields and we will be eligible to receive the development, regulatory and sales-based milestone payments and royalty payments as set forth above from Myeloid with respect to such products.

Unless earlier terminated based on customary termination rights, the Myeloid Agreement will continue on a Prime Product-by-Prime Product and country-by-country basis until the expiration of the royalty term for such Prime Product in such country. If we exercise our option, neither party will have the right to terminate the Myeloid Agreement for any reason.

Competition

The pharmaceutical and biotechnology industries, including the gene therapy and gene editing fields, are characterized by rapidly advancing technologies, intense competition and a strong defense of intellectual property. We believe that our Prime Editing technology is highly differentiated and that our considerable expertise in Prime Editing and expanding its capabilities, as well as our team's extensive drug development and manufacturing experience, together with exclusive licenses to this technology have positioned us at the forefront of the field of advanced precision genetic medicines and provided us with significant competitive advantages. Nevertheless, we face potential competition from a variety of companies. There are several companies utilizing CRISPR/Cas9 nuclease technology, including Caribou Biosciences, Inc., Editas Medicine, Inc., CRISPR Therapeutics AG, Intellia Therapeutics, Inc. and Graphite Bio, Inc., among others. Several additional companies such as Sangamo Therapeutics, Inc., Precision BioSciences, Inc. and bluebird bio, Inc. utilize alternative nuclease-based genome editing technologies, including Zinc Fingers, Arcuses and TAL Nucleases. Beam Therapeutics Inc. utilizes base editing technology. In addition, other private companies such as Tessara Therapeutics Pty. Ltd. and Tome Biosciences, Inc. have announced their work in recombinase DNA and RNA gene writers, although little is known publicly about their science or portfolio. Other companies have announced intentions to enter the gene editing field, such as Moderna, Inc. and Pfizer Inc. Most recently, new epigenetic editing companies have emerged, such as Chroma Medicine, Inc. and Tune Therapeutics, Inc. In addition, we face competition from companies utilizing gene therapy, oligonucleotides and cell therapy therapeutic approaches. Several companies such as Arbor Biotechnologies, Inc., Scribe Therapeutics Inc., Mammoth Biosciences, Inc. and Metagenomi, Inc. are actively searching for novel genome editing components and have reported the discovery of new DNA-cutting enzymes. Other companies are active in LNP delivery technologies and advancing those into therapeutics using genetic therapies, including Recode Therapeutics, Inc., Verve Therapeutics, Inc., Generation Bio Co. and Beam Therapeutics Inc., among others.

Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future that are approved to treat the same diseases for which we may obtain approval for our product candidates. This may include gene editing companies with other approaches to editing, as well as other types of therapies, such as small molecule, RNAi, antibody and/or protein therapies.

In addition, many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials and approved products than we do today. Mergers and acquisitions in the pharmaceutical, biotechnology and gene therapy industries may result in resources becoming increasingly concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. We

also compete with these companies in recruiting, hiring and retaining qualified scientific and management talent, establishing clinical trial sites and patient registration for clinical trials, obtaining manufacturing slots at contract manufacturing organizations and in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, particularly if they represent cures, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. The key competitive factors affecting the success of all of our programs are likely to be their efficacy, safety, convenience and availability of reimbursement.

Manufacturing

We currently have no commercial manufacturing capabilities. For our initial wave of clinical programs, we intend to use qualified third-party contract manufacturing organizations, or CMOs, with relevant manufacturing experience in genetic medicines. We plan to partner with suppliers and CMOs to produce or process critical raw materials, bulk compounds, formulated compounds, viral vectors or engineered cells for IND-supporting activities and early-stage clinical trials. At the appropriate time in the product development process, we will determine whether to establish in-house GMP manufacturing capabilities for some core technologies or continue to rely on third parties to manufacture commercial quantities for any products that we may successfully develop.

Intellectual Property

Our success depends in large part on our ability to obtain and maintain intellectual property protection for our platform technology, our programs and know-how related to our business, defend and enforce our intellectual property rights, in particular, our patent rights, preserve the confidentiality of our trade secrets and other confidential or proprietary information and operate without infringing, misappropriating or otherwise violating any intellectual property rights of others. We seek to protect our proprietary position by, among other things, exclusively licensing and filing U.S. and certain foreign patent applications related to our platform technology, existing and planned programs and improvements that are important to the development of our business, where patent protection is available. We do not currently own or in-license any issued patents in any jurisdiction covering our Prime Editing technology or product candidates. Notwithstanding our efforts, we cannot be sure that patents will be issued with respect to any patent applications we have licensed or filed or may license or file in the future, and we cannot be sure that any patents that may be licensed or issued to us in the future will not be challenged, invalidated, narrowed in scope, rendered unenforceable or circumvented or that such patents will be commercially useful in protecting our technology. For more information regarding the risks related to our intellectual property, please see “Risk Factors—Risks Related To Our Intellectual Property.”

Our wholly owned and our in-licensed patent applications cover various aspects of our Prime Editing platform and our programs, including:

- Prime Editors
- Prime Editing guide RNA, or pegRNA, and modified pegRNAs
- Prime Editing complexes and methods
- Dual-Flap Prime Editing technology
- Program-specific pegRNAs and therapeutic methods
- Prime Editors with enhanced activity
- Engineered pegRNAs
- Delivery modalities

We intend to continue to pursue, when possible, additional patent protection, including composition of matter, method of use, delivery modality and process claims, directed to our platform technology and the programs in our portfolio. We also intend to expand and extend our Prime Editing platform and programs, as well as obtain rights to delivery modalities, through one or more licenses from third parties.

As of February 4, 2022, we owned approximately 28 pending U.S. provisional patent applications. Our owned patent applications are generally related to our Prime Editing technology, including claims to modified pegRNAs, Prime Editors with enhanced activities (e.g., improved Prime Editing efficiency), methods of using such Prime Editors and pegRNAs, program-specific pegRNAs directed to targeting and correcting specific mutations and methods of using such pegRNAs therapeutically. These provisional patent applications are not eligible to become issued patents until, among other things, we file non-provisional patent applications within 12 months of filing one or more of our related provisional patent applications. Any U.S. non-provisional patent applications timely filed based on any of these U.S. provisional patent applications, if issued, and if the appropriate maintenance or annuity fees are paid, are expected to expire in 2042, excluding any additional term for patent term adjustments or patent term extensions or similar provisions in foreign jurisdictions.

As of February 4, 2022, we have in-licensed approximately four pending U.S. patent applications, two pending PCT applications, two pending U.S. provisional applications and 41 pending ex-U.S. patent applications, in each case, related to Prime Editing, from Broad Institute. The patents and patent applications outside of the United States were filed in the European Patent Office, Japan, China and certain other foreign jurisdictions. The patent applications from our in-licensed portfolio for Prime Editing are generally related to Prime Editors, pegRNAs, Prime Editing complexes and systems; compositions including the Prime Editors, pegRNAs and Prime Editing complexes as a component; methods of using such Prime Editors, pegRNAs and Prime Editing complexes and systems, including methods for therapeutic indications; pegRNAs that target and correct therapeutically relevant DNA sequences; and delivery modalities for Prime Editing systems, including the use of adeno-associated viral vectors, or AAV, in a split AAV system for viral delivery of a Prime Editor. The in-licensed patent applications cover various aspects related to the Prime Editing platform technology, including Prime Editors that employ CRISPR-Cas protein domains, such as Cas9 nickases and DNA polymerase domains, such as reverse transcriptase domains. The exclusive in-licensed patent applications also cover dual-flap Prime Editing technology, including dual-flap Prime Editing compositions and methods of using such technology for therapeutic indications and engineered pegRNAs, including compositions and methods comprising such pegRNAs. Our current in-licensed U.S. and foreign patent applications, if issued and if the appropriate maintenance or annuity fees are paid, are expected to expire as early as 2040, excluding any additional term for patent term adjustments or patent term extensions or similar provisions in foreign jurisdictions.

The term of individual patents depends upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country. However, the actual protection afforded by a patent varies from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. In the United States, a patent's term may, in certain cases, be lengthened by patent term adjustment, or PTA, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent or may be shortened, e.g., if a patent is terminally disclaimed over a commonly owned patent having an earlier expiration date. In some instances, such a PTA may result in a U.S. patent term extending beyond 20 years from the earliest date of filing a non-provisional patent application related to the U.S. patent. Patent term extensions, or PTE, under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the Hatch-Waxman Amendments, are also possible for patents that cover an FDA-approved drug as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Amendments permit a PTE of up to five years beyond the expiration of the patent. The length of the PTE is related to the length of time the drug is under regulatory review. PTE cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent per product may be extended and only those claims covering an approved product, a method for using it or a method of manufacturing it, may be extended. Similar provisions are available in Europe and certain other jurisdictions to extend the term of a patent that covers an approved drug. In the future, if our products receive regulatory approval, we may be eligible to apply for PTEs on

patents covering such products, however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such PTE should be granted, and if granted, the length of such PTE. For more information regarding the risks related to our intellectual property, please see “Risk Factors—Risks Related To Our Intellectual Property.”

We also rely on trade secrets, know-how, continuing technological innovation and confidential information to develop and maintain our proprietary position and protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have implemented measures to protect and preserve our trade secrets, such measures can be breached, and we may not have adequate remedies for any such breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. For more information regarding the risks related to our intellectual property, please see “Risk Factors—Risks Related To Our Intellectual Property.”

Government Regulation

In the United States, biological products, including gene therapy products, are subject to regulation under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, and the Public Health Service Act, or PHS Act, and other federal, state, local and foreign statutes and regulations. Both the FD&C Act and the PHS Act and their corresponding regulations govern, among other things, the research, development, clinical trial, testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, reporting, advertising and other promotional practices involving biological products. Each clinical trial protocol for a gene therapy product must be reviewed by the FDA. FDA approval must be obtained before the marketing of biological products. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and we may not be able to obtain the required regulatory approvals.

Ethical, social and legal concerns about gene therapy, genetic testing and genetic research could result in additional laws and regulations restricting or prohibiting the processes we may use. Federal and state legislatures, agencies, congressional committees and foreign governments have expressed interest in further regulating biotechnology. More restrictive laws and regulations or interpretations of existing laws or regulations, or claims that our products are unsafe or pose a hazard, could prevent us from commercializing any products. New government requirements may be established that could delay or prevent regulatory approval of our product candidates under development. It is impossible to predict whether legislative changes will be enacted, regulations, policies or guidance changed, or interpretations by agencies or courts changed, or what the impact of such changes, if any, may be.

U.S. Biological Products Development Process

The process required by the FDA before a biological product may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests and animal studies according to good laboratory practices, or GLPs, unless justified and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- submission to the FDA of an application for an investigational new drug application, or IND, which must become effective before human clinical trials may begin;
- approval of the protocol and related documentation by an independent institutional review board, or IRB, or ethics committee at each clinical trial site before each study may be initiated;
- performance of adequate and well-controlled human clinical trials according to the FDA’s regulations commonly referred to as good clinical practices, or GCPs, and any additional requirements for the

protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biological product for its intended use;

- submission to the FDA of a biologics license application, or BLA, for marketing approval that includes sufficient evidence of establishing the safety, purity and potency of the proposed biological product for its intended indication, including from results of nonclinical testing and clinical trials;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with current good manufacturing practice, or cGMP, to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity and, if applicable, the FDA's current good tissue practices, or CGTPs, for the use of human cellular and tissue products;
- potential FDA audit of the nonclinical study and clinical trial sites that generated the data in support of the BLA in accordance with any applicable expedited programs or designations;
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- payment of user fees for FDA review of the BLA (unless a fee waiver applies); and
- FDA review and approval, or licensure, of the BLA.

Before testing any biological product candidate, including a gene therapy product, in humans, the product candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product biological characteristics, chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs.

An IND is an exemption from the FD&C Act that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. Such authorization must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved BLA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, must be submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Information about certain clinical trials, including clinical trial results, must be submitted within specific timeframes for publication on the www.clinicaltrials.gov website.

A sponsor may choose, but is not required, to conduct a foreign clinical trial under an IND. When a foreign clinical trial is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical trial is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval or

licensing. In particular, such studies must be conducted in accordance with GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The FDA must be able to validate the data through an onsite inspection, if deemed necessary by the FDA.

An IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee, or DSMB. This group provides authorization as to whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study.

In addition to the submission of an IND to the FDA before initiation of a clinical trial in the United States, certain human clinical trials involving recombinant or synthetic nucleic acid molecules are subject to oversight of institutional biosafety committees, or IBCs, as set forth in the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines. Specifically, under the NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

Information about clinical trials must be submitted within specific timeframes to the NIH for public dissemination on its [ClinicalTrials.gov](https://clinicaltrials.gov) website.

Clinical trials typically are conducted in three sequential phases that may overlap or be combined:

- Phase 1. The biological product is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- Phase 2. The biological product is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for approval and product labeling.

Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up. The FDA generally recommends that sponsors of human gene therapy products integrating vectors such as gammaretroviral and lentiviral vectors and transposon elements as well as genome editing products observe subjects for potential gene therapy-related delayed adverse events for up to a 15-year period, including five years of annual examinations followed by ten years of annual queries, either by telephone or by questionnaire, of study subjects.

Both the FDA and the European Medicines Agency, or EMA, provide expedited pathways for the development of drug product candidates for treatment of rare diseases, particularly life-threatening diseases with high unmet medical need. Such drug product candidates may be eligible to proceed to registration following a single clinical trial in a limited patient population, sometimes referred to as a Phase 1/2 trial, but which may be deemed a pivotal or registrational trial following review of the trial's design and primary endpoints by the applicable regulatory agencies. Determination of the requirements to be deemed a pivotal or registrational trial is subject to the applicable regulatory authority's scientific judgement and these requirements may differ in the U.S. and the European Union, or EU.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA, the NIH and the investigators for serious and unexpected adverse events, any findings from other studies, tests in laboratory animals or *in vitro* testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within 7 calendar days after the sponsor's initial receipt of the information. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor, acting on its own or based on a recommendation from the sponsor's data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biological product has been associated with unexpected serious harm to patients.

Human gene therapy products are still a relatively new category of therapeutics. Because this is a still an expanding area of novel therapeutic interventions, there can be no assurance as to the length of the study period, the number of patients the FDA will require to be enrolled in the studies in order to establish the safety, purity and potency of human gene therapy products, or that the data generated in these studies will be acceptable to the FDA to support marketing approval.

Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the physical characteristics of the biological product as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHS Act emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

U.S. Review and Approval Processes

After the completion of clinical trials of a biological product, FDA approval of a BLA must be obtained before commercial marketing of the biological product. The BLA must include results of product development, laboratory and animal studies, human studies, information on the manufacture and composition of the product, proposed labeling and other relevant information. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the FDA accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. In most cases, the submission of a BLA is subject to a substantial

application user fee, although the fee may be waived under certain circumstances. Under the performance goals and policies implemented by the FDA under the Prescription Drug User Fee Act, or PDUFA, for original BLAs, the FDA targets ten months from the filing date in which to complete its initial review of a standard application and respond to the applicant, and six months from the filing date for an application with priority review. The FDA does not always meet its PDUFA goal dates, and the review process is often significantly extended by FDA requests for additional information or clarification. This review typically takes twelve months from the date the BLA is submitted to the FDA because the FDA has approximately two months to make a “filing” decision. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe, pure and potent, for its intended use, and whether the product is being manufactured in accordance with cGMP to ensure the continued safety, purity and potency of such product. The FDA may refer applications for novel biological products or biological products that present difficult or novel questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the biological product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to assure the safe use of the biological product. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

Before approving a BLA, the FDA typically will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. For a gene therapy product, the FDA also will not approve the product if the manufacturer is not in compliance with the CGTPs. These are FDA regulations that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues and cellular and tissue-based products, or HCT/Ps, which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the CGTP requirements is to ensure that cell and tissue-based products are manufactured in a manner designed to prevent the introduction, transmission and spread of communicable disease. FDA regulations also require tissue establishments to register and list their HCT/Ps with the FDA and, when applicable, to evaluate donors through appropriate screening and testing. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND study requirements and GCP requirements. During the ongoing COVID-19 pandemic, restrictions preventing the conduct or completion of facility or clinical site inspections can lead to FDA deferred action on marketing applications or the issuance of complete response letters. To assure cGMP, CGTP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production and quality control.

Under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA for a novel product (e.g., new active ingredient, new indication, etc.) must contain data to assess the safety and effectiveness of the biological product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the BLA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. If the FDA decides not to approve the BLA in its present form, the FDA will issue a complete response letter that usually describes all of the specific deficiencies in the BLA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the

complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, including to subpopulations of patients, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings precautions or interactions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing or dispensing in the form of a REMS, or otherwise limit the scope of any approval. In addition, the FDA may require post-marketing clinical trials, sometimes referred to as Phase 4 clinical trials, designed to further assess a biological product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug or biological product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting a BLA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same biological product for the same use or indication, and we are unable to demonstrate that our product is clinically superior to the previously approved drug for the same use or indication. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. Orphan drug status in the European Union has similar, but not identical, benefits.

Rare Pediatric Disease Designation and Priority Review Vouchers

Under the FD&C Act, the FDA incentivizes the development of drugs and biological products that meet the definition of a "rare pediatric disease," defined to mean a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years and the disease affects fewer than 200,000 individuals in the United States or affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making in the United States a drug or biological product for such disease or condition will be received from sales in the United States of such drug or biological product. The sponsor of a product candidate for a rare pediatric disease may be eligible for a voucher that can be used to obtain a priority review for a subsequent human drug or biological product application after the date of approval of the rare pediatric disease drug or biological product, referred to as a priority review voucher, or PRV. A sponsor may request rare pediatric disease designation from the FDA prior to the submission of its BLA. A rare pediatric disease designation does not guarantee that a sponsor will receive a PRV upon approval of its BLA. Moreover, a sponsor who chooses not to submit a rare pediatric disease designation request may nonetheless receive a PRV upon approval of their marketing application if they request such a voucher in their original marketing application and meet all of the eligibility criteria. If a PRV is received, it may be sold or transferred an unlimited number of times.

Congress has extended the PRV program through September 30, 2024, with the potential for PRVs to be granted through September 30, 2026.

Expedited Development and Review Programs

The FDA has various programs, including fast track designation, breakthrough therapy designation, accelerated approval and priority review, that are intended to expedite or simplify the process for the development and FDA review of drugs and biologics that are intended for the treatment of serious or life-threatening diseases or conditions. These programs do not change the standards for approval but may help expedite the development or approval process. To be eligible for fast track designation, new drugs and biological products must be intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug or biologic may request the FDA to designate the drug or biologic as a fast track product at any time during the clinical development of the product. One benefit of fast track designation, for example, is that the FDA may consider for review sections of the marketing application for a product that has received fast track designation on a rolling basis before the complete application is submitted.

Under the FDA's breakthrough therapy program, products intended to treat a serious or life-threatening disease or condition may be eligible for the benefits of the Fast Track program when preliminary clinical evidence demonstrates that such product may have substantial improvement on one or more clinically significant endpoints over existing therapies. Additionally, the FDA will seek to ensure the sponsor of a breakthrough therapy product receives timely advice and interactive communications to help the sponsor design and conduct a development program as efficiently as possible.

Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological product designated for priority review in an effort to facilitate the review. Under priority review, the FDA's goal is to review an application in six months once it is filed, compared to ten months for a standard review.

Additionally, a product may be eligible for accelerated approval. Drug or biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on an intermediate clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

RMAT Designation

As part of the 21st Century Cures Act, enacted in December 2016, Congress amended the FD&C Act to facilitate an efficient development program for, and expedite review of regenerative medicine advanced therapy, or RMAT, which include cell and gene therapies, therapeutic tissue engineering products, human cell and tissue products and combination products using any such therapies or products. RMAT do not include those HCT/Ps regulated solely under section 361 of the PHS Act and 21 CFR Part 1271. This program is intended to facilitate efficient development and expedite review of regenerative medicine therapies, which are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition and qualify for RMAT designation. A drug sponsor may request that FDA designate a drug as a RMAT concurrently with or at any time after submission of an IND. FDA has 60 calendar days to determine whether the drug meets the criteria, including whether there is preliminary clinical evidence indicating that the drug has the potential to address unmet medical needs for a serious or life-threatening disease or condition. A BLA for a regenerative medicine therapy that has received RMAT designation may be eligible for priority review or accelerated approval through use of surrogate or intermediate endpoints

reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites. Benefits of RMAT designation also include early interactions with FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A regenerative medicine therapy with RMAT designation that is granted accelerated approval and is subject to post-approval requirements may fulfill such requirements through the submission of clinical evidence from clinical trials, patient registries, or other sources of real world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post-approval monitoring of all patients treated with such therapy prior to its approval. Like some of the FDA's other expedited development programs, RMAT designation does not change the standards for approval but may help expedite the development or approval process.

Post-Approval Requirements

Maintaining substantial compliance with applicable federal, state and local statutes and regulations requires the expenditure of substantial time and financial resources. Rigorous and extensive FDA regulation of biological products continues after approval, particularly with respect to cGMP. We currently rely, and may continue to rely, on third parties for the production of clinical and commercial quantities of any products that we may commercialize. Manufacturers of our products are required to comply with applicable requirements in the cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to biological products, include reporting of cGMP deviations that may affect the identity, potency, purity and overall safety of a distributed product, record-keeping requirements, reporting of adverse effects, reporting updated safety and efficacy information, and complying with electronic record and signature requirements. After a BLA is approved, the product also may be subject to official lot release. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA also may perform certain confirmatory tests on lots of some products, such as viral vaccines, before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency and effectiveness of biological products.

We also must comply with the FDA's advertising and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical holds, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors or other stakeholders, debarment, restitution, disgorgement of profits, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Biological product manufacturers and other entities involved in the manufacture and distribution of approved biological products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved BLA, including withdrawal of the product from the market. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of the use of our product candidates, some U.S. patents that may issue from our pending patent applications may be eligible for limited patent term extension under the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved biological product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. In addition, only those claims covering the approved product, a method for using it, or a method for manufacturing it may be extended, and a patent can only be extended once and only for a single product. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for one of the patents that may issue from our pending patent applications, if and as applicable, to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA. However, there can be no assurance that our pending patent applications will issue or that we will benefit from any patent term extension or favorable adjustments to the terms of any patents we may own or in-license in the future.

A biological product can obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods, including some regulatory exclusivity periods tied to patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

The ACA, signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 which created an abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product. This amendment to the PHS Act attempts to minimize duplicative testing. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, animal studies and a clinical trial or trials. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

A reference biological product is granted four- and 12-year exclusivity periods from the time of first licensure of the product. FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product, and FDA will not approve an application for a biosimilar or interchangeable product based on the reference biological product until twelve years after the date of first licensure of the reference product. "First licensure" typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength, or for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency. Therefore, one must determine whether a new product includes a modification to the structure of a previously licensed product that results in a change in safety, purity, or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of exclusivity. Whether a subsequent application, if approved, warrants exclusivity as the "first licensure" of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act, to which we are subject, prohibits corporations and individuals from engaging in certain activities to obtain or retain business or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity.

Government Regulation Outside of the United States

In addition to regulations in the United States, we are subject to a variety of regulations in other jurisdictions governing, among other things, research and development, clinical trials, testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, reporting, advertising and other promotional practices involving biological products as well as authorization and approval of our products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials must be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension of clinical trials, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

European Union Clinical Trials Regulation

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a clinical trial application, or CTA, must be submitted for each clinical trial to each country's National Competent Authority, or NCA, and at least one independent Ethics Committee, or EC, much like the FDA and an IRB, respectively. Once the CTA is approved in accordance with a country's requirements, the corresponding clinical trial may proceed. Under the current regime (the EU Clinical Trials Directive 2001/20/EC and corresponding national laws) all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the EU Member State where they occurred.

In April 2014, the European Union adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to come in to effect and replace the current Clinical Trials Directive 2001/20/EC on January 31, 2022. It will overhaul the current system of approvals for clinical trials in the European Union. Specifically, the new regulation, which will be directly applicable in all Member States (meaning that no national implementing legislation in each European Union Member State is required), aims at simplifying and streamlining the approval of clinical trials in the European Union. For instance, the new Clinical Trials Regulation provides for a streamlined application procedure via a single entry point and strictly defined deadlines for the assessment of clinical trial applications.

EU Drug Review and Approval

In the EU, medicinal products can only be commercialized after obtaining a marketing authorization. To obtain regulatory approval of a medicinal product in the EU, we must submit a marketing authorization application, or MAA. A centralized marketing authorization is issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA, and is valid throughout the EU. The centralized procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicinal products (gene-therapy, somatic cell-therapy or tissue-engineered medicines), and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions, and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

Under the centralized procedure the maximum timeframe for the evaluation of a MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of a MAA considerably beyond 210 days. Where the CHMP gives a positive opinion, it provides the opinion together with supporting documentation to the European Commission, who make the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of a MAA under the accelerated assessment procedure is 150 days, excluding clock stops, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.

Now that the UK (which comprises Great Britain and Northern Ireland) has left the European Union, Great Britain will no longer be covered by centralized marketing authorizations (under the Northern Ireland Protocol, centralized marketing authorizations will continue to be recognized in Northern Ireland). All medicinal products with a current centralized marketing authorization were automatically converted to Great Britain marketing authorizations on January, 1 2021. For a period of two years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, the UK medicines regulator, may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain marketing authorization. A separate application will, however, still be required.

Periods of Authorization and Renewals

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a re-evaluation of the risk benefit balance by the EMA for a centrally authorized product, or by the competent authority of the authorizing Member State for a nationally authorized product. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any authorization that is not followed by the placement of the drug on the EU market (in the case of the centralized procedure) or on the market of the authorizing Member State for a nationally authorized product within three years after authorization, or if the drug is removed from the market for three consecutive years, ceases to be valid.

Data and Marketing Exclusivity

The EU also provides opportunities for market exclusivity. Upon receiving marketing authorization in the EU, innovative medicinal products generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents generic or biosimilar applicants from referencing the innovator's preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EU, during a period of eight years from the date on which the reference product was first authorized in the EU. During the additional two-year period of market exclusivity, a generic or

biosimilar marketing authorization can be submitted and the innovator's data may be referenced, but no generic or biosimilar product can be marketed until the expiration of the market exclusivity period. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if an innovative medicinal product gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained a marketing authorization based on a MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials. There is, however, no guarantee that a product will be considered by the European Union's regulatory authorities to be an innovative medicinal product, and products may therefore not qualify for data exclusivity.

Orphan Drug Designation and Exclusivity

Products with an orphan designation in the EEA can receive ten years of market exclusivity, during which time "no similar medicinal product" for the same indication may be placed on the market. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. An orphan product can also obtain an additional two years of market exclusivity in the EEA where an agreed Pediatric Investigation Plan for pediatric studies has been complied with. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

The criteria for designating an "orphan medicinal product" in the EEA are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as an orphan medicinal product if it meets the following criteria: (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; and (2) either the prevalence of such condition must not be more than five in 10,000 persons in the EEA when the application is made, or without the benefits derived from orphan status, it must be unlikely that the marketing of the medicine would generate sufficient return in the EEA to justify the investment needed for its development; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EEA, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. The application for orphan drug designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the MAA if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Otherwise, orphan medicine marketing exclusivity may be revoked only in very select cases, such as if:

- a second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- the marketing authorization holder consents to a second orphan medicinal product application; or
- the marketing authorization holder cannot supply enough orphan medicinal product.

Pediatric Development

In the EEA, companies developing a new medicinal product must agree upon a Pediatric Investigation Plan, or PIP, with the EMA's Pediatric Committee, or PDCO, and must conduct pediatric clinical trials in accordance with that PIP, unless a waiver applies, (e.g., because the relevant disease or condition occurs only in adults). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The marketing authorization application for the product must include the

results of pediatric clinical trials conducted in accordance with the PIP, unless a waiver applies or a deferral has been granted by the PDCO of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults, in which case the pediatric clinical trials must be completed at a later date. Products that are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six month extension of the protection under a supplementary protection certificate (if any is in effect at the time of approval) even where the trial results are negative. In the case of orphan medicinal products, a two year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

PRIME Designation

In March 2016, the EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation, where the marketing authorization application will be made through the centralized procedure. Eligible products must target conditions for which there is an unmet medical need (there is no satisfactory method of diagnosis, prevention or treatment in the EEA or, if there is, the new medicine will bring a major therapeutic advantage) and they must demonstrate the potential to address the unmet medical need by introducing new methods of therapy or improving existing ones. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated Agency contact and rapporteur from the CHMP or CAT are appointed early in PRIME scheme facilitating increased understanding of the product at EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies. Where, during the course of development, a medicine no longer meets the eligibility criteria, support under the PRIME scheme may be withdrawn.

Post-Approval Controls

Following approval, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of the medicinal product. These include the following:

- The holder of a marketing authorization must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.
- All new MAAs must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the marketing authorization. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs or the conduct of additional clinical trials or post-authorization safety studies. RMPs and PSURs are routinely available to third parties requesting access, subject to limited redactions.
- All advertising and promotional activities for the product must be consistent with the approved Summary of Product Characteristics and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the European Union. Although general requirements for advertising and promotion of medicinal products are established under European Union directives, the details are governed by regulations in each European Union Member State and can differ from one country to another.

Brexit and the Regulatory Framework in the United Kingdom

In June 2016, the electorate in the United Kingdom voted in favor of leaving the European Union (commonly referred to as “Brexit”). Thereafter, in March 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The United Kingdom formally left the European Union on January 31, 2020. A transition period began on February 1, 2020, during which European Union pharmaceutical law remained applicable to the United Kingdom. This transition period ended on December 31, 2020. Since the regulatory framework in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union Directives and Regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom as United Kingdom legislation now has the potential to diverge from European Union legislation. It remains to be seen how Brexit will impact regulatory requirements for product candidates and products in the United Kingdom in the long-term. The MHRA, the United Kingdom medicines and medical devices regulator, has recently published detailed guidance for industry and organizations to follow from January 1, 2021 now that the transition period is over, which will be updated as the United Kingdom’s regulatory position on medicinal products evolves over time. Brexit has also created uncertainty with regard to data protection regulation in the United Kingdom, and in particular, how data transfers from the European Union to the United Kingdom will be regulated. The European Union and the United Kingdom have agreed a bridging period of up to 6 months to allow the continued free flow of data from the European Union to the United Kingdom, during which time the European Commission will assess whether the United Kingdom will be granted adequacy status. There is no certainty that an adequacy decision will be granted. If it is not, legal uncertainties regarding the flow of data across borders could increase the complexity and cost of transferring personal data from the European Union to the United Kingdom.

Other Healthcare Laws and Compliance Requirements

Insurance and Coverage

In the United States and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments such as gene therapy products. Sales of these or other product candidates that we may identify will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is also significant uncertainty related to the insurance coverage and reimbursement of newly approved products and coverage may be more limited than the purposes for which the medicine is approved by the FDA or comparable foreign regulatory authorities. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or HHS. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;

- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

In addition, many third-party payors are increasingly limiting both coverage and the level of reimbursement of new drugs. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price, or ASP, and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs. Net prices for drugs may be also reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States.

Further, due to the COVID-19 pandemic, millions of individuals have lost/will be losing employer-based insurance coverage, which may adversely affect our ability to commercialize our products. As noted above, in the U.S., we plan to have various programs to help patients afford our products, including patient assistance programs and co-pay coupon programs for eligible patients.

Other healthcare laws and compliance requirements

In the United States, our current and future operations are subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, CMS, other divisions of HHS (such as the Office of Inspector General, Office for Civil Rights and the Health Resources and Service Administration), the U.S. Department of Justice, or DOJ, and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, our clinical research, sales, marketing and scientific/educational grant programs may have to comply with the anti-fraud and abuse provisions of the Social Security Act, the false claims laws, the privacy and security provisions of the Health Insurance Portability and Accountability Act of 1996, or HIPAA, and similar state laws, each as amended, as applicable:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order, arrangement or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs; a person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers, among others, on the other. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act or federal civil money penalties statute;
- the federal civil and criminal false claims laws and civil monetary penalty laws, including the False Claims Act, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false or fraudulent claims for payment to, or approval by, Medicare, Medicaid, or other federal healthcare programs, knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government, or knowingly concealing or knowingly and improperly avoiding or decreasing or concealing an obligation to pay money to the federal government. A claim that includes items or services resulting

from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim under the False Claims Act. Manufacturers can be held liable under the False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. The False Claims Act also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the False Claims Act and to share in any monetary recovery;

- HIPAA, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious, or fraudulent statements or representations in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions;
- the federal transparency requirements under the Affordable Care Act, or ACA, including the provision commonly referred to as the Physician Payments Sunshine Act, and its implementing regulations, which require applicable manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program (with certain exceptions) to report annually to CMS, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners;
- federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- analogous state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers or patients; state laws that require pharmaceutical companies to comply with the industry’s voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state and local laws that require the licensure of sales representatives; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information; data privacy and security laws and regulations in foreign jurisdictions that may be more stringent than those in the United States (such as the European Union, which adopted the General Data Protection Regulation, which became effective in May 2018); state laws governing the privacy and security of health information in

certain circumstances, many of which differ from each other in significant ways and may not have the same effect; and state laws related to insurance fraud in the case of claims involving private insurers.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws.

Law enforcement authorities are increasingly focused on enforcing fraud and abuse laws, and it is possible that some of our practices may be challenged under these laws. Efforts to ensure that our current and future business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. If our operations, including our arrangements with physicians and other healthcare providers, are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, administrative, criminal and/or civil penalties, damages, fines, disgorgement, reputational harm, imprisonment, the exclusion or suspension from federal and state healthcare programs such as Medicare and Medicaid and debarment from contracting with the U.S. government, and/or the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. If any of the physicians or other healthcare providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to similar penalties.

The risk of our being found in violation of these laws is increased by the fact that many of these laws have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain a robust system to comply with multiple jurisdictions with different compliance and reporting requirements increases the possibility that a healthcare company may violate one or more of the requirements. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial cost.

Healthcare reform

In the United States and some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system directed at broadening the availability of healthcare, improving the quality of healthcare, and containing or lowering the cost of healthcare. For example, in March 2010, the ACA, was enacted which includes changes to the coverage and payment for products under government health care programs. Among other things, the ACA:

- increases the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program;
- addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- extends the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care plans;
- establishes annual fees and taxes on manufacturers of certain branded prescription drugs;
- creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50 percent (increased to 70 percent pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.;
- expanded the entities eligible for discounts under the PHS Act's pharmaceutical pricing program, also known as the 340B Drug Pricing Program;

There have been executive, judicial and congressional challenges to certain aspects of the ACA. On February 10, 2021, the Biden administration withdrew the federal government's support for overturning the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, from February 15, 2021 through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden administration or other efforts, if any, to challenge, repeal, or replace the ACA will impact our business. There is no assurance that federal or state health care reform will not adversely affect our future business and financial results, and we cannot predict how future federal or state legislative, judicial or administrative changes relating to healthcare reform will affect our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, on March 22, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100 percent of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. Further, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. Specifically, the Joint Select Committee on Deficit Reduction, asked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2 percent per fiscal year, which went into effect in April 2013, and, due to subsequent legislative amendments, will remain in effect through 2030 unless additional Congressional action is taken. However, COVID-19 relief legislation suspended the 2 percent Medicare sequester reductions from May 1, 2020 through December 31, 2021. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. The Bipartisan Budget Act, or BBA, also amended the ACA, effective January 1, 2019, by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole."

Furthermore, the prices of prescription pharmaceuticals in the United States and foreign jurisdictions is subject to considerable legislative and executive actions and could impact the prices we obtain for our products, if and when licensed. At the U.S. federal level, the former Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. As a result, the FDA released a final rule on September 24, 2020, effective November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Medicare Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed until January 1, 2023. On November 20, 2020, CMS, issued an interim final rule implementing the Trump administration's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021.

On December 28, 2020, the U.S. District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. It is unclear whether the Biden administration will work

to reverse these measures or pursue similar policy initiatives. In addition to pricing regulations, reforms of regulatory approval frameworks may adversely affect our pricing strategy. For example, on July 9, 2021, President Biden issued an executive order directing the FDA to, among other things, continue to clarify and improve the approval framework for biosimilars, including the standards for interchangeability of biological products, facilitate the development and approval of biosimilar and interchangeable products, clarify existing requirements and procedures related to the review and submission of BLAs, and identify and address any efforts to impede biosimilar competition. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. It is difficult to predict the future legislative landscape in healthcare and the effect on our business, results of operations, financial condition and prospects. However, we expect that additional state and federal healthcare reform measures will be adopted in the future, particularly in light of the new presidential administration. Further, it is possible that additional governmental action is taken in response to the ongoing COVID-19 pandemic. At the state level, legislatures have also been increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Employees and Human Capital Resources

As of December 31, 2021, we had 81 full-time employees, of which 50 have M.D. or Ph.D. degrees. Within our workforce, 69 employees are engaged in research and development and 12 are engaged in business development, finance, legal, and general management and administration. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity incentive plans are to attract, retain and reward personnel through the granting of equity-based compensation awards in order to increase shareholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

Facilities

Our corporate headquarters is located in Cambridge, Massachusetts, where we lease and occupy approximately 10,000 square feet of office space at 21 Erie Street, Cambridge, MA 02139. The current term of our lease expires in March 14, 2023. The company also occupies approximately 13,000 square feet of office space at 38 Sidney Street, Cambridge, MA 02139 and, in April 2022, will occupy approximately 27,000 square feet of combined laboratory and office space at 64 Sidney Street, Cambridge, MA 02139. In addition, we have secured approximately 148,941 square feet in new office and laboratory space at 60 First Street, Cambridge, MA 02141 that we do not expect to occupy until 2024.

We believe that our facilities are adequate for our current needs and for the foreseeable future. To meet the future needs of our business, we may lease additional or alternate space. We believe that suitable additional or substitute space at commercially reasonable terms will be available as needed to accommodate any future expansion of our operations.

Legal proceedings

From time to time, we may become involved in litigation or other legal proceedings arising in the ordinary course of business. We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are probable to have a material adverse effect on our business. Regardless of outcome, litigation can

have an adverse impact on our business, financial condition, results of operations and prospects because of defense and settlement costs, diversion of management resources and other factors.

MANAGEMENT

The following table sets forth information about our executive officers, significant employees and directors as of the date of this prospectus.

Name	Age	Position(s)
<i>Executive Officers and Significant Employees</i>		
Keith Gottesdiener, M.D.	68	President, Chief Executive Officer and Director
Jeremy Duffield, M.D. Ph.D., FRCP	53	Chief Scientific Officer
Ann Lee, Ph.D.	60	Chief Technical Officer
Carman Alenson	57	Chief Accounting Officer and Senior Vice President, Finance
Meredith Goldwasser, Sc.D.	51	Senior Vice President, Strategy and Corporate Operations
Andrew Anzalone	35	Senior Scientist II, Head of Prime Editing Platform
<i>Non-Employee Directors</i>		
John Evans	44	Director
Stephen Knight, M.D.	61	Director
Robert Nelsen ⁽²⁾	58	Director
Thomas Cahill, M.D., Ph.D. ⁽¹⁾⁽³⁾	35	Director
David Schenkein, M.D. ⁽²⁾⁽³⁾	64	Director
Wendy Chung, M.D., Ph.D. ⁽¹⁾⁽³⁾	53	Director
Michael Kelly ⁽¹⁾	65	Director
Kaye Foster ⁽²⁾	62	Director

(1) Member of our audit committee

(2) Member of our compensation committee

(3) Member of our nominating and corporate governance committee

The following is a biographical summary of the experience of our executive officers and directors. There are no family relationships among any of our executive officers or directors.

Executive Officers and Significant Employees

Keith Gottesdiener, M.D. has served as our Chief Executive Officer and a member of our board of directors since July 2020. Prior to that, from October 2011 until March 2020, Dr. Gottesdiener served as the Chief Executive Officer and a director of Rhythm Pharmaceuticals, Inc., a biopharmaceutical company. Dr. Gottesdiener joined Rhythm after 16 years at Merck Research Laboratories, where he held positions of increasing responsibility, including serving as a leader of Merck's late clinical development organization from 2006 to 2011 and leading Merck's early clinical development across all therapeutic areas from 2001 through early 2006. Dr. Gottesdiener currently serves as a director of Intercept Pharmaceuticals, Inc., and Cardurion Pharmaceuticals, both biotechnology companies. He received his M.D. from the University of Pennsylvania and his B.A. in Applied Mathematics from Harvard College.

We believe that Dr. Gottesdiener is qualified to serve on our board of directors based on his extensive experience as a senior executive in the pharmaceutical industry, his drug development and regulatory affairs expertise, his research work for both medical and academic institutions, his public company experience, as well as his knowledge of our company based on his role as our President and Chief Executive Officer.

Jeremy Duffield, M.D., Ph.D., FRCP, has served as our Chief Scientific Officer since January 2021. Prior to that, he served at Vertex Pharmaceuticals Incorporated, a biopharmaceutical company, as Vice President of Business Development from December 2018 to January 2021 and Global Head of Human Biology from July 2016 to November 2018, where his team worked on discovering and advancing candidates to clinical studies in rare diseases. Dr. Duffield also practiced Internal Medicine and Nephrology at Massachusetts General Hospital from November 2013 to September 2019. Prior to that, he served as Senior Research Fellow and Vice President at Biogen Inc. and as

a member of the faculty at University of Washington and Harvard Medical School. Dr. Duffield received his Ph.D. in Immunology from the University of Edinburgh in the laboratory of Sir John Savill, and his M.D. (B.M., B.Ch.) and B.A. in Physiological Sciences from Oxford University.

Ann L. Lee, Ph.D., has served as our Chief Technical Officer since October 2021. Prior to that, Dr. Lee served as Senior Vice President and Head of Cell Therapy Development and Operations at Bristol-Myers Squibb Company, a biopharmaceutical company, from November 2019 to July 2021, as Executive Vice President of Cell Therapy Development and Operations at Celgene Corporation, a biopharmaceutical company, from April 2018 to November 2019 and as Executive Vice President of Technical Operations at Juno Therapeutics, Inc., a biotechnology company, from November 2017 to April 2018. From April 2009 to November 2017, Dr. Lee served as Senior Vice President and Global Head of Pharma Technical Development at Genentech, Inc., a Roche Group subsidiary and a biotechnology company. Dr. Lee received her Ph.D. in biochemical engineering from Yale University and her B.S. in chemical engineering from Cornell University.

Carman Alenson, CPA, MBA, has served as our Chief Accounting Officer and Senior Vice President, Finance since August 2021. Prior to that, she served as Vice President, Accounting, Treasury and Tax at Agios Pharmaceuticals, Inc., a biopharmaceutical company, from November 2016 to July 2021. Prior to that, from April 2015 to October 2016, she was Executive Director of Accounting, Controller, and Assistant Treasurer at AMAG Pharmaceuticals, Inc., a specialty pharmaceuticals company, where she managed the corporate accounting group. Ms. Alenson is a certified public accountant, and received her M.B.A. and B.A. in Economics and Business Administration from Boston University.

Meredith Goldwasser, Sc.D., has served as our Head of Strategy and Corporate Operations since September 2020. Prior to that, Dr. Goldwasser held leadership roles at Agios Pharmaceuticals, Inc., including Vice President and Development Lead for the IDH Hematology program from November 2017 to September 2020 as well as Oncology Business Development Lead from July 2019 to September 2020. She was also Vice President and Head of Biometrics and Data Management at Agios from August 2014 to July 2019. From February 2011 to July 2014, Dr. Goldwasser served as the U.S. Group Head of Biostatistics and Oncology Translational Medicine at Novartis International AG. Dr. Goldwasser received her Sc.D. in Biostatistics from Harvard. She holds a B.A. in Psychology from the University of Pennsylvania.

Andrew Anzalone, M.D., Ph.D., joined Prime Medicine in August 2020 as Co-Founder and Head of the Prime Editing Platform. Prior to this, Dr. Anzalone was a postdoctoral researcher as a Jane Coffin Childs Memorial Fund Postdoctoral Fellow at Broad Institute. Dr. Anzalone received his Sc.B. in Chemistry from Brown University and his M.D. and Ph.D. from Columbia University.

Non-Employee Directors

John Evans has served as a member of our board of directors since September 2019 pursuant to Beam's right to appoint a representative to our board of directors under our Voting Agreement, dated as of September 26, 2019, in connection with our Series A preferred stock financing, which was amended and restated on April 20, 2021 in connection with our Series B preferred stock financing. Mr. Evans has served as Chief Executive Officer of Beam Therapeutics Inc., a biotechnology company, since January 2018, as its President and Chief Executive Officer from January 2018 through January 2020, and as its interim Chief Executive Officer from April 2017 through January 2018. Mr. Evans previously was a Venture Partner with ARCH Venture Partners L.P., a venture capital firm, from April 2017 to March 2021. Mr. Evans was previously at Agios Pharmaceuticals, Inc., a biopharmaceutical company, from September 2009 until April 2017, most recently serving as Senior Vice President for Corporate Development and Portfolio Leadership. Prior to joining Agios, Mr. Evans worked at Infinity Pharmaceuticals, McKinsey & Company's pharmaceuticals practice and MedImmune. Mr. Evans currently serves as a director of Verve Therapeutics, Inc. a biotechnology company. He received his M.B.A. in Healthcare Management from Wharton, an M.S. in Biotechnology from the University of Pennsylvania, and his B.A. in English with distinction from Yale University.

We believe that Mr. Evans is qualified to serve on our board of directors based on his extensive experience in the pharmaceutical industry.

Stephen C. Knight, M.D. has served as a member of our board of directors since September 2019 pursuant to F-Prime Capital's right to appoint a representative to our board of directors under our Voting Agreement, dated as of September 26, 2019, in connection with our Series A preferred stock financing, which was amended and restated on April 20, 2021 in connection with our Series B preferred stock financing. Dr. Knight is President and Managing Partner of F-Prime Capital, a venture capital firm, where he has served since October 2003. He has worked in the pharmaceutical and biotechnology industries for over 25 years and invests broadly across healthcare. Dr. Knight previously served on the boards of several private and public health care companies including Beam Therapeutics Inc., Semma Therapeutics, Inc., Innovent Biologics, Inc., Blueprint Medicines Corporation, Denali Therapeutics Inc., FoldRx Pharmaceuticals, Inc., Ironwood Pharmaceuticals, Inc., NextWave Pharmaceuticals, Inc., Proteostasis Therapeutics, Inc., and Respivert Ltd. Dr. Knight has held various senior management roles in private and public biotechnology and consulting companies. He was also a researcher at AT&T Bell Laboratories, the National Institutes of Health, and Yale University. He received an M.D. from the Yale University School of Medicine, an M.B.A. from the Yale School of Organization and Management, and received his B.S. in Biology from Columbia University.

We believe that Dr. Knight is qualified to serve on our board of directors based on his extensive experience in the medical industry. Dr. Knight will resign from our board of directors prior to our initial public offering.

Robert Nelsen has served as a member of our board of directors since September 2020 pursuant to ARCH's right to appoint a representative to our board of directors under our Voting Agreement, dated as of September 26, 2019, in connection with our Series A preferred stock financing, which was amended and restated on April 20, 2021 in connection with our Series B preferred stock financing. Mr. Nelsen co-founded ARCH Venture Partners, L.P., a venture capital firm focused on early-stage technology companies, in 1986 and has served as a Managing Director of ARCH Venture Partners or its affiliated entities since 1994. Mr. Nelsen currently serves on the board of directors of Bria Biosciences Limited, Denali Therapeutics Inc., Vir Biotechnology, Inc., Sana Biotechnology, Inc., Lyell Immunopharma, Inc., Revolution Healthcare Acquisition Corp., and Hua Medicine, Inc., each a public biotechnology company, and currently serves on the board of directors of a number of private companies. Mr. Nelsen previously served on the board of directors of a number of public biotechnology companies, including Unity Biotechnology, Inc. from 2015 to December 2020, Agios Pharmaceuticals, Inc. from 2007 to June 2017, Syros Pharmaceuticals, Inc. from 2012 to June 2018, Juno Therapeutics, Inc. (acquired by Celgene Corporation in January 2018) from 2013 to March 2018, Sienna Biopharmaceuticals, Inc. from 2015 to September 2018 and Gossamer Bio, Inc. from 2017 to December 2018 (prior to its initial public offering). Mr. Nelsen received his M.B.A. from the University of Chicago and his B.S. from the University of Puget Sound in Economics and Biology.

We believe that Mr. Nelsen is qualified to serve on our board of directors because of his extensive experience as a venture capitalist, building and serving boards of many public and private emerging companies, including multiple life sciences, biotechnology and pharmaceutical companies.

Thomas Cahill, M.D., Ph.D. has served as a member of our board of directors since November 2021. Dr. Cahill is the Founder and Managing Partner of Newpath Partners, a Boston based life science venture fund focused on therapeutic companies. Dr. Cahill is the founding investor and director of Chroma Medicine, Exo Therapeutics, Kisbee Therapeutics, Kojin Therapeutics, Magnet Biomedicine, Myeloid Therapeutics, and Resonance Medicine. Prior to Newpath Partners, Dr. Cahill served as an Advisor at Raptor Group Holdings, where he helped further establish and lead the life science and technology investment portfolio, from September 2016 to May 2018. Dr. Cahill received both his M.D. and Ph.D. from Duke University and his M.S. from Stanford University.

We believe that Dr. Cahill is qualified to serve on our board of directors based on his experience in the medical and venture capital industries.

David Schenkein, M.D. has served as a member of our board of directors since September 2019 pursuant to GV's right to appoint a representative to our board of directors under our Voting Agreement, dated as of September 26, 2019, in connection with our Series A preferred stock financing, which was amended and restated on April 20, 2021 in connection with our Series B preferred stock financing. Dr. Schenkein currently serves as a partner in GV, the venture capital investment arm of Alphabet Inc., which he joined in February 2019. Previously, Dr. Schenkein served as President and Chief Executive Officer of Agios Pharmaceuticals from August 2009 to February 2019.

From April 2006 to July 2009, Dr. Schenkein served as a Senior Vice President of Oncology Development at Genentech Inc. Dr. Schenkein currently serves as the Executive Chairman of the board of directors of Agios Pharmaceuticals and as a member of the board of directors of Denali Therapeutics Inc. Previously, Dr. Schenkein served on the board of directors of Foundation Medicine, Inc. and bluebird bio, Inc. He also currently serves as an adjunct attending physician in hematology at Tufts Medical Center. Dr. Schenkein received his M.D. from the State University of New York Upstate Medical School and his B.A. in Chemistry from Wesleyan University.

We believe that Dr. Schenkein is qualified to serve on our board of directors because of his extensive background in the biotechnology industry and leadership experience as a senior executive and director of biotechnology companies.

Wendy Chung, M.D., Ph.D., has served as a member of our board of directors since November 2021. Dr. Chung is an American Board of Medical Genetics certified clinical and molecular geneticist and leads the Precision Medicine Resource in the Irving Institute at Columbia University, a position she has held since February 2014. Dr. Chung has been on the faculty at Columbia University since 2002, most recently as the Kennedy Family Professor of Pediatrics and Medicine at Columbia University, a position she has held since July 2017. Prior to that, from June 2014 to July 2017, she was an Associate Professor at Columbia University. She received her B.A. in Biochemistry from Cornell University, her M.D. from Cornell University Medical College, and her Ph.D. in Genetics from The Rockefeller University.

We believe that Dr. Chung is qualified to serve on our board of directors because of her extensive experience in medicine and genetics research.

Michael A. Kelly has served as a member of our board of directors since November 2021. Mr. Kelly is currently acting as Founder & President of Sentry Hill Partners, LLC, a global life sciences transformation and management consulting business founded by Mr. Kelly in January 2018. From February 2003 to December 2017 he was a senior executive of Amgen, Inc., a biotechnology company, where he most recently served as Senior Vice President, Global Business Services and Vice President & Chief Financial Officer, International Commercial Operations. He also serves on the boards of directors of: Amicus Therapeutics, Inc., a biotechnology company, which he joined in December 2020; Aprea Therapeutics, Inc., a biotechnology company, which he joined in September 2020; DMC Global Inc., a composite materials and oil field products company, which he joined in July 2020; NeoGenomics Laboratories, Inc., a genetics testing company, which he joined in July 2020; and Hookipa Pharma Inc., a biopharmaceutical company, which he joined in February 2019. Mr. Kelly has also held positions at Tanox, Inc., Biogen, Inc., and Nutrasweet Kelco Company, a division of Monsanto Life Sciences. He also serves on the Council of Advisors and was the former audit committee chairman for Direct Relief, a humanitarian aid organization focused on health outcomes and disaster relief. Mr. Kelly received his B.Sc. in Business Administration from Florida A&M University, concentrating in Finance and Industrial Relations.

We believe that Mr. Kelly is qualified to serve on our board of directors because of his extensive experience in managing and growing global healthcare and biotechnology companies.

Kaye Foster has served as a member of our board of directors since December 2021. Ms. Foster has been a Senior Advisor at the Boston Consulting Group since August 2014. Previously, she was Senior Vice President, Global Human Resources at Onyx Pharmaceuticals, Inc., an Amgen, Inc. subsidiary and a biopharmaceutical company, from October 2010 to January 2014. At Onyx, she led all aspects of human resources for U.S. and global operations. Prior to joining Onyx, Ms. Foster was Global Vice President of Human Resources and an Executive Committee member at Johnson and Johnson Corporation, a healthcare company, from May 2003 to March 2010. Before Johnson and Johnson, Ms. Foster held several senior human resources executive positions with Pfizer Inc., a pharmaceuticals company. She currently serves on the board of directors and compensation and community equity committees of Resilience Inc.; on the board of directors and real estate and nominations committees of Stanford Health Care, a hospital and healthcare system; on the board of trustees and the human resources committee of Spelman College; and chairs the Glide Memorial Foundation Board of Trustees. She received her B.B.A. in Business Administration from Baruch College of the City University of New York and her M.B.A. from Columbia University, Graduate School of Business.

We believe Ms. Foster is qualified to serve on our board of directors because of her extensive experience as an executive in the pharmaceuticals industry, including her experience in people management, compensation planning and driving and maintaining corporate culture.

Board Composition

Our board of directors currently consists of eight members, each of whom is a member pursuant to the board composition provisions of our current certificate of incorporation and agreements with our stockholders, which agreements are described in the section of this prospectus entitled “Certain Relationships and Related Person Transactions.” These board composition provisions will terminate upon the closing of this offering. Upon the termination of these provisions, there will be no further contractual obligations regarding the election of our directors. Our nomination and corporate governance committee and our board of directors may therefore consider a broad range of factors relating to the qualifications and background of nominees. Our nomination and corporate governance committee’s and our board of directors’ priority in selecting board members is identification of persons who will further the interests of our stockholders through their established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business, understanding of the competitive landscape, professional and personal experiences and expertise relevant to our growth strategy. Our directors hold office until their successors have been elected and qualified or until their earlier resignation or removal. Our third amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least two-thirds of the votes that all our stockholders would be entitled to cast in an annual election of directors, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

Staggered Board

In accordance with the terms of our third amended and restated certificate of incorporation and our amended and restated bylaws that will become effective upon the closing of this offering, our board of directors will be divided into three staggered classes of directors and each director will be assigned to one of the three classes. At each annual meeting of the stockholders, one class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. The terms of the directors will expire upon the election and qualification of successor directors at the annual meeting of stockholders to be held during the years 2023 for Class I directors, 2024 for Class II directors and 2025 for Class III directors.

- Our Class I directors will be John Evans, Michael Kelly and David Schenkein;
- Our Class II directors will be Kaye Foster, Wendy Chung and Keith Gottesdiener; and
- Our Class III directors will be Thomas Cahill and Robert Nelsen.

Our third amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering will provide that the number of our directors shall be fixed from time to time by a resolution of the majority of our board of directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our management or a change in control.

Director Independence

We have applied to list our common stock on The Nasdaq Global Market. Under the Nasdaq listing rules, independent directors must comprise a majority of a listed company’s board of directors within twelve months from the date of listing. In addition, the Nasdaq listing rules require that, subject to specified exceptions, each member of a listed company’s audit, compensation and nominating and governance committees be independent within twelve months from the date of listing. Audit committee members must also satisfy additional independence criteria, including those set forth in Rule 10A-3 under the Securities Exchange Act of 1934, or the Exchange Act, and

compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Exchange Act. Under Nasdaq listing rules, a director will only qualify as an “independent director” if, in the opinion of that company’s board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3 under the Exchange Act, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee: (i) accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries, other than compensation for board service; or (ii) be an affiliated person of the listed company or any of its subsidiaries. In order to be considered independent for purposes of Rule 10C-1, the board of directors must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director’s ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: the source of compensation of the director, including any consulting advisory or other compensatory fee paid by such company to the director, and whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In February 2022, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his background, employment and affiliations, including family relationships, our board of directors has determined that all members of our board of directors, except Keith Gottesdiener and John Evans, are independent directors, including for purposes of Nasdaq and the SEC rules. In making that determination, our board of directors considered the relationships that each director has with us and all other facts and circumstances the board of directors deemed relevant in determining independence, including the potential deemed beneficial ownership of our capital stock by each director, including non-employee directors that are affiliated with certain of our major stockholders. Upon the completion of this offering, we expect that the composition and functioning of our board of directors and each of our committees will comply with all applicable requirements of Nasdaq and the rules and regulations of the SEC. There are no family relationships among any of our executive officers and directors.

We intend to adopt a policy, subject to and effective upon the effectiveness of the registration statement of which this prospectus forms a part, that outlines a process for our securityholders to send communications to the board of directors.

Board Committees

Our board of directors has established an audit committee, a compensation committee and a nomination and corporate governance committee, each of which will operate pursuant to a charter to be adopted by our board of directors and will be effective upon the effectiveness of the registration statement of which this prospectus forms a part. We believe that the composition and functioning of all of our committees will comply with the applicable requirements of Nasdaq, the Sarbanes-Oxley Act of 2002 and SEC rules and regulations that will be applicable to us. We intend to comply with future requirements to the extent they become applicable to us.

Following the consummation of this offering, the full text of our audit committee charter, compensation committee charter and nomination and corporate governance committee charter will be posted on the investor relations portion of our website at <https://www.primemedicine.com>. We do not incorporate the information contained on, or accessible through, our corporate website into this prospectus, and you should not consider it a part of this prospectus.

Audit Committee

Upon the effectiveness of the registration statement of which this prospectus forms a part, our audit committee will consist of Michael Kelly, Thomas Cahill and Wendy Chung and will be chaired by Mr. Kelly. The functions of the audit committee will include:

- appointing, approving the compensation of, and assessing the independence of our independent registered public accounting firm;

- pre-approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the overall audit plan with our independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- coordinating the oversight and reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending based upon the audit committee’s review and discussions with management and our independent registered public accounting firm whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;
- preparing the audit committee report required by SEC rules to be included in our annual proxy statement;
- reviewing all related person transactions for potential conflict of interest situations and approving all such transactions; and
- reviewing quarterly earnings releases.

All members of our audit committee will meet the requirements for financial literacy under the applicable rules and regulations of the SEC and the Nasdaq listing rules. Our board of directors has determined that Michael Kelly qualifies as an “audit committee financial expert” within the meaning of applicable SEC regulations. In making this determination, our board of directors considered the nature and scope of experience that Michael Kelly has previously had with public reporting companies, including service as a principal financial officer and principal accounting officer. Our board of directors has determined that all of the directors that will become members of our audit committee upon the effectiveness of the registration statement of which this prospectus forms a part satisfy the relevant independence requirements for service on the audit committee set forth in the rules of the SEC and the Nasdaq listing rules. Both our independent registered public accounting firm and management will periodically meet privately with our audit committee.

Compensation Committee

Upon the effectiveness of the registration statement of which this prospectus forms a part, our compensation committee will consist of Kaye Foster, David Schenkein and Robert Nelsen, and will be chaired by Ms. Foster. The functions of the compensation committee will include:

- annually reviewing and recommending to the board of directors the corporate goals and objectives relevant to the compensation of our Chief Executive Officer;
- evaluating the performance of our Chief Executive Officer in light of such corporate goals and objectives and based on such evaluation (i) reviewing and determining the cash compensation of our Chief Executive Officer and (ii) reviewing and approving grants and awards to our Chief Executive Officer under equity-based plans;
- reviewing and approving the compensation of our other executive officers;
- reviewing and establishing our overall management compensation, philosophy and policy;

- overseeing and administering our compensation and similar plans;
- evaluating and assessing potential and current compensation advisors in accordance with the independence standards identified in the applicable Nasdaq listing rules;
- reviewing and approving our policies and procedures for the grant of equity-based awards;
- reviewing and recommending to the board of directors the compensation of our directors;
- preparing our compensation committee report if and when required by SEC rules;
- reviewing and discussing annually with management our “Compensation Discussion and Analysis,” if and when required, to be included in our annual proxy statement; and
- reviewing and approving the retention or termination of any consulting firm or outside advisor to assist in the evaluation of compensation matters.

Each member of our compensation committee will be a non-employee director, as defined in Rule 16b-3 promulgated under the Exchange Act, and an outside director, as defined pursuant to Section 162(m) of the Internal Revenue Code of 1986, as amended (the Code).

Nominating and Corporate Governance Committee

Upon the effectiveness of the registration statement of which this prospectus forms a part, our nominating and corporate governance committee will consist of David Schenkein, Wendy Chung and Thomas Cahill and will be chaired by Mr. Schenkein. The functions of the nominating and corporate governance committee will include:

- developing and recommending to the board of directors criteria for board and committee membership;
- establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by stockholders;
- reviewing the composition of the board of directors to ensure that it is composed of members containing the appropriate skills and expertise to advise us;
- identifying individuals qualified to become members of the board of directors;
- recommending to the board of directors the persons to be nominated for election as directors and to each of the board’s committees;
- developing and recommending to the board of directors a code of business conduct and ethics and a set of corporate governance guidelines; and
- overseeing the evaluation of our board of directors and management.

Our board of directors may from time to time establish other committees.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee is, or has at any time during the prior three years been, one of our officers or employees. None of our executive officers currently serve, or have in the past fiscal year served, as a member of the board of directors or compensation committee of any entity that has one or more of its executive officers serving as a member of our board of directors or our compensation committee.

Code of Business Conduct and Ethics

Our board of directors intends to adopt, subject to and effective upon the effectiveness of the registration statement of which this prospectus forms a part, a Code of Business Conduct and Ethics in connection with this offering. The Code of Business Conduct and Ethics will apply to all of our employees, officers (including our

principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions), agents and representatives, including directors and consultants.

We intend to disclose future amendments to certain provisions of our Code of Business Conduct and Ethics and our Code of Ethics on our website identified below. Upon the completion of this offering, the full text of our Code of Business Conduct and Ethics and our Code of Ethics will be posted on our website at <https://www.primemedicine.com>. The inclusion of our website address in this prospectus does not include or incorporate by reference the information on our website into this prospectus, and you should not consider that information a part of this prospectus.

Limitations on Liability and Indemnification Agreements

As permitted by Delaware law, provisions in our third amended and restated certificate of incorporation and amended and restated bylaws, both of which will become effective upon the closing of this offering, limit or eliminate the personal liability of directors for a breach of their fiduciary duty of care as a director. The duty of care generally requires that, when acting on behalf of the corporation, a director exercise an informed business judgment based on all material information reasonably available to him or her. Consequently, a director will not be personally liable to us or our stockholders for monetary damages or breach of fiduciary duty as a director, except for liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any act related to unlawful stock repurchases, redemptions or other distributions or payments of dividends; or
- any transaction from which the director derived an improper personal benefit.

These limitations of liability do not limit or eliminate our rights or any stockholder's rights to seek non-monetary relief, such as injunctive relief or rescission. These provisions will not alter a director's liability under other laws, such as the federal securities laws or other state or federal laws. Our third amended and restated certificate of incorporation that will become effective upon the closing of this offering also authorizes us to indemnify our officers, directors and other agents to the fullest extent permitted under Delaware law.

As permitted by Delaware law, our amended and restated bylaws to be effective upon the consummation of this offering will provide that:

- we will indemnify our directors, officers, employees and other agents to the fullest extent permitted by law;
- we must advance expenses to our directors and officers, and may advance expenses to our employees and other agents, in connection with a legal proceeding to the fullest extent permitted by law; and
- the rights provided in our amended and restated bylaws are not exclusive.

If Delaware law is amended to authorize corporate action further eliminating or limiting the personal liability of a director or officer, then the liability of our directors or officers will be so eliminated or limited to the fullest extent permitted by Delaware law, as so amended. Our amended and restated bylaws will also permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in connection with their services to us, regardless of whether our amended and restated bylaws permit such indemnification. We have obtained such insurance.

In addition to the indemnification that will be provided for in our third amended and restated certificate of incorporation and amended and restated bylaws, we plan to enter into separate indemnification agreements with each of our directors and executive officers, which may be broader than the specific indemnification provisions contained in the Delaware General Corporation Law. These indemnification agreements may require us, among other things, to indemnify our directors and executive officers for some expenses, including attorneys' fees, expenses, judgments,

finances and settlement amounts incurred by a director or executive officer in any action or proceeding arising out of his service as one of our directors or executive officers or any other company or enterprise to which the person provides services at our request. We believe that these provisions and agreements are necessary to attract and retain qualified individuals to serve as directors and executive officers.

This description of the indemnification provisions of our third amended and restated certificate of incorporation, our amended and restated bylaws and our indemnification agreements is qualified in its entirety by reference to these documents, each of which is attached as an exhibit to the registration statement of which this prospectus forms a part.

Insofar as indemnification for liabilities arising under the Securities Act, may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable.

There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

EXECUTIVE COMPENSATION

The following discussion contains forward looking statements that are based on our current plans, considerations, expectations and determinations regarding our future compensation programs. The actual amount and form of compensation and the compensation policies and practices that we adopt in the future may differ materially from currently planned programs as summarized in this discussion.

As an emerging growth company, we have opted to comply with the executive compensation disclosure rules applicable to “smaller reporting companies,” as such term is defined in the rules promulgated under the Securities Act. The compensation provided to our named executive officers for the fiscal years ended December 31, 2020 and December 31, 2021 are detailed in the 2021 Summary Compensation Table and accompanying footnotes and narrative that follow. Our named executive officers for the fiscal year ended December 31, 2021 are:

- Keith Gottesdiener, M.D., President and Chief Executive Officer;
- Jeremy S. Duffield, M.D., Ph.D., FRCP, Chief Scientific Officer; and
- Ann L. Lee, Ph.D., Chief Technical Officer.

To date, the compensation of our named executive officers has consisted of a combination of base salary, cash bonuses and long-term incentive compensation in the form of restricted stock awards and stock options. Our named executive officers, like all our full-time employees, are eligible to participate in our health and welfare benefit plans. As we transition from a private company to a publicly traded company, we intend to evaluate our compensation values and philosophy and compensation plans and arrangements as circumstances require.

2021 Summary Compensation Table

The following table shows the total compensation awarded to, earned by, or paid to, our named executive officers for services rendered to us in all capacities during the fiscal years indicated.

Name and Principal Position	Year	Salary (\$)	Bonus (\$) ⁽¹⁾	Stock Awards (\$) ⁽²⁾	Option Awards (\$) ⁽³⁾	Non-Equity Incentive Plan Compensation (\$)	All Other Compensation (\$)	Total (\$)
Keith Gottesdiener, MD <i>President and Chief Executive Officer</i>	2021	524,000	327,500	—	2,072,325	—	15,608 ⁽⁴⁾	2,939,433
	2020	252,068	257,500	323,943	—	—	101,413	394,924
Jeremy Duffield, MD, PhD ⁽⁵⁾ <i>Chief Scientific Officer</i>	2021	428,400	566,000	264,000	138,155	—	—	1,396,555
Ann Lee, PhD ⁽⁶⁾ <i>Chief Technical Officer</i>	2021	108,750	54,247	—	4,144,650	—	8,193 ⁽⁷⁾	4,315,840

- (1) The amounts reflect discretionary bonuses earned by our named executive officers during the fiscal years ended December 31, 2021 and December 31, 2020, as applicable. Dr. Duffield’s bonus amount also reflects a \$350,000 signing bonus paid to him at the time of hire.
- (2) The amounts reported represent the aggregate grant date fair value of the restricted stock awards granted to our named executive officers during the applicable fiscal year, calculated in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 718. Such grant date fair values do not take into account any estimated forfeitures. The assumptions used in calculating the grant date fair value of the restricted stock awards reported in this column are set forth in note 8 of our consolidated financial statements included elsewhere in this prospectus. The amounts reported in this column reflect the accounting cost for these awards and do not correspond to the actual economic value that may be received by our named executive officers upon the vesting of the awards or any sale of the underlying shares of common stock. For Dr. Gottesdiener’s performance-based restricted stock awards, the grant date fair values based on probable level of achievement of the applicable performance metrics were \$0.00 for his 2021 and 2020 grants and the grant date fair values of such awards based on maximum level of achievement of the applicable performance metrics were \$66,000 and \$64,786, for his 2021 and 2020 grants, respectively. For Dr. Duffield’s performance-based restricted stock award, the grant date fair value based on probable level of achievement of the applicable performance metrics was \$0.00 and the grant date fair value of such award based on maximum level of achievement of the applicable performance metrics was \$66,000.
- (3) The amounts reported represent the aggregate grant date fair value of the stock options granted to our named executive officers during the applicable fiscal year, calculated in accordance with FASB ASC Topic 718. Such grant date fair values do not take into account any estimated forfeitures. The assumptions used in calculating the grant date fair value of the stock options reported in this column are set forth in note 8 of our consolidated financial statements included elsewhere in this prospectus. The amounts reported in this column reflect the

accounting cost for these awards and do not correspond to the actual economic value that may be received by our named executive officers upon the exercise of the awards or any sale of the underlying shares of common stock. One third of Dr. Lee's performance-based stock option to purchase 250,000 shares of common stock granted on October 27, 2021 will vest based on the Company's achievement of a third performance-based milestone requiring the building of a chemistry facility, initiation of pegRNA piloting operations, and production of a GLP toxicology lot suitable for *in vivo* non-human primate studies. This performance-based milestone was not determined in 2021, and was determined in 2022. As such, there was no grant date fair value associated with this tranche of the performance-based stock option for 2021. For the remainder of Dr. Lee's performance-based stock option, the grant date fair value based on probable level of achievement of the applicable performance metrics was \$0.00 and the grant date fair value of such award based on maximum level of achievement of the applicable performance metrics was \$1,381,550.

- (4) Includes (i) \$14,408 for reimbursements for commuting expenses incurred by Dr. Gottesdiener in 2021 for travel to and from New York, New York to our corporate headquarters in Cambridge, Massachusetts and (ii) \$1,200 for reimbursements for cell phone expenses.
- (5) Dr. Duffield commenced employment with us on January 4, 2021 and his 2021 base salary was pro-rated accordingly. His annual base salary rate for 2021 was \$432,000. Dr. Duffield's 2021 annual bonus was not pro-rated, per the terms of his offer letter.
- (6) Dr. Lee commenced employment with us on October 4, 2021 and her 2021 base salary was pro-rated accordingly. Her annual base salary for 2021 was \$450,000. Dr. Lee's 2021 annual bonus was pro-rated per the terms, per the terms of her offer letter.
- (7) Includes reimbursements for \$5,530 in relocation expenses incurred by Dr. Lee in 2021 for travel from her residence in Seattle, Washington to our corporate headquarters in Cambridge, Massachusetts, house hunting trips and \$2,663 in tax-gross up expenses on her relocation benefits.

Narrative Disclosure to Summary Compensation Table

2021 Base Salaries

Our named executive officers each receive a base salary to compensate them for services rendered to our Company. The base salary payable to each named executive officer is intended to provide a fixed component of compensation reflecting the executive's skill set, experience, role and responsibilities. Base salaries may be adjusted from time to time to realign salaries with market levels after taking into account individual responsibilities, performance and experience.

2021 Cash Bonuses

For the fiscal year ended December 31, 2021, each of the named executive officers was eligible to earn a discretionary annual cash bonus determined by our board of directors in its sole discretion, based on corporate and/or individual performance. The target annual bonus for each of our named executive officers for the fiscal year ended December 31, 2021 was equal to the percentage of the executive's respective annual base salary specified below:

Name	Target Bonus Percentage
Keith Gottesdiener, M.D.	50 %
Jeremy S. Duffield, M.D., Ph.D., FRCP	40 %
Ann Lee, Ph.D.	40 %

In addition, in the fiscal year ended December 31, 2021, Dr. Duffield received (i) a \$350,000 signing bonus payable pursuant to the terms of his offer letter with the Company and (ii) a milestone bonus equal to \$300,000, which can be earned and payable based on achievement of the following milestones, subject to Dr. Duffield's continued employment with the Company on each such date: one-third of the bonus will be earned and payable upon achievement of proof of concept in lead indication, one-third of the bonus will be earned and payable upon IND acceptance, and the remaining one-third of the bonus will be earned and payable upon the consummation of the Company's initial public offering.

Equity-Based Compensation

Although we do not yet have a formal policy with respect to the grant of equity incentive awards to our executive officers, we believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. In addition, we believe that equity grants promote executive retention because they incentivize our executive officers to remain in our employment during the vesting period. Accordingly, our board of directors periodically reviews the equity incentive compensation of our named executive officers and may grant equity incentive

awards to them from time to time. In furtherance of these goals, in 2021 each of our named executive officers was granted restricted stock award(s) and/or stock option(s). For additional information regarding outstanding equity awards held by our named executive officers as of December 31, 2021, see the “Outstanding Equity Awards at 2021 Fiscal Year End” table below.

Perquisites/Personal Benefits

Perquisites or other personal benefits are not a significant component of our executive compensation program. Accordingly, we do not provide significant perquisites or other personal benefits to our executive officers, including our named executive officers, except for reimbursements for relocation, commuting and/or cell phone expenses for certain named executive officers, as described above in the “2021 Summary Compensation Table”.

401(k) Plan

We maintain a retirement savings plan, or 401(k) plan, that is intended to qualify for favorable tax treatment under Section 401(a) of the Code, and contains a cash or deferred feature that is intended to meet the requirements of Section 401(k) of the Code. U.S. employees are generally eligible to participate in the 401(k) plan, subject to certain criteria. Participants may make pre-tax and certain after-tax (Roth) salary deferral contributions to the plan from their eligible earnings up to the statutorily prescribed annual limit under the Code. Participants who are 50 years of age or older may contribute additional amounts based on the statutory limits for catch-up contributions. Participant contributions are held in trust as required by law. We do not provide any matching contributions under our 401(k) plan.

Outstanding Equity Awards at 2021 Fiscal Year End

The following table lists all outstanding equity awards held by our named executive officers as of December 31, 2021.

Name	Grant Date	Vesting Commencement Date	Options ⁽¹⁾				Stock Awards ⁽¹⁾				
			Number of Securities Underlying Unexercised Option (#) Exercisable	Number of Securities Underlying Unexercised Option (#) Unexercisable	Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Unearned Option (#)	Option Exercise Price	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested (\$) ⁽²⁾	Equity Incentive Plan Awards: Number of Unearned Shares, Units or Other Rights That Have Not Vested (#)	Equity Incentive Plan Awards: Market or Payout Value of Unearned Shares, Units or Other Rights That Have Not Vested (\$) ⁽²⁾
Keith Gottesdiener, M.D.	10/27/2021	10/27/2021	31,250 ⁽³⁾	718,750 ⁽³⁾		1.18	10/26/2031				
	3/4/2021									600,000 ⁽⁴⁾	2,106,000
	7/28/2020 7/28/2020	6/20/2020						6,748,816 ⁽⁵⁾	23,688,344	2,159,621 ⁽⁴⁾	7,580,270
Jeremy Duffield, M.D., Ph.D.	10/27/2021	10/27/2021	2,083 ⁽³⁾	47,917 ⁽³⁾		1.18	10/26/2031				
	1/16/2021	1/4/2021						2,400,000 ⁽⁵⁾	8,424,000		
	1/16/2021									600,000 ⁽⁴⁾	2,106,000
Ann Lee, Ph.D.	10/27/2021	10/4/2021	— ⁽⁶⁾	1,500,000		1.18	10/26/2031				
	10/27/2021				750,000 ⁽⁷⁾	1.18	10/26/2031				

(1) Each equity award was granted under the Company’s 2019 Stock Option and Grant Plan, or the 2019 Plan.

(2) Assumes a market value of \$3.51 per share, based on an independent valuation report in effect as of December 31, 2021.

(3) The shares underlying these options vest in equal monthly installments over 48 months commencing on the vesting commencement date, subject to the applicable named executive officer’s continuous service relationship with the Company through each applicable vesting date. In the event of a termination of Dr. Gottesdiener’s employment by the Company without Cause or by Dr. Gottesdiener for Good Reason (such terms as defined in Dr. Gottesdiener’s offer letter), in either case within three months prior to or 12 months after a Sale Event (as defined in the 2019 Plan), all unvested shares will immediately vest as of the date of such termination event or Sale Event, as applicable. In addition, if upon a Sale Event, Dr. Gottesdiener is offered substantially equivalent employment terms by the successor and he remains employed by the Company or its successor for up to 6 months, all unvested shares will vest upon the 6-month anniversary of the Sale Event. In the event of a termination of Dr. Duffield’s employment by the Company without Cause or by Dr. Duffield for Good Reason

- (such terms as defined in Dr. Duffield's offer letter), in either case on or within 12 months after a Sale Event (as defined in the 2019 Plan), all unvested shares will immediately vest as of the date of such termination event.
- (4) The underlying shares vest upon achievement of the following pre-determined milestone: one-third of the shares will vest upon achievement of proof of concept in lead indication, one-third will vest upon IND acceptance, and the remaining one-third will vest upon the consummation of the Company's initial public offering. 100 percent of the underlying shares will immediately vest upon a Sale Event (as defined in the 2019 Plan) if (i) a Sale Event occurs prior to the date the Board determines in good faith that the milestones are achieved and prior to the Company's initial public offering or the Company otherwise becoming a public company, (ii) the per share proceeds distributable to the holders of preferred stock of the Company upon the consummation of such Sale Event is at least equal to the original issue price of the Company's most recently completed preferred stock financing and (iii) the applicable named executive officer continuous to have a service relationship with the Company at such time.
 - (5) The restricted shares vest as follows: 25 percent vest on the one year anniversary of the vesting commencement date, and 1/48th of the shares vest on a monthly basis thereafter, in each case subject to the applicable named executive officer's continuous service relationship with the Company through each applicable vesting date. In the event of a termination by the Company without Cause or by Dr. Gottesdiener for Good Reason (such terms as defined in Dr. Gottesdiener's offer letter), in either case within three months prior to or twelve months after a Sale Event (as defined in the 2019 Plan), all unvested shares will immediately vest as of the date of such termination event or Sale Event, as applicable. In addition, if upon a Sale Event, Dr. Gottesdiener is offered substantially equivalent employment terms by the successor and he remains employed by the Company or its successor for up to 6 months, all unvested shares will vest upon the six-month anniversary of the Sale Event. In the event of a termination of Dr. Duffield's employment by the Company without Cause or by Dr. Duffield for Good Reason (such terms as defined in Dr. Duffield's offer letter), in either case on or within 12 months after a Sale Event (as defined in the 2019 Plan), all unvested shares will immediately vest as of the date of such termination event.
 - (6) The shares underlying this option vest as follows: 25 percent vest on the one year anniversary of the vesting commencement date, and 1/48th of the shares vest on a monthly basis thereafter, in each case subject to Dr. Lee's continuous service relationship with the Company through each applicable vesting date. In the event of a termination by the Company without Cause or by Dr. Lee for Good Reason (such terms as defined in Dr. Lee's offer letter), in either case on or within 12 months after a Sale Event (as defined in the 2019 Plan), all unvested shares will immediately vest as of the date of such termination event.
 - (7) The underlying shares vest upon achievement of the following milestones: one-third will vest upon IND acceptance, one-third will vest upon the consummation of the Company's initial public offering and the remaining one-third will vest upon the achievement of a performance-based milestone requiring the building of a chemistry facility, initiation of pegRNA piloting operations, and production of a GLP toxicology lot suitable for *in vivo* non-human primate studies.

Executive Compensation Arrangements

We have entered into offer letters with each of our named executive officers. Each offer letter provides for "at-will" employment and the compensation and benefits described below. In connection with this offering, we intend to enter into a new employment agreement with our named executive officers that will be effective as of the closing of this offering.

Employment Arrangements in Place Prior to The Offering for Named Executive Officers

Keith M. Gottesdiener, M.D.

On June 24, 2020, we entered into an offer letter with Dr. Gottesdiener, or the Gottesdiener Offer Letter, for the position of President and Chief Executive Officer. The Gottesdiener Offer Letter provides for Mr. Gottesdiener's at-will employment. Dr. Gottesdiener's current base salary is \$542,340 and he is eligible to receive an annual bonus with an annual target amount of 50 percent of his annual base salary. Dr. Gottesdiener is eligible to participate in the employee benefit plans available to our employees, subject to the terms of such plan and is entitled to reimbursement for commuting expenses between New York, New York and Cambridge, Massachusetts for the first three years of his employment. In accordance with the Gottesdiener Offer Letter, the Company paid Dr. Gottesdiener a bonus of \$100,000 in 2020 to cover personal taxes incurred in 2020 from the grants of restricted stock awards made to him in 2020. In addition, the Gottesdiener Offer Letter provides that in the event of a Qualified Departure (as defined in the Gottesdiener Offer Letter), the post-termination exercise period of any vested options on such date will be extended until 12 months after such termination, inclusive of any period of consulting service. Furthermore, upon a Qualified Departure other than due to death or disability, the Company will negotiate in good faith to establish a non-exclusive consulting relationship with Dr. Gottesdiener for a period of up to one year after the date of such termination pursuant to which Dr. Gottesdiener will receive no cash compensation other than severance benefits as described below. In the event Dr. Gottesdiener's employment is terminated by us without Cause or he resigns for Good Reason (as such terms are defined in the Gottesdiener Offer Letter), in each case, within three months prior to or 12 months after a Sale Event (as such term is defined in the 2019 Plan), then all of the unvested portion of Dr. Gottesdiener's initial time-based restricted stock grant for 10,798,106 shares of Company common stock (the "Initial Time-Based Award") will immediately vest as of the date of such termination event or Sale Event, as applicable. Notwithstanding the foregoing, if upon a Sale Event, Dr. Gottesdiener agrees, if

offered substantially equivalent employment terms, to remain employed by the Company (or any successor) for up to six months, the unvested portion of the Initial Time-Based Award shall vest upon the 6-month anniversary of the Sale Event (unless otherwise vested upon a Qualified Departure).

Upon a termination of Dr. Gottesdiener's employment by us without Cause or his resignation for Good Reason, subject to his execution and non-revocation of a separation agreement, including, without limitation, a general release of claims in favor of the Company and, in the Company's discretion, a one year post-employment noncompetition agreement, Dr. Gottesdiener will be entitled to (i) a payment equal to the sum of 12 months of his base salary and annual target bonus, and (ii) if Dr. Gottesdiener is participating in the Company's group health plan immediately prior to his last day of employment and he elects COBRA health continuation, a monthly cash payment to the group health plan provider, COBRA provider or him until the earlier of (A) the 12-month anniversary of his termination, (B) his eligibility for group health plan benefits under any other employer's group health plan, or (C) the end of his COBRA continuation rights period, in an amount equal to the monthly employer contribution the Company would have paid to provide him with health insurance had he remained employed. If Dr. Gottesdiener's employment is terminated prior to a Sale Event, such severance amounts will be paid out in substantially equal installments in accordance with the Company's payroll practice over 12 months. Notwithstanding the foregoing, if a Sale Event occurs during the 12-month period during which the Company is paying severance, then such remaining severance amounts will be paid in a lump sum within 10 business days after the Sale Event. If the termination occurs on or after a Sale Event, then the severance amounts will be paid in a lump sum within 60 days after the date of such termination.

Dr. Gottesdiener has entered into an Employee Confidentiality, Assignment and Nonsolicitation Agreement that contains various restrictive covenants, including, nonsolicitation provisions that apply during his employment and for up to one year thereafter (or, in certain situations, for up to two years thereafter).

Jeremy Duffield, M.D., Ph.D., FRCP

On December 8, 2020, we entered into an offer letter with Dr. Duffield, or the Duffield Offer Letter, for the position of Chief Scientific Officer beginning January 4, 2021. The Duffield Offer Letter provides for Dr. Duffield's at-will employment. Dr. Duffield's current base salary is \$447,120 and he is eligible to receive an annual bonus with an annual target amount of 40 percent of his annual base salary. Dr. Duffield is eligible to participate in the employee benefit plans available to our employees, subject to the terms of such plans. In accordance with the Duffield Offer Letter, the Company (i) paid Dr. Duffield a one-time signing bonus of \$350,000 in 2021, and (ii) committed to an additional \$300,000 bonus that will be earned and payable as follows: one-third of the bonus will be earned and payable upon achievement of proof of concept in lead indication, one-third of the bonus will be earned and payable upon IND acceptance, and the remaining one-third of the bonus will be earned and payable upon the consummation of the Company's initial public offering, in each case subject to Dr. Duffield's continued employment with us through the date of achievement of the applicable milestone.

Upon a termination of Dr. Duffield's employment by us without Cause or his resignation for Good Reason (as such terms are defined in the Duffield Offer Letter, subject to his execution and non-revocation of a separation agreement, including, without limitation, a general release of claims in favor of the Company and, in the Company's discretion, a one year post-employment noncompetition agreement, Dr. Duffield is entitled to (i) a payment equal to 12 months of his base salary, reduced by any amount he may receive pursuant to the Restrictive Covenants Agreement (as defined in the Duffield Offer Letter), and (ii) if Dr. Duffield is participating in the Company's group health plan immediately prior to his last day of employment and he elects COBRA health continuation, a monthly cash payment to the group health plan provider, COBRA provider or him until the earlier of (A) the 12 month anniversary of his termination, (B) his eligibility for group health plan benefits under any other employer's group health plan, or (C) the end of his COBRA continuation rights period, in an amount equal to the monthly employer contribution the Company would have paid to provide him with health insurance had he remained employed. Such severance amounts will be paid out in substantially equal installments in accordance with the Company's payroll practice over 12 months. In addition, in the event Dr. Duffield's employment is terminated by us without Cause or he resigns for Good Reason, in each case, on or within 12 months after a Sale Event (as such term is defined in the 2019 Plan), then all of the unvested portion of his new hire grant of time-based restricted stock shall immediately vest as of the date of such termination.

Dr. Duffield has entered into an Employee Confidentiality, Assignment, Nonsolicitation and Noncompetition Agreement that contains various restrictive covenants, including, noncompetition and nonsolicitation provisions that apply during his employment and for up to one year thereafter (or, in certain situations, for up to two years thereafter).

Ann L. Lee, Ph.D.

On September 21, 2021, we entered into an offer letter with Dr. Lee, or the Lee Offer Letter, for the position of Chief Technical Officer. The Lee Offer Letter provides for Dr. Lee's at-will employment. Dr. Lee's current base salary is \$453,797 and she is eligible to receive an annual bonus with an annual target amount of 40 percent of her annual base salary, prorated for 2021 based on her October 4, 2021 start date. Dr. Lee is eligible to participate in the employee benefit plans available to our employees, subject to the terms of such plans. In addition, Dr. Lee is also eligible to receive certain relocation benefits pursuant to the Lee Offer Letter, including (i) temporary living accommodations paid by the Company in the greater Boston/Cambridge area beginning for a period of four months starting on January 2022, (ii) reasonable cost for bi-weekly travel to Dr. Lee's current residence on the West Coast, (iii) two house hunting trips for her spouse, including reasonable expense for travel, meal, hotel and other accommodations and (iv) net relocation benefit of up to \$150,000, to be used towards eligible costs for ongoing living expenses and (collectively, the "relocation benefits"). The Company will provide a tax gross-up for the relocation benefits.

Upon a termination of Dr. Lee's employment by us without Cause or her resignation for Good Reason (as such terms are defined in the Lee Offer Letter, subject to her execution and non-revocation of a separation agreement, including, without limitation, a general release of claims in favor of the Company and, in the Company's discretion, a one year post-employment noncompetition agreement, Dr. Lee is entitled to (i) a payment equal to six months of her base salary, reduced by any amount she may receive pursuant to a Noncompete Agreement (as defined in the Lee Offer Letter), and (ii) if Dr. Lee is participating in the Company's group health plan immediately prior to her last day of employment and she elects COBRA health continuation, a monthly cash payment to the group health plan provider, COBRA provider or her until the earlier of (A) the six month anniversary of her termination, (B) her eligibility for group health plan benefits under any other employer's group health plan, or (C) the end of her COBRA continuation rights period, in an amount equal to the monthly employer contribution the Company would have paid to provide her with health insurance had she remained employed. Such severance amounts will be paid out in substantially equal installments in accordance with the Company's payroll practice over six months. In addition, in the event Dr. Lee's employment is terminated by us without Cause or she resigns for Good Reason, in each case, on or within twelve months after a Sale Event (as such term is defined in the 2019 Plan), then all of the unvested portion of her new hire time-based option grant shall immediately vest as of the date of such termination.

Dr. Lee has entered into an Employee Confidentiality, Assignment and Nonsolicitation Agreement that contains various restrictive covenants, including, nonsolicitation provisions that apply during her employment and for up to one year thereafter (or, in certain situations, for up to two years thereafter).

New Employment Agreements for Our Named Executive Officers

In 2022, we entered into employment agreements with each of Dr. Gottesdiener, Dr. Duffield and Dr. Lee, effective as of the completion of our IPO, pursuant to which the executives will continue to serve as our Chief Executive Officer, Chief Scientific Officer and Chief Technical Officer, respectively, as summarized below.

Each of Dr. Gottesdiener, Dr. Duffield and Dr. Lee will be subject to standard confidentiality and nondisclosure, assignment of intellectual property work product and post-termination nonsolicitation of employees, consultants and customers covenants and, in certain circumstances, noncompetition covenants.

Keith M. Gottesdiener, M.D.

The employment agreement with Dr. Gottesdiener, or the Gottesdiener Employment Agreement, provides for at-will employment. The agreement also sets forth initial base salary, initial annual target bonus and eligibility to participate in our benefit plans generally. Effective upon the IPO, the base salary for Dr. Gottesdiener will be \$542,340, and the annual target bonus will be equal to 55% of his annual base salary. In addition, Dr. Gottesdiener

will be entitled to reimbursement for commuting expenses for three (3) years from the commencement of his employment with the Company, which include all reasonable costs for his commute between his family's residence in New York, New York and our corporate headquarters in Cambridge, Massachusetts.

Pursuant to the Gottesdiener Employment Agreement, in the event Dr. Gottesdiener is terminated by us without "cause" or he resigns for "good reason" (as such terms are defined in the Gottesdiener Employment Agreement), in each case subject to the delivery of and compliance with a fully effective separation agreement that shall include, without limitation, a release of claims, reaffirmation of applicable restrictive covenants and, in the Company's discretion, a one year noncompetition agreement, Dr. Gottesdiener will be entitled to (i) an amount equal to the sum of (A) 12 months of his then-current base salary plus (B) 1.0 times his target annual bonus for the then current year, in each case subject to reductions by any amount received by him pursuant to a restrictive covenant agreement, (ii) subject to Dr. Gottesdiener's copayment of premium amounts at the applicable active employees' rate and proper election to continue COBRA health coverage, payment of the portion of the premium equal to the amount we would have paid to provide health insurance had he remained employed by us until the earliest of (A) 12 months following his termination, (B) his eligibility for group medical plan benefits under any other employer's group medical plan or (C) the end of his COBRA health continuation period. These amounts shall be paid out in substantially equal installments in accordance with the Company's payroll practice over a period of 12 months. In addition, subject to the delivery of the fully effective separation agreement, the bonus amount (if any) that Dr. Gottesdiener would have been paid if he had remained employed through the payment date, if such termination occurs on or after January 1 but before the date bonuses are paid for the prior year to the Company's other executives, will be paid to Dr. Gottesdiener on the date the Company's other executives receive their bonuses. In addition, the Company has agreed to negotiate in good faith a non-exclusive limited consulting relationship with Dr. Gottesdiener for a period up to one year under similar terms as described above pursuant to the Gottesdiener Offer Letter.

In the event Dr. Gottesdiener is terminated by us without cause or he resigns for good reason, in each case within 12 months following a change in control (as defined in the Gottesdiener Employment Agreement), or 3 months prior to such change in control, subject to the delivery of and compliance with a fully effective separation agreement as described above, Dr. Gottesdiener will be entitled to the following, in lieu of the benefits above: (i) a lump sum cash payment equal to the sum of (A) 18 months of his then-current base salary (or his base salary in effect immediately prior to the change in control, if higher) plus (B) 1.5 times his target annual bonus for the then current year (or target in effect immediately prior to the change in control, if higher), in each case subject to reductions by any amount received by him pursuant to a restrictive covenant agreement, (ii) subject to Dr. Gottesdiener's copayment of premium amounts at the applicable active employees' rate and proper election to continue COBRA health coverage, payment of the portion of the premium equal to the amount we would have paid to provide health insurance had he remained employed by us until the earliest of (A) 18 months from the date of his separation, (B) his eligibility for group medical plan benefits under any other employer's group medical plan or (C) the end of his COBRA health continuation period, and (iii) the bonus amount (if any) that Dr. Gottesdiener would have been paid if he had remained employed through the payment date, if such termination occurs on or after January 1 but before the date bonuses are paid for the prior year to the Company's other executives. In addition, in the event Dr. Gottesdiener is terminated by us without cause or he resigns for good reason, in each case within 12 months following a change in control, or 3 months prior to such change in control, all of the then-outstanding and unvested portion of his stock options and other stock-based awards that (i) are subject solely to time-based vesting or (ii) were granted to Dr. Gottesdiener prior to the effective date of the Gottesdiener Employment Agreement and are subject to performance-based vesting shall become fully vested and exercisable or nonforfeitable immediately as of the date of termination or, if later, the change in control event, with any such performance-based awards vesting at target.

The payments and benefits provided under the Gottesdiener Employment Agreement in connection with a change in control may not be eligible for federal income tax deduction for the Company pursuant to Section 280G of the Code. These payments and benefits may also be subject to an excise tax under Section 4999 of the Code. If the payments or benefits payable to Dr. Gottesdiener in connection with a change in control would be subject to the excise tax imposed under Section 4999 of the Code, then those payments or benefits will be reduced if such reduction would result in a higher net after-tax benefit to him.

Jeremy Duffield, M.D., Ph.D., FRCP

The employment agreement with Dr. Duffield, or the Duffield Employment Agreement, provides for at-will employment. The agreement also sets forth initial base salary, initial annual target bonus and eligibility to participate in our benefit plans generally. Effective upon the IPO, the base salary for Dr. Duffield will be \$447,120, and the annual target bonus will be equal to 40% of his annual base salary. In addition, Dr. Duffield will remain eligible to receive the milestone bonuses set forth in the Duffield Offer Letter.

Pursuant to the Duffield Employment Agreement, in the event Dr. Duffield is terminated by us without “cause” or he resigns for “good reason” (as such terms are defined in the Duffield Employment Agreement), in each case subject to the delivery of and compliance with a fully effective separation agreement that shall include, without limitation, a release of claims, reaffirmation of applicable restrictive covenants and, in the Company’s discretion, a one year noncompetition agreement, Dr. Duffield will be entitled to (i) an amount equal to the sum of (A) 9 months of his then-current base salary plus (B) 0.75 times his target annual bonus for the then current year, in each case subject to reductions by any amount received by him pursuant to a restrictive covenant agreement, (ii) subject to Dr. Duffield’s copayment of premium amounts at the applicable active employees’ rate and proper election to continue COBRA health coverage, payment of the portion of the premium equal to the amount we would have paid to provide health insurance had he remained employed by us until the earliest of (A) 12 months following his termination, (B) his eligibility for group medical plan benefits under any other employer’s group medical plan or (C) the end of his COBRA health continuation period. These amounts shall be paid out in substantially equal installments in accordance with the Company’s payroll practice over a period of 9 months. In addition, subject to the delivery of the fully effective separation agreement, the bonus amount (if any) that Dr. Duffield would have been paid if he had remained employed through the payment date, if such termination occurs on or after January 1 but before the date bonuses are paid for the prior year to the Company’s other executives, will be paid to Dr. Duffield on the date the Company’s other executives receive their bonuses.

In the event Dr. Duffield is terminated by us without cause or he resigns for good reason, in each case within 12 months following a change in control (as defined in the Duffield Employment Agreement), subject to the delivery of and compliance with a fully effective separation agreement (as described above), Dr. Duffield will be entitled to the following, in lieu of the benefits above: (i) a lump sum cash payment equal to the sum of (A) 12 months of his then-current base salary (or his base salary in effect immediately prior to the change in control, if higher) plus (B) 1.0 times his target annual bonus for the then current year (or target in effect immediately prior to the change in control, if higher), in each case subject to reductions by any amount received by him pursuant to a restrictive covenant agreement, (ii) subject to Dr. Duffield’s copayment of premium amounts at the applicable active employees’ rate and proper election to continue COBRA health coverage, payment of the portion of the premium equal to the amount we would have paid to provide health insurance had he remained employed by us until the earliest of (A) 12 months from the date of his separation, (B) his eligibility for group medical plan benefits under any other employer’s group medical plan or (C) the end of his COBRA health continuation period, and (iii) the bonus amount (if any) that Dr. Duffield would have been paid if he had remained employed through the payment date, if such termination occurs on or after January 1 but before the date bonuses are paid for the prior year to the Company’s other executives. In addition, in the event Dr. Duffield is terminated by us without cause or he resigns for good reason, in each case within 12 months following a change in control, all of the then-outstanding and unvested portion of his stock options and other stock-based awards that (i) are subject solely to time-based vesting or (ii) were granted to Dr. Duffield prior to the effective date of the Duffield Employment Agreement and are subject to performance-based vesting shall become fully vested and exercisable or nonforfeitable immediately as of the date of termination, with any such performance-based awards vesting at target.

The payments and benefits provided under the Duffield Employment Agreement in connection with a change in control may not be eligible for federal income tax deduction for the Company pursuant to Section 280G of the Code. These payments and benefits may also be subject to an excise tax under Section 4999 of the Code. If the payments or benefits payable to Dr. Duffield in connection with a change in control would be subject to the excise tax imposed under Section 4999 of the Code, then those payments or benefits will be reduced if such reduction would result in a higher net after-tax benefit to him.

Ann L. Lee, Ph.D.

The employment agreement with Dr. Lee, or the Lee Employment Agreement, provides for at-will employment. The agreement also sets forth initial base salary, initial annual target bonus and eligibility to participate in our benefit plans generally. Effective upon the IPO, the base salary for Dr. Lee will be \$453,797, and the annual target bonus will be equal to 40% of her annual base salary. Dr. Lee will also be entitled to a temporary relocation benefit, which includes (i) living accommodations in the greater Boston/Cambridge area beginning in January 2022 and continuing for four (4) months, (ii) reasonable costs for bi-weekly travel to her residence on the West Coast and rental car or other transportation as needed in the Boston/Cambridge area, and (iii) the cost of two house hunting trips. In addition, Dr. Lee will also be entitled to a net relocation benefit of up to \$150,000, which can be used towards eligible costs for ongoing living expenses, including rental assistance or home purchase of a new Massachusetts primary residence and current home sale. The Company will cover additional tax-gross-up costs on the provided benefit expenses.

Pursuant to the Lee Employment Agreement, in the event Dr. Lee is terminated by us without “cause” or she resigns for “good reason” (as such terms are defined in the Lee Employment Agreement), in each case subject to the delivery of and compliance with a fully effective separation agreement that shall include, without limitation, a release of claims, reaffirmation of applicable restrictive covenants and, in the Company’s discretion, a one year noncompetition agreement, Dr. Lee will be entitled to (i) an amount equal to the sum of (A) 9 months of her then-current base salary plus (B) 0.75 times her target annual bonus for the then current year, in each case subject to reductions by any amount received by her pursuant to a restrictive covenant agreement, and (ii) subject to Dr. Lee’s copayment of premium amounts at the applicable active employees’ rate and proper election to continue COBRA health coverage, payment of the portion of the premium equal to the amount we would have paid to provide health insurance had she remained employed by us until the earliest of (A) 9 months following her termination, (B) her eligibility for group medical plan benefits under any other employer’s group medical plan or (C) the end of her COBRA health continuation period. These amounts shall be paid out in substantially equal installments in accordance with the Company’s payroll practice over a period of 9 months. In addition, subject to the delivery of the fully effective separation agreement, the bonus amount (if any) that Dr. Lee would have been paid if she had remained employed through the payment date, if such termination occurs on or after January 1 but before the date bonuses are paid for the prior year to the Company’s other executives, will be paid to Dr. Lee on the date the Company’s other executives receive their bonuses.

In the event Dr. Lee is terminated by us without cause or she resigns for good reason, in each case within 12 months following a change in control (as defined in the Lee Employment Agreement), subject to the delivery of and compliance with a fully effective separation agreement (as described above), Dr. Lee will be entitled to the following, in lieu of the benefits above: (i) a lump sum cash payment equal to the sum of (A) 12 months of her then-current base salary (or her base salary in effect immediately prior to the change in control, if higher) plus (B) 1.0 times her target annual bonus for the then current year (or target in effect immediately prior to the change in control, if higher), in each case subject to reductions by any amount received by her pursuant to a restrictive covenant agreement, (ii) subject to Dr. Lee’s copayment of premium amounts at the applicable active employees’ rate and proper election to continue COBRA health coverage, payment of the portion of the premium equal to the amount we would have paid to provide health insurance had she remained employed by us until the earliest of (A) 12 months from the date of her separation, (B) her eligibility for group medical plan benefits under any other employer’s group medical plan or (C) the end of her COBRA health continuation period, and (iii) the bonus amount (if any) that Dr. Lee would have been paid if she had remained employed through the payment date, if such termination occurs on or after January 1 but before the date bonuses are paid for the prior year to the Company’s other executives. In addition, in the event Dr. Lee is terminated by us without cause or she resigns for good reason, in each case within 12 months following a change in control (as defined in the Lee Employment Agreement), all of the then-outstanding and unvested portion of her stock options and other stock-based awards that (i) are subject solely to time-based vesting or (ii) were granted to Dr. Lee prior to the effective date of the Lee Employment Agreement and are subject to performance-based vesting shall become fully vested and exercisable or nonforfeitable immediately as of the date of termination, with any such performance-based awards vesting at target.

The payments and benefits provided under the Lee Employment Agreement in connection with a change in control may not be eligible for federal income tax deduction for the Company pursuant to Section 280G of the Code.

These payments and benefits may also be subject to an excise tax under Section 4999 of the Code. If the payments or benefits payable to Dr. Lee in connection with a change in control would be subject to the excise tax imposed under Section 4999 of the Code, then those payments or benefits will be reduced if such reduction would result in a higher net after-tax benefit to her.

Employee Benefit and Equity Compensation Plans

2019 Stock Option and Grant Plan

Our 2019 Plan was approved by our board of directors and our stockholders on September 26, 2019, and most recently amended on April 19, 2021. Under the 2019 Plan, we have reserved for issuance an aggregate of 35,943,372 shares of our common stock. The number of shares of common stock reserved for issuance is subject to adjustment in the event of any merger, consolidation, sale of all or substantially all of our assets, reorganization, recapitalization, reclassification, stock split, stock dividend, reverse stock split or other similar transaction.

The shares of common stock underlying awards that are forfeited, canceled, reacquired by us prior to vesting, satisfied without the issuance of stock or otherwise terminated (other than by exercise) and shares of common stock that are withheld upon exercise of an option or settlement of an award to cover the exercise price or tax withholding are currently added back to the shares of common stock available for issuance under the 2019 Plan.

Our board of directors has acted as administrator of the 2019 Plan. The administrator has full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted, and to determine the specific terms and conditions of each award, subject to the provisions of the 2019 Plan. Persons eligible to participate in the 2019 Plan are those employees, officers and directors of, and consultants and advisors to, our company as selected from time to time by the administrator in its discretion.

The 2019 Plan permits the granting of (1) options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Internal Revenue Code of 1986, as amended, or the Code, and (2) options that do not so qualify. The per share exercise price of each option is determined by the administrator but may not be less than 100 percent of the fair market value of the common stock on the date of grant. The term of each option is fixed by the administrator but may not exceed 10 years from the date of grant. The administrator determines at what time or times each option may be exercised. In addition, the 2019 Plan permits the granting of restricted shares of common stock, unrestricted shares of common stock, and restricted stock units.

The 2019 Plan provides that upon the occurrence of a “sale event,” as defined in the 2019 Plan, all outstanding stock options will terminate at the effective time of such sale event, unless the parties to the sale event agree that such awards will be assumed or continued by the successor entity. In the event of a termination of the 2019 Plan and all options issued thereunder in connection with a sale event, optionees will be provided an opportunity to exercise options that are then exercisable or will become exercisable as of the effective time of the sale event within a specified period of time prior to the consummation of the sale event. In addition, we have the right to provide for cash payment to holders of options, in exchange for the cancellation thereof, in an amount per share equal to the difference between the value of the consideration payable per share of common stock in the sale event and the per share exercise price of such options. In the event of, and subject to the consummation of, a sale event, restricted stock and restricted stock units (other than those becoming vested as a result of the sale event) will be forfeited immediately prior to the effective time of a sale event unless such awards are assumed or continued by the successor entity. In the event that shares of restricted stock are forfeited in connection with a sale event, such shares of restricted stock shall be repurchased at a price per share equal to the original per share purchase price of such shares. We have the right to provide for cash payment to holders of restricted stock or restricted stock units, in exchange for the cancellation thereof, in an amount per share equal to the value of the consideration payable per share of common stock in the sale event.

Additionally, the 2019 Plan provides for certain drag along rights pursuant to which grantees may be obligated to, on the request of the Company or the accepting requisite holder, sell, transfer and deliver, or cause to be sold, transferred and delivered, to a buyer, their shares in the event the Company or the accepting requisite holder determine to enter into a sale event with a buyer.

The board of directors may amend or discontinue the 2019 Plan at any time, subject to stockholder approval where such approval is required by applicable law. The administrator of the 2019 Plan may also amend or cancel any outstanding award, provided that no amendment to an award may adversely affect a participant's rights without his or her consent. The administrator of the 2019 Plan is specifically authorized to exercise its discretion to reduce the exercise price of outstanding stock options or effect the repricing of such awards through cancellation and re-grants.

The 2019 Plan will automatically terminate upon the earlier of 10 years from the date on which the 2019 Plan was initially adopted by our board of directors or 10 years from the date the 2019 Plan was initially approved by our stockholders. As of _____, 2022, options to purchase _____ shares of common stock and _____ restricted share awards were outstanding under the 2019 Plan. Our board of directors has determined not to make any further awards under the 2019 Plan following the closing of this offering.

2022 Stock Option and Incentive Plan

Our 2022 Plan was adopted by our board of directors on February 9, 2022, approved by our stockholders on _____, 2022 and will become effective upon the date immediately preceding the date on which the registration statement of which this prospectus is part is declared effective by the SEC. The 2022 Plan will replace the 2019 Plan as our board of directors has determined not to make additional awards under the 2019 Plan following the closing of our initial public offering. However, the 2019 Plan will continue to govern outstanding equity awards granted thereunder. The 2022 Plan allows us to make equity-based and cash-based incentive awards to our officers, employees, directors and consultants.

We have initially reserved the sum of (i) _____ shares plus (ii) the number of shares available for grants under the 2019 Plan, as of the effective date, for the issuance of awards under the 2022 Plan, or the Initial Limit. The 2022 Plan provides that the number of shares reserved and available for issuance under the 2022 Plan will automatically increase on January 1, 2023 and each January 1 thereafter, by five percent of the outstanding number of shares of our common stock on the immediately preceding December 31 or such lesser number of shares as determined by our compensation committee, or the Annual Increase. The number of shares reserved under the 2022 Plan is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

The shares we issue under the 2022 Plan will be authorized but unissued shares or shares that we reacquire. The shares of common stock underlying any awards under the 2022 Plan and the 2019 Plan that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by us prior to vesting, satisfied without the issuance of stock, expire or are otherwise terminated (other than by exercise) will be added back to the shares of common stock available for issuance under the 2022 Plan.

The maximum number of shares of common stock that may be issued in the form of incentive stock options shall not exceed the Initial Limit, cumulatively increased on January 1, 2023 and on each January 1 thereafter by the lesser of the Annual Increase for such year or _____ shares of common stock, in each case subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

The grant date fair value of all awards made under our 2022 Plan and all other cash compensation paid by us to any non-employee director in any calendar year for services as a non-employee director shall not exceed \$ _____; provided, however, that such amount shall be \$ _____ for the calendar year in which the applicable non-employee director is initially elected or appointed to the board of directors.

The 2022 Plan will be administered by our compensation committee. Our compensation committee has the full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted and the number of shares subject to such awards, to make any combination of awards to participants, to accelerate at any time the exercisability or vesting of any award and to determine the specific terms and conditions of each award, subject to the provisions of the 2022 Plan. Persons eligible to participate in the 2022 Plan will be those full or part-time officers, employees, non-employee directors and consultants as selected from time to time by our compensation committee in its discretion.

The 2022 Plan permits the granting of both options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Code and options that do not so qualify. The option exercise price of each option will be determined by our compensation committee but generally may not be less than 100 percent of the fair market value of our common stock on the date of grant unless the option (i) is granted pursuant to a transaction described in, and in a manner consistent with Section 424(a) of the Code, (ii) is granted to an individual who is not subject to U.S. income tax or (iii) complies with Section 409A of the Code. The term of each option will be fixed by our compensation committee and may not exceed 10 years from the date of grant. Our compensation committee will determine at what time or times each option may be exercised.

Our compensation committee may award stock appreciation rights under the 2022 Plan subject to such conditions and restrictions as it may determine. Stock appreciation rights entitle the recipient to shares of common stock, or cash, equal to the value of the appreciation in our stock price over the exercise price. The exercise price of each stock appreciation right will be determined by our compensation committee but generally may not be less than 100 percent of the fair market value of our common stock on the date of grant unless the stock appreciation right (i) is granted pursuant to a transaction described in, and in a manner consistent with Section 424(a) of the Code, (ii) is granted to an individual who is not subject to U.S. income tax or (iii) complies with Section 409A of the Code. The term of each stock appreciation right will be fixed by our compensation committee and may not exceed 10 years from the date of grant. Our compensation committee will determine at what time or times each stock appreciation right may be exercised.

Our compensation committee may award restricted shares of common stock and restricted stock units to participants subject to such conditions and restrictions as it may determine. These conditions and restrictions may include the achievement of certain performance goals and/or continued employment with us through a specified vesting period. Our compensation committee may also grant shares of common stock that are free from any restrictions under the 2022 Plan. Unrestricted stock may be granted to participants in recognition of past services or for other valid consideration and may be issued in lieu of cash compensation due to such participant.

Our compensation committee may grant dividend equivalent rights to participants that entitle the recipient to receive credits for dividends that would be paid if the recipient had held a specified number of shares of common stock.

Our compensation committee may grant cash bonuses under the 2022 Plan to participants, subject to the achievement of certain performance goals and/or continued employment or service relationship with us through a specified vesting period.

The 2022 Plan provides that upon the effectiveness of a “sale event,” as defined in the 2022 Plan, an acquirer or successor entity may assume, continue or substitute outstanding awards under the 2022 Plan. To the extent that awards granted under the 2022 Plan are not assumed or continued or substituted by the successor entity, upon the effective time of the sale event, such awards shall terminate. In such case, except as may be otherwise provided in the relevant award agreement, all awards with time-based vesting, conditions or restrictions shall become fully vested and nonforfeitable as of the effective time of the sale event and all awards with conditions and restrictions relating to the attainment of performance goals may become vested and nonforfeitable in connection with a sale event in the plan administrator’s discretion or to the extent specified in the relevant award agreement. In the event of such termination, (i) individuals holding options and stock appreciation rights will be permitted to exercise such options and stock appreciation rights (to the extent exercisable) within a specified period of time prior to the sale event or (ii) we may make or provide for a payment, in cash or in kind, to participants holding vested and exercisable options and stock appreciation rights equal (A) the difference between the per share cash consideration payable to stockholders in the sale event and the per share exercise price of the options or stock appreciation rights, multiplied by (B) the number of shares subject to such outstanding vested and exercisable options and stock appreciation rights (to the extent exercisable at prices not in excess of the per share cash consideration), and we may make or provide for a payment, in cash or in kind, to participants holding other vested awards equal to the per share cash consideration multiplied by the number of vested shares underlying such awards.

Our board of directors may amend or discontinue the 2022 Plan and our compensation committee may amend or cancel outstanding awards for purposes of satisfying changes in law or any other lawful purpose, but no such

action may adversely affect rights under an award without the holder's consent. Certain amendments to the 2022 Plan require the approval of our stockholders. The plan administrator cannot, without prior stockholder approval, reduce the exercise price of outstanding stock options or stock appreciation rights or effect the repricing of such awards through cancellation and re-grants or cancellation of stock options or stock appreciation rights in exchange for cash or other awards. No awards may be granted under the 2022 Plan after the date that is 10 years from the effective date of the 2022 Plan. No awards under the 2022 Plan have been made prior to the date of this prospectus.

2022 Employee Stock Purchase Plan

Our ESPP was adopted by our board of directors on February 9, 2022, approved by our stockholders on _____, 2022 and will become effective on the date immediately preceding the date on which the registration statement of which this prospectus forms a part is declared effective by the SEC. The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of the Code. The ESPP initially reserves and authorizes the issuance of up to a total of _____ shares of our common stock to participating employees. The ESPP provides that the number of shares reserved and available for issuance will automatically increase on January 1, 2023 and each January 1 thereafter through January 1, 2032, by the least of (i) _____ shares of our common stock, (ii) _____ percent of the outstanding number of shares of our common stock on the immediately preceding December 31, or (iii) such lesser number of shares of common stock as determined by the administrator of the ESPP. The number of shares reserved under the ESPP is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

All employees who are customarily employed by us or one of our designated subsidiaries for more than twenty hours per week and who we have employed for at least 6 months are eligible to participate in the ESPP. However, any employee who owns five percent or more of the total combined voting power or value of all classes of our stock will not be eligible to purchase shares of common stock under the ESPP.

We may make one or more offerings each year to our employees to purchase shares under the ESPP. The plan administrator may, in its discretion, designate the start and end dates of any offering; provided, that no offering will exceed twenty-seven months in duration. Each eligible employee may elect to participate in any offering by submitting an enrollment form at least fifteen business days before the applicable offering date.

Each employee who is a participant in the ESPP may purchase shares of our common stock by authorizing contributions of between one and fifteen percent of his or her eligible compensation during an offering period. Unless the participating employee has previously withdrawn from the offering, his or her accumulated contributions will be used to purchase shares of our common stock on the last business day of the offering period at a price equal to 85 percent of the fair market value of the shares of our common stock on the first business day or the last business day of the offering period, whichever is lower, provided that no more than 7,000 shares of common stock (or a lesser number as established by our plan administrator in advance of the offering period) may be purchased by any one employee during each offering period. In addition, under applicable tax rules, an employee may purchase no more than \$25,000 worth of shares of our common stock, valued at the start of the offering period, under the ESPP for each calendar year in which a purchase right is outstanding.

The accumulated payroll deductions of any employee who is not a participant on the last day of an offering period will be refunded. An employee's rights under the ESPP terminate upon voluntary withdrawal from the plan or when the employee ceases employment with us for any reason.

In the case of and subject to the consummation of a "sale event," the plan administrator, in its discretion, and on such terms and conditions as it deems appropriate, is hereby authorized to take any one or more of the following actions under the ESPP or with respect to any right under the ESPP or to facilitate such transactions or events: (i) to provide for either (A) termination of any outstanding option in exchange for an amount of cash, if any, equal to the amount that would have been obtained upon the exercise of such option had such option been currently exercisable or (B) the replacement of such outstanding option with other options or property selected by the plan administrator in its sole discretion; (ii) to provide that the outstanding options under the ESPP shall be assumed by the successor or survivor corporation, or a parent or subsidiary thereof, or shall be substituted for similar options covering the stock of the successor or survivor corporation, or a parent or subsidiary thereof, with appropriate adjustments as to

the number and kind of shares and prices; (iii) to make adjustments in the number and type of shares of common stock (or other securities or property) subject to outstanding options under the ESPP and/or in the terms and conditions of outstanding options and options that may be granted in the future; (iv) to provide that the offering with respect to which an option relates will be shortened by setting a new exercise date on which such offering will end; and (v) to provide that all outstanding options shall terminate without being exercised and all amounts in the accounts of participants shall be promptly refunded.

The ESPP may be terminated or amended by our board of directors at any time. An amendment that increases the number of shares of our common stock authorized under the ESPP and certain other amendments require the approval of our stockholders. The plan administrator may adopt subplans under the ESPP for employees of our non-U.S. subsidiaries

Senior Executive Cash Incentive Bonus Plan

On February 9, 2022 our board of directors adopted the Senior Executive Cash Incentive Bonus Plan, or the Bonus Plan. The Bonus Plan provides for annual cash bonus payments based upon the attainment of Company and individual performance targets established by our compensation committee. The payment targets may be related to financial and operational measures or objectives with respect to our Company, or the Corporate Performance Goals, as well as individual performance objectives.

Our compensation committee may select Corporate Performance Goals from among the following: developmental, publication, clinical or regulatory milestones; cash flow (including, but not limited to, operating cash flow and free cash flow); revenue; corporate revenue; earnings before interest, taxes, depreciation and amortization; net income (loss) (either before or after interest, taxes, depreciation and/or amortization); changes in the market price of our common stock; economic value-added; acquisitions, licenses, collaborations or strategic transactions; financing or other capital raising transactions; operating income (loss); return on capital, assets, equity, or investment; stockholder returns; return on sales; total shareholder return; gross or net profit levels; productivity; expense efficiency; margins; operating efficiency; customer satisfaction; working capital; earnings (loss) per share of the company's common stock; bookings, new bookings or renewals; sales or market shares; number of prescriptions or prescribing physicians; coverage decisions; leadership development, employee retention and recruiting and other human resources matters; operating income and/or net annual recurring revenue, any of which may be measured in absolute terms, as compared to any incremental increase, in terms of growth, as compared to results of a peer group, against the market as a whole, compared to applicable market indices and/or measured on a pre-tax or post-tax basis.

Each executive officer who is selected to participate in the Bonus Plan will have a target bonus opportunity set for each performance period. The bonus formulas will be adopted in each performance period by the compensation committee and communicated to each executive. The Corporate Performance Goals will be measured at the end of each performance period after our financial reports have been published or such other appropriate time as the compensation committee determines. If the Corporate Performance Goals and individual performance objectives are met, payments will be made as soon as practicable following the end of each performance period, but no later than two and one-half months after the end of the fiscal year in which such performance period ends. Subject to the rights contained in any agreement between the executive officer and us, and unless otherwise determined by the compensation committee, an executive officer must be employed by us on the bonus payment date to be eligible to receive a bonus payment. The Bonus Plan also permits the compensation committee to approve additional bonuses to executive officers in its sole discretion.

DIRECTOR COMPENSATION

Prior to this offering, we did not have a formal non-employee director compensation policy. We have historically provided equity grants to certain of our non-employee directors not associated with ARCH Venture Partners, F-Prime Capital, Newpath Partners or GV. In 2021, we granted each of Mr. Kelly and Dr. Chung an option to purchase 42,000 shares of our common stock. The options vest in equal annual installments over three years, subject to continued service with the Company.

The following table presents the total compensation for each person who served as a non-employee member of our board of directors during the year ended December 31, 2021. Other than as set forth in the table and described more above, we did not pay any compensation, make any equity awards or non-equity awards to, or pay any other compensation to any of the non-employee members of our board of directors in 2021. We reimburse non-employee members of our board of directors for reasonable travel and out-of-pocket expenses incurred in attending meetings of our board of directors and committees of our board of directors. Dr. Gottesdiener, who is our Chief Executive Officer, did not receive any additional compensation for his service as a director. The compensation received by Dr. Gottesdiener, as a named executive officer of the Company, is presented in “Executive Compensation-2021 Summary Compensation Table” above.

Name	Fees Earned or Paid in Cash (\$)	Option Awards (\$) ⁽¹⁾	All Other Compensation (\$)	Total (\$)
Tom Cahill ⁽²⁾	—	—	—	—
Wendy Chung ⁽³⁾	—	96,134	—	96,134
John Evans ⁽⁴⁾	—	—	—	—
Kaye Foster ⁽⁵⁾	—	—	—	—
Michael Kelly ⁽⁶⁾	—	96,134	—	96,134
Robert Nelson ⁽⁷⁾	—	—	—	—
Stephen Knight ⁽⁸⁾	—	—	—	—
David Schenkein ⁽⁹⁾	—	—	—	—

(1) The amounts reported represent the aggregate grant date fair value of the stock options granted to our directors during the fiscal year, calculated in accordance with FASB ASC Topic 718. Such grant date fair values do not take into account any estimated forfeitures. The assumptions used in calculating the grant date fair value of the stock options reported in this column are set forth in note 8 of our consolidated financial statements included elsewhere in this prospectus. The amounts reported in this column reflect the accounting cost for these awards and do not correspond to the actual economic value that may be received by our directors upon the exercise of the awards or any sale of the underlying shares of common stock.

(2) As of December 31, 2021, Dr. Cahill did not hold any outstanding equity awards.

(3) As of December 31, 2021, Dr. Chung held options to purchase an aggregate of 42,000 shares of our common stock.

(4) As of December 31, 2021, Mr. Evans did not hold any outstanding equity awards.

(5) As of December 31, 2021, Ms. Foster did not hold any outstanding equity awards.

(6) As of December 31, 2021, Mr. Kelly held options to purchase an aggregate of 42,000 shares of our common stock.

(7) As of December 31, 2021, Mr. Nelson did not hold any outstanding equity awards.

(8) As of December 31, 2021, Mr. Knight did not hold any outstanding equity awards.

(9) As of December 31, 2021, Mr. Schenkein did not hold any outstanding equity awards.

Non-Employee Director Compensation Policy

In connection with this offering, we intend to adopt a new non-employee director compensation policy that will become effective as of the completion of this offering and will be designed to enable us to attract and retain, on a long term basis, highly qualified non-employee directors. Under the policy, our non-employee directors will be

eligible to receive cash retainers (which will be payable quarterly in arrears and prorated for partial years of service) and equity awards as set forth below:

Annual Retainer for Board Membership

\$40,000 for general availability and participation in meetings and conference calls of our Board of Directors

Additional Annual Retainer for Committee Membership

Audit Committee Chairperson: \$15,000

Audit Committee member (other than Chairperson): \$7,500

Compensation Committee Chairperson: \$12,000

Compensation Committee member (other than Chairperson): \$6,000

Nominating and Corporate Governance Committee Chairperson: \$10,000

Nominating and Corporate Governance Committee member (other than Chairperson): \$5,000

In addition, our policy will provide that, upon initial election or appointment to our board of directors, each new non-employee director will be granted a one-time grant of a non-statutory stock option to purchase shares of our common stock equivalent to \$800,000 in value on the date of such director's election or appointment to the board of directors, or the Director Initial Grant. The Director Initial Grant will vest in substantially equal annual installments over three years, subject to the non-employee director's continued services to the Company. On the date of each annual meeting of stockholders of our company following the completion of this offering, each non-employee director who has served as a director for at least 6 months prior to the annual meeting and will continue as a non-employee director following such meeting will be granted an annual award of a non-statutory stock option to purchase shares of common stock equivalent to \$400,000 in value, or the Director Annual Grant. The Director Annual Grant will vest in full on the earlier of the one-year anniversary of the grant date or on the date of our next annual meeting of stockholders, subject to the non-employee director's continued services to the Company. Such awards are subject to full acceleration vesting upon the sale of our company.

The aggregate amount of compensation, including both equity compensation and cash compensation, paid to any non-employee director for service as a non-employee director in a calendar year period will not exceed \$ _____ in the first calendar year such individual becomes a non-employee director and \$ _____ in any other calendar year.

We will reimburse all reasonable out-of-pocket expenses incurred by directors for their attendance at meetings of our board of directors or any committee thereof.

Employee directors will receive no additional compensation for their service as a director.

CERTAIN RELATIONSHIPS AND RELATED PERSON TRANSACTIONS

The following is a description of transactions or series of transactions since our inception in September 2019, to which we were or will be a party, in which:

- the amount involved in the transaction exceeds, or will exceed, \$120,000; and
- in which any of our executive officers, directors or holder of five percent or more of any class of our capital stock, including their immediate family members or affiliated entities, had or will have a direct or indirect material interest.

Compensation arrangements for our named executive officers and our directors are described elsewhere in this prospectus under “Executive Compensation” and “Director Compensation.”

Series A Preferred Stock Financing

In 2019, 2020 and 2021, we sold an aggregate of 115,761,842 Series A convertible preferred shares in multiple closings at a purchase price of \$1.00 per share for an aggregate amount of \$115.8 million. The following table summarizes purchases of our Series A convertible preferred shares by related persons:

Stockholder	Shares of Series A convertible preferred shares	Total purchase price
F-Prime Capital Partners Life Sciences Fund VI LP ⁽¹⁾	33,333,331	\$ 33,333,331
GV 2019, L.P. ⁽²⁾	33,333,331	\$ 33,333,331
Entities affiliated with ARCH Venture Partners ⁽³⁾	33,333,331	\$ 33,333,331
Newpath Partners, L.P. ⁽⁴⁾	9,999,999	\$ 9,999,999
David Liu ⁽⁵⁾	1,000,001	\$ 1,000,001

(1) Stephen Knight serves as a member of our board of directors and is an affiliate of F-Prime Capital, of which F-Prime Capital Partners Life Sciences Fund VI LP is an affiliated fund. F-Prime Capital Partners Life Sciences Fund VI LP holds more than 5 percent of our voting securities.

(2) David Schenkein serves as a member of our board of directors and is an affiliate of GV, of which GV 2019, L.P. is an affiliated fund. Entities affiliated with GV collectively hold more than 5 percent of our voting securities.

(3) Represents 16,666,664 shares of Series A convertible preferred stock purchased by ARCH Venture Fund X Overage, L.P. and 16,666,667 shares of Series A convertible preferred stock purchased by ARCH Venture Fund X, L.P. Robert Nelsen serves as a member of our board of directors and is an affiliate of ARCH Venture Partners, of which ARCH Venture Fund X Overage, L.P. and ARCH Venture Fund X, L.P. are affiliated funds. Entities affiliated with ARCH Venture Partners collectively hold more than 5 percent of our voting securities.

(4) Thomas Cahill serves as a member of our board of directors and is an affiliate of Newpath Partners, of which Newpath Partners, L.P. is an affiliated fund. Newpath Partners, L.P. holds more than 5 percent of our voting securities.

(5) David Liu is our founder and holds more than 5 percent of our voting securities.

Series B Preferred Stock Financing

In 2021, we sold an aggregate of 45,658,957 Series B convertible preferred shares in multiple closings at a purchase price of \$4.3803 per share for an aggregate amount of \$200.0 million. The following table summarizes purchases of our Series B convertible preferred shares by related persons:

Stockholder	Shares of Series B convertible preferred shares	Total purchase price
F-Prime Capital Partners Life Sciences Fund VI LP ⁽¹⁾	2,282,948	\$ 9,999,997
GV 2021, L.P. ⁽²⁾	5,479,076	\$ 23,999,997
Entities affiliated with ARCH Venture Partners ⁽³⁾	2,282,948	\$ 9,999,997
Newpath Partners, L.P. ⁽⁴⁾	5,250,781	\$ 22,999,996

(1) Stephen Knight serves as a member of our board of directors and is an affiliate of F-Prime Capital, of which F-Prime Capital Partners Life Sciences Fund VI LP is an affiliated fund. F-Prime Capital Partners Life Sciences Fund VI LP holds more than 5 percent of our voting securities.

- (2) David Schenkein serves as a member of our board of directors and is an affiliate of GV, of which GV 2021, L.P. is an affiliated fund. Entities affiliated with GV collectively hold more than 5 percent of our voting securities.
- (3) Represents 1,141,474 shares of Series B convertible preferred stock purchased by ARCH Venture Fund X Overage, L.P. and 1,141,474 shares of Series B convertible preferred stock purchased by ARCH Venture Fund X, L.P. Robert Nelsen serves as a member of our board of directors and is an affiliate of ARCH Venture Partners, of which ARCH Venture Fund X Overage, L.P. is an affiliated fund. Entities affiliated with ARCH Venture Partners collectively hold more than 5 percent of our voting securities.
- (4) Thomas Cahill serves as a member of our board of directors and is an affiliate of Newpath Partners, of which Newpath Partners, L.P. is an affiliated fund. Newpath Partners, L.P. holds more than 5 percent of our voting securities.

Consulting Agreement with David Liu

In September 2019, we entered into a consulting agreement with David Liu, which was amended in October 2022, or the Liu Consulting Agreement. Dr. Liu is a beneficial owner of more than 5 percent of our voting securities. Pursuant to the Liu Consulting Agreement, we agreed to pay Dr. Liu an annual fee of \$150,000 and to reimburse Dr. Liu's reasonable business expenses. Dr. Liu agreed to provide services, including serving as Chairman of our Scientific Advisory Board and advisory services related to any and all gene editing and related technology for any and all human or prophylactic uses, including without limitation, participation in corporate and research and development strategy sessions, recruiting and interviewing activities, finding and establishing laboratory space, advising on the design of experiments and other research and development activities.

Pursuant to the Liu Consulting Agreement, for the term of the Liu Consulting Agreement and six months thereafter, Dr. Liu cannot directly provide material services to any third party in the field of gene editing for therapeutics or become an owner, partner, shareholder, consultant, agent, employee or co-venturer of any third party that has committed, or intends to commit, significant resources to that field, with certain exceptions, including a previous commitment with respect to Beam Therapeutics, Inc., or Beam (see below).

The Liu Consulting Agreement does not prevent David Liu from conducting research funded by a third-party sponsor at the HHMI, Harvard or Broad Institute, or collectively, the Institutions, provided that any inventions conceived in the course of such research will be owned by such Institution. Furthermore, David Liu is not restricted from publishing the results of such research or providing education, clinical or other such services for an Institution. Additionally, pursuant to a consulting agreement entered into between Dr. Liu and Beam in March 2017, or the Beam Consulting Agreement, Dr. Liu is permitted to provide consulting services to Beam, subject to certain limitations, one of which includes not providing Beam services related to our Prime Editing technology. If there is any conflict between the Liu Consulting Agreement and the Beam Consulting Agreement, the Beam Consulting Agreement prevails. The current term of the Liu Consulting Agreement runs through September 2025, following which it may be terminated by either party with 30 days prior notice. As of December 31, 2021, we have paid Dr. Liu \$345,000 under the Liu Consulting Agreement.

Agreement with Myeloid

In December 2021, we entered into the Myeloid Agreement. Newpath Partners, L.P. holds more than 5 percent of our voting securities, and holds more than 5 percent of Myeloid's voting securities as well. Under the Myeloid Agreement, we collaborate with Myeloid on the research and development of LINE-1 retrotransposon technology. In connection with this agreement, Myeloid received an upfront payment of \$30.0 million in cash and was issued an aggregate of 3,424,422 shares of our common stock.

See "Business—Our License and Collaboration Agreements—Research Collaboration, Option and License Agreement with Myeloid Therapeutics, Inc."

Agreements with Stockholders

In connection with our Series A preferred stock financing and Series B preferred stock financing, we entered into investors' rights, voting and right of first refusal and co-sale agreements containing registration rights, information rights, voting rights and rights of first refusal, among other things, with certain holders of our preferred stock and certain holders of our common stock. These stockholder agreements will terminate upon the closing of this offering, except for the registration rights granted under our investors' rights agreement, as more fully described in "Description of Capital Stock—Registration Rights."

Stock Option Grants to Executive Officers

We have granted stock options to our named executive officers as more fully described in the section entitled “Executive Compensation.”

Indemnification Agreements

In connection with this offering, we intend to enter into new agreements to indemnify our directors and executive officers. These agreements will, among other things, require us to indemnify these individuals for certain expenses (including attorneys’ fees), judgments, fines and settlement amounts reasonably incurred by such person in any action or proceeding, including any action by or in our right, on account of any services undertaken by such person on behalf of our company or that person’s status as a member of our board of directors to the maximum extent allowed under Delaware law.

Policies for Approval of Related Party Transactions

Our board of directors reviews and approves transactions with directors, officers and holders of five percent or more of our voting securities and their affiliates, each a related party. Prior to this offering, the material facts as to the related party’s relationship or interest in the transaction were disclosed to our board of directors prior to their consideration of such transaction, and the transaction was not considered approved by our board of directors unless a majority of the directors who are not interested in the transaction approved the transaction. Further, when stockholders are entitled to vote on a transaction with a related party, the material facts of the related party’s relationship or interest in the transaction were disclosed to the stockholders, who must approve the transaction in good faith.

In connection with this offering, we expect to adopt a written related party transactions policy that will provide that such transactions must be approved by our audit committee. This policy will become effective on the date on which the registration statement of which this prospectus forms a part is declared effective by the SEC. Pursuant to this policy, the audit committee has the primary responsibility for reviewing and approving or disapproving “related party transactions,” which are transactions between us and related persons in which the aggregate amount involved exceeds or may be expected to exceed \$120,000 and in which a related person has or will have a direct or indirect material interest. In reviewing any such proposal, our audit committee or other committee of independent directors are to consider the relevant facts of the transaction, including the risks, costs and benefits to us and whether the transaction is on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances. For purposes of this policy, a related person will be defined as a director, executive officer, nominee for director, or greater than 5 percent beneficial owner of our common stock, in each case since the beginning of the most recently completed year, and their immediate family members.

PRINCIPAL STOCKHOLDERS

The following table sets forth, as of December 31, 2021, information regarding the beneficial ownership of our common stock by:

- each person, or group of affiliated persons, who is known by us to be the beneficial owner of five percent or more of our outstanding common stock (on an as-converted to common stock basis);
- each of our directors;
- each of our named executive officers; and
- all of our current directors and executive officers as a group.

The information in the following table is calculated based on 265,613,476 shares (which includes 47,734,388 shares of unvested restricted common stock) of common stock deemed to be outstanding before this offering and _____ shares of common stock outstanding after this offering, assuming no exercise by the underwriters of their option to purchase additional shares of common stock. The number of shares outstanding is based on the number of shares of common stock outstanding as of December 31, 2021 as adjusted to give effect to:

- the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 161,420,799 shares of common stock upon the completion of this offering; and
- the sale of _____ shares of common stock in this offering (assuming no exercise of the underwriters' option to purchase additional shares).

Each individual or entity shown on the table has furnished information with respect to beneficial ownership. Except as otherwise indicated below, the address of each officer, director and five percent stockholder listed below is c/o Prime Medicine, Inc., 21 Erie Street, Cambridge, MA 02139.

We have determined beneficial ownership in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities as well as any shares of common stock that the person has the right to acquire within 60 days of December 31, 2021 through the exercise of stock options or other rights. These shares are deemed to be outstanding and beneficially owned by the person holding those options for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the

percentage ownership of any other person. Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them.

	Shares of common stock beneficially owned	Percentage of shares beneficially owned	
		Before offering	After offering
5% or Greater Stockholders			
David Liu ⁽¹⁾	65,833,288	24.80 %	
Entities affiliated with GV ⁽²⁾	38,812,407	14.61 %	
Entities affiliated with ARCH Venture Partners ⁽³⁾	35,616,279	13.41 %	
F-Prime Capital Partners Life Sciences Fund VI LP ⁽⁴⁾	35,616,279	13.41 %	
Newpath Partners, L.P. ⁽⁵⁾	15,250,780	5.74 %	
Directors, Named Executive Officers and Other Executive Officers			
Keith Gottesdiener ⁽⁶⁾	10,365,143	3.90 %	
Jeremy Duffield ⁽⁷⁾	3,004,167	1.13 %	
Ann Lee	—	— %	
John Evans ⁽⁸⁾	5,000,000	1.88 %	
Stephen Knight	—	— %	
Robert Nelsen ⁽³⁾	35,616,279	13.41 %	
Thomas Cahill	—	— %	
David Schenkein	—	— %	
Michael Kelly	—	— %	
Wendy Chung	—	— %	
Kaye Foster	—	— %	
All executive officers and directors as a group (14 persons)	56,710,158	21.34 %	

* Less than one percent.

(1) Consists of: (a) 64,772,720 shares of common stock, (b) 1,000,001 shares of common stock issuable upon conversion of Series A convertible preferred stock and (c) 60,567 shares of common stock underlying options exercisable within 60 days of December 31, 2021.

(2) Consists of: (a) 33,333,331 shares of common stock issuable upon conversion of Series A convertible preferred stock held by GV 2019, L.P., or GV 2019, and (b) 5,479,076 shares of common stock issuable upon conversion of Series B convertible preferred stock held by GV 2021, L.P., or GV 2021.

GV 2019 GP, L.P., the general partner of GV 2019, GV 2019 GP, L.L.C., the general partner of GV 2019 GP, L.P., Alphabet Holdings LLC, the sole member of GV 2019 GP, L.L.C., XXVI Holdings Inc., the sole member of Alphabet Holdings LLC, and Alphabet Inc., the controlling stockholder of XXVI Holdings Inc., may each be deemed to have sole power to vote or dispose of the shares held directly by GV 2019.

GV 2021 GP, L.P., the general partner of GV 2021, GV 2021 GP, L.L.C., the general partner of GV 2021 GP, L.P., Alphabet Holdings LLC, the sole member of GV 2021 GP, L.L.C., XXVI Holdings Inc., the sole member of Alphabet Holdings LLC, and Alphabet Inc., the controlling stockholder of XXVI Holdings Inc., may each be deemed to have sole power to vote or dispose of the shares held directly by GV 2021.

The principal business address for all entities referenced in this footnote is 1600 Amphitheatre Parkway, Mountain View, CA 94043.

(3) Consists of: (a) 16,666,667 shares of common stock issuable upon conversion of Series A convertible preferred stock held by ARCH Venture Fund X, L.P., or ARCH X, (b) 1,141,474 shares of common stock issuable upon conversion of Series B convertible preferred stock held by ARCH X, (c) 16,666,664 shares of common stock issuable upon conversion of Series A convertible preferred stock held by ARCH Venture Fund X Overage, L.P., or ARCH X Overage, and (d) 1,141,474 shares of common stock issuable upon conversion of Series B convertible preferred stock held by ARCH X Overage.

ARCH Venture Partners X, L.P., or AVP X LP, is the sole general partner of ARCH X. ARCH Venture Partners X Overage, L.P., or AVP X Overage LP, is the sole general partner of ARCH X Overage. ARCH Venture Partners X, LLC, or AVP X LLC, is the sole general partner of each of AVP X LP and AVP X Overage LP. Keith Crandell, Kristina Burow, Steven Gillis, and Robert Nelsen comprise the investment committee of AVP X LLC, or the AVP X Committee Members. AVP X LP and AVP X Overage LP may be deemed to

beneficially own the shares held by ARCH X and ARCH X Overage, respectively, AVP X LLC may be deemed to beneficially own the shares held by ARCH X and ARCH X Overage, and each of the AVP X Committee Members may be deemed to share the power to direct the disposition and vote of the shares held by ARCH X and ARCH X Overage. AVP X LP, AVP X Overage LP, AVP X LLC, and the AVP X Committee Members each disclaim beneficial ownership except to any pecuniary interest therein. The address of the ARCH Venture Partners is 8755 W. Higgins Road, Suite 1025, Chicago, IL 60631.

- (4) Consists of: (a) 33,333,331 shares of common stock issuable upon conversion of Series A convertible preferred stock and (b) 2,282,948 shares of common stock issuable upon conversion of Series B convertible preferred stock.
F-Prime Capital Partners Life Sciences Advisors Fund VI LP, or F-Prime Advisors, is the general partner of F-Prime Capital Partners Life Sciences Fund VI LP. F-Prime Advisors is solely managed by Impresa Management LLC, the managing member of its general partner and its investment manager. Impresa Management LLC is owned, directly or indirectly, by various shareholders and employees of FMR LLC. Each of the entities listed above expressly disclaims beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein, if any. The address of the above entities is 245 Summer Street, Boston, Massachusetts 02210.
- (5) Consists of: (a) 9,999,999 shares of common stock issuable upon conversion of Series A convertible preferred stock and (b) 5,250,781 shares of common stock issuable upon conversion of Series B convertible preferred stock.
Newpath Partners GP, L.P. is the general partner of Newpath Partners L.P. Newpath Partners GP, LLC is the general partner of Newpath Partners GP, L.P. Each of the entities listed above expressly disclaims beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein, if any. The address of Newpath Partners, L.P. is 800 Boylston Street, Suite 2222, Boston, Massachusetts 02199.
- (6) Consists of: (a) 10,302,642 shares of common stock held by Dr. Gottesdiener and (b) 62,500 shares of common stock underlying options exercisable within 60 days of December 31, 2021.
- (7) Consists of: (a) 3,000,000 shares of common stock and (b) 4,167 shares of common stock underlying options exercisable within 60 days of December 31, 2021.
- (8) Consists of 5,000,000 shares of common stock held by Beam Therapeutics Inc., or Beam. Mr. Evans is a director of Beam and shares voting and dispositive power with respect to the shares held by Beam. The principal business address of Beam is 26 Landsdowne Street, Cambridge, MA 02139. Mr. Evans disclaims beneficial ownership of these shares except to the extent of any pecuniary interest therein.

DESCRIPTION OF CAPITAL STOCK

The following descriptions are summaries of the material terms of our third amended and restated certificate of incorporation and amended and restated bylaws, which will be effective immediately upon the closing of this offering. The descriptions of the common stock and preferred stock give effect to changes to our capital structure that will occur immediately upon the closing of this offering. We refer in this section to our third amended and restated certificate of incorporation as our certificate of incorporation, and we refer to our amended and restated bylaws as our bylaws.

General

Upon completion of this offering, our authorized capital stock will consist of 775,000,000 shares of common stock, par value \$0.00001 per share, and 10,000,000 shares of preferred stock, par value \$0.00001 per share, all of which shares of preferred stock will be undesignated.

As of December 31, 2021, 100,768,255 shares of our common stock (which includes 47,734,388 shares of unvested restricted common stock) were outstanding and held of record by 20 stockholders, and 115,761,842 shares of Series A convertible preferred stock and 45,658,957 shares of Series B convertible preferred stock were outstanding and held of record by 40 stockholders. This amount does not take into account the conversion of all outstanding shares of our preferred stock into common stock upon the closing of this offering.

Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the common stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock. The shares to be issued by us in this offering will be, when issued and paid for, validly issued, fully paid and non-assessable.

Preferred Stock

Upon the completion of this offering, all outstanding shares of our preferred stock will be converted into shares of our common stock. Upon the closing of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to _____ shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. Immediately after consummation of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

Options

As of December 31, 2021, options to purchase 9,335,220 shares of common stock at a weighted-average exercise price of \$1.27 per share were outstanding under our 2019 Stock Option and Grant Plan, as amended, or the 2019 Plan.

Registration Rights

Upon the completion of this offering, the holders of _____ shares of our common stock, including those issuable upon the conversion of preferred stock upon closing of this offering, will be entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of an amended and restated investors' rights agreement between us, certain holders of our common stock and holders of our preferred stock. The amended and restated investors' rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses of underwritten registrations under this agreement will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand Registration Rights

Beginning 180 days after the effective date of this registration statement, the holders of _____ shares of our common stock, including those issuable upon the conversion of shares of our preferred stock upon closing of this offering, are entitled to demand registration rights. Under the terms of the amended and restated investors' rights agreement, we will be required, upon the written request of holders of at least a majority of the securities eligible for registration then outstanding to file a registration statement with respect to at least a majority of the securities eligible for registration then outstanding, we will be required to file a registration statement within 60 days of such request covering all securities eligible for registration that our stockholders request to be included in such registration. We are required to effect only one registration pursuant to this provision of the amended and restated investors' rights agreement in any twelve-month period.

Short-Form Registration Rights

Pursuant to the amended and restated investors' rights agreement, if we are eligible to file a registration statement on Form S-3, upon the written request of stockholders holding at least twenty percent of the securities eligible for registration then outstanding we will be required to file a Form S-3 registration restatement with respect to outstanding securities of such stockholders having an anticipated aggregate offering, net of related fees and expenses, of at least \$3.0 million. We are required to effect only two registrations in any twelve month period pursuant to this provision of the amended and restated investors' rights agreement. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations.

Piggyback Registration Rights

Pursuant to the amended and restated investors' rights agreement, if we register any of our securities either for our own account or for the account of other security holders, the holders of our common stock, including those issuable upon the conversion of our preferred stock, are entitled to include their shares in the registration. Subject to certain exceptions contained in the amended and restated investors' rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

Our amended and restated investors' rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of Registration Rights

The demand registration rights and short form registration rights granted under the amended and restated investors' rights agreement will terminate on the earliest to occur of (a) the closing of certain liquidation events, (b) the fifth anniversary of the completion of this offering or (c) at such time after this offering when the holders' shares may be sold without restriction pursuant to Rule 144 under the Securities Act within a three month period.

Expenses

Ordinarily, other than underwriting discounts and commissions, we are generally required to pay all expenses incurred by us related to any registration effected pursuant to the exercise of these registration rights. These expenses may include all registration and filing fees, printing expenses, fees and disbursements of our counsel, reasonable fees and disbursements of a counsel for the selling security holders and blue-sky fees and expenses.

Anti-Takeover Effects of Delaware Law and Certain Provisions of Our Certificate of Incorporation and Bylaws

Some provisions of Delaware law, our certificate of incorporation and bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies

Our certificate of incorporation provides for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

No Written Consent of Stockholders

Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

Meetings of Stockholders

Our certificate of incorporation and bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements

Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our bylaws specify the requirements as to form and content of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

Amendment to Certificate of Incorporation and Bylaws

Any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our certificate of incorporation, must thereafter be approved by a majority of the

outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, limitation of liability and the amendment of our bylaws and certificate of incorporation must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of at least two-thirds of the outstanding shares entitled to vote on the amendment, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated Preferred Stock

Our certificate of incorporation provides for 10,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Delaware Anti-Takeover Statute

Upon completion of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85 percent of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge, exchange, mortgage or other disposition involving the interested stockholder of 10 percent or more of the assets of the corporation;

- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15 percent or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Choice of Forum

Our bylaws will provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any state law claims for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, and employees to us or our stockholders, (3) any action asserting a claim arising pursuant to the Delaware General Corporation Law, our certificate of incorporation or our bylaws (including the interpretation, validity or enforceability thereof), or (4) any action asserting a claim that is governed by the internal affairs doctrine; provided, however, that this provision shall not apply to any causes of action arising under the Securities Act or Exchange Act. In addition, our bylaws will provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in our securities shall be deemed to have notice of and consented to these forum provisions. These forum provisions may impose additional costs on stockholders, may limit our stockholders' ability to bring a claim in a forum they find favorable, and the designated courts may reach different judgments or results than other courts. In addition, there is uncertainty as to whether the federal forum provision for Securities Act claims will be enforced, which may impose additional costs on us and our stockholders.

Stock Exchange Listing

We intend to apply to list our common stock on The Nasdaq Global Market under the proposed trading symbol "PRME".

Transfer Agent and Registrar

The Transfer Agent and Registrar for our common stock will be Computershare Inc. and Computershare Trust Company, N.A.

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our shares. Future sales of our common stock in the public market, or the availability of such shares for sale in the public market, could adversely affect market prices prevailing from time to time. As described below, only a limited number of shares will be available for sale shortly after this offering due to contractual and legal restrictions on resale. Nevertheless, sales of shares of our common stock in the public market after such restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price at such time and our ability to raise equity capital in the future.

Based on the number of shares outstanding as of December 31, 2021, upon the completion of this offering, _____ shares of our common stock will be outstanding, assuming the issuance of _____ shares offered by us in this offering, no exercise of the underwriters' option to purchase additional shares and no exercise of outstanding options. Of the outstanding shares, all of the shares sold in this offering will be freely tradable, except that any shares held by our affiliates, as that term is defined in Rule 144 under the Securities Act, may only be sold in compliance with the limitations described below, and restricted shares of common stock are subject to time-based vesting terms. All remaining shares of common stock held by existing stockholders immediately prior to the completion of this offering will be "restricted securities" as such term is defined in Rule 144 under the Securities Act. These restricted securities were issued and sold by us in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act, including the exemptions provided by Rule 144 or Rule 701, summarized below.

Rule 144

In general, a person who has beneficially owned restricted stock for at least six months would be entitled to sell their securities provided that (i) such person is not deemed to have been one of our affiliates at the time of, or at any time during the 90 days preceding, a sale and (ii) we are subject to the periodic reporting requirements of the Exchange Act for at least 90 days before the sale. Persons who have beneficially owned restricted shares for at least six months but who are our affiliates at the time of, or any time during the 90 days preceding, a sale, would be subject to additional restrictions, by which such person would be entitled to sell within any three-month period only a number of securities that does not exceed the greater of either of the following:

- 1 percent of the number of shares then outstanding, which will equal approximately _____ shares immediately after this offering, assuming no exercise of the underwriters' option to purchase additional shares, based on the number of shares outstanding as of December 31, 2021; or
- the average weekly trading volume of our common stock on The Nasdaq Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale;

provided, in each case, that we are subject to the periodic reporting requirements of the Exchange Act for at least 90 days before the sale. Such sales both by affiliates and by non-affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144.

Rule 701

Rule 701 under the Securities Act, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, executive officers or directors who purchased shares under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701, but all holders of Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares.

However, substantially all Rule 701 shares are subject to lock-up agreements as described below and under "Underwriting" included elsewhere in this prospectus and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

Lock-Up Agreements

We, all of our directors and officers and substantially all of our stockholders have agreed not to sell or otherwise transfer or dispose of any of our securities for a period of 180 days from the date of this prospectus, subject to certain exceptions. The representatives of the underwriters in this offering may, in their sole discretion, permit early release of shares subject to the lock-up agreements. See the section entitled “Underwriting,” included elsewhere in this prospectus for more information.

Registration Rights

Upon completion of this offering, certain holders of our securities will be entitled to various rights with respect to registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. See the section entitled “Description of Capital Stock—Registration Rights” included elsewhere in this prospectus for more information.

Equity Incentive Plans

We intend to file one or more registration statements on Form S-8 under the Securities Act to register our shares issued or reserved for issuance under our equity incentive plans. The first such registration statement is expected to be filed soon after the date of this prospectus and will automatically become effective upon filing with the SEC. Accordingly, shares registered under such registration statement will be available for sale in the open market, unless such shares are subject to vesting restrictions with us or the lock-up restrictions described above. As of the date of this prospectus, we estimate that such registration statement on Form S-8 will cover approximately shares.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following discussion is a summary of certain material U.S. federal income tax considerations applicable to non-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering. For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes:

- a non-resident alien individual;
- a foreign corporation or other foreign organization taxable as a corporation; or
- a foreign trust or estate the income of which is not subject to U.S. federal income tax on a net income basis.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons that hold their common stock through partnerships or other pass-through entities. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any such change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus. There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset within the meaning of Section 1221 of the Code, generally property held for investment.

This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any aspects of U.S. state, local or non-U.S. taxes, the alternative minimum tax, the Medicare contribution tax on net investment income, the rules regarding qualified small business stock within the meaning of Section 1202 of the Code, or any other aspect of any U.S. federal tax other than income taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt or governmental organizations;
- financial institutions;
- brokers or dealers in securities;
- "regulated investment companies" and "real estate investment trusts";
- pension plans;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- "qualified foreign pension funds," or entities wholly owned by a "qualified foreign pension fund";
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and partners and investors therein);
- persons deemed to sell our common stock under the constructive sale provisions of the Code;

- persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment; and
- U.S. expatriates.

This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

Distributions on Our Common Stock

We have never declared or paid any cash distributions on our capital stock and we do not anticipate paying cash distributions on our common stock for the foreseeable future. Distributions, if any, on our common stock will generally constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in "Gain on Sale or Other Taxable Disposition of Our Common Stock." Any such distributions will also be subject to the discussions below under the sections entitled "Backup Withholding and Information Reporting" and "Withholding and Information Reporting Requirements—FATCA."

Subject to the discussion in the following two paragraphs in this section, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30 percent rate or a reduced rate specified by an applicable income tax treaty between the United States and such holder's country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30 percent withholding tax if the non-U.S. holder satisfies applicable certification requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30 percent rate or a reduced rate specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or other applicable or successor form) to the applicable withholding agent and satisfy applicable certification and other requirements. Any documentation provided to an applicable withholding agent may need to be updated in certain circumstances. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS.

Gain on Sale or Other Taxable Disposition of Our Common Stock

Subject to the discussions below under "Backup Withholding and Information Reporting" and "Withholding and Information Reporting Requirements—FATCA," a non-U.S. holder generally will not be subject to any U.S. federal income or withholding tax on any gain realized upon such holder's sale or other taxable disposition of shares of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed base maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to United States

persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in “Distributions on Our Common Stock” also may apply;

- the non-U.S. holder is a nonresident alien individual who is present in the United States for a period or periods aggregating 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30 percent tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses; or
- we are, or have been, at any time during the five-year period preceding such sale or other taxable disposition (or the non-U.S. holder’s holding period, if shorter) a “U.S. real property holding corporation,” as described below, unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5 percent of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a U.S. real property holding corporation if the fair market value of its U.S. real property interests, as defined in the Code and applicable Treasury regulations, equals or exceeds 50 percent of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Backup Withholding and Information Reporting

We (or the applicable paying agent) must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. A non-U.S. holder may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in “Distributions on Our Common Stock,” generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker.

Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them. Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder’s U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

Withholding and Information Reporting Requirements—FATCA

Provisions of the Code commonly referred to as the Foreign Account Tax Compliance Act (FATCA) generally impose a U.S. federal withholding tax at a rate of 30 percent on payments of dividends on, or, subject to the

discussion of certain proposed U.S. Treasury regulations below, gross proceeds from the sale or other disposition of, our common stock paid to a foreign entity unless (i) if the foreign entity is a “foreign financial institution,” such foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a “foreign financial institution,” such foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA. However, the U.S. Treasury released proposed regulations which, if finalized in their present form, would eliminate the federal withholding tax of 30 percent applicable to the gross proceeds of a sale or other disposition of our common stock. In the preamble to such proposed regulations, the U.S. Treasury stated that taxpayers (including withholding agents) may generally rely on the proposed regulations until final regulations are issued. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of this withholding tax. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their tax advisors regarding the possible implications of this legislation on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30 percent withholding tax under FATCA.

UNDERWRITING

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC, Goldman Sachs & Co. LLC, Morgan Stanley & Co. LLC and Jefferies LLC are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

Name	Number of shares of common stock
J.P. Morgan Securities LLC	
Goldman Sachs & Co. LLC	
Morgan Stanley & Co. LLC	
Jefferies LLC	
Total	

The underwriters are committed to purchase all the shares of common stock offered by us if they purchase any shares of common stock. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the shares of common stock directly to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of \$ _____ per share. After the initial offering of the shares of common stock to the public, if all of the shares of common stock are not sold at the initial public offering price, the underwriters may change the offering price and the other selling terms. Sales of any shares of common stock made outside of the United States may be made by affiliates of the underwriters.

The underwriters have an option to buy up to _____ additional shares of common stock from us to cover sales of shares of common stock by the underwriters which exceed the number of shares of common stock specified in the table above. The underwriters have 30 days from the date of this prospectus to exercise this option to purchase additional shares of common stock. If any shares of common stock are purchased with this option to purchase additional shares of common stock, the underwriters will purchase shares of common stock in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares of common stock on the same terms as those on which the shares of common stock are being offered.

The underwriting fee is equal to the public offering price per common share less the amount paid by the underwriters to us per common share. The underwriting fee is \$ _____ per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares of common stock.

	Without option to purchase additional shares of common stock exercise	With full option to purchase additional shares of common stock exercise
Per Common Share	\$	\$
Total	\$	\$

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be

approximately \$ million. We have agreed to reimburse the underwriters for expenses relating to clearance of this offering with the Financial Industry Regulatory Authority, Inc. of up to \$.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares of common stock to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, or submit to, or file with, the SEC a registration statement under the Securities Act relating to, any of our shares of common stock or securities convertible into or exercisable or exchangeable for any of our shares of common stock, or publicly disclose the intention to undertake any of the foregoing, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences of ownership of any shares of common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise), in each case without the prior written consent of the representatives for a period of 180 days after the date of this prospectus, other than our shares of common stock to be sold in this offering.

Our directors and executive officers, and substantially all of our stockholders (such persons, the “lock-up parties”) have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each lock-up party, with limited exceptions, for a period of 180 days after the date of this prospectus (such period, the “restricted period”), may not (and may not cause any of their direct or indirect affiliates to), without the prior written consent of the representatives, (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for common stock (including without limitation, common stock or such other securities which may be deemed to be beneficially owned by the lock-up party in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant) (collectively with the common stock, “lock-up securities”), (2) enter into any hedging, swap, or other agreement or transaction that transfers, in whole or in part, any of the economic consequences of ownership of the lock-up securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of lock-up securities, in cash or otherwise, (3) make any demand for or exercise any right with respect to the registration of any lock-up securities, or (4) publicly disclose the intention to do any of the foregoing. Each lock-up party will further acknowledge that the foregoing precludes the lock-up party from engaging in any hedging or other transactions or arrangements (including, without limitation, any short sale or the purchase or sale of, or entry into, any put or call option, or combination thereof, forward, swap or any other derivative transaction or instrument, however described or defined) designed or intended, or which could reasonably be expected to lead to or result in, a sale or disposition or transfer (whether by the lock-up party or any other person) of any economic consequences of ownership, in whole or in part, directly or indirectly, of any lock-up securities, whether any such transaction or arrangement (or instrument provided for thereunder) would be settled by delivery of lock-up securities, in cash or otherwise. Each lock-up party will further confirm subject to limited exceptions and conditions that (1) neither the lock-up party, nor any of its affiliates, is party to as of the date of the lock-up agreement, any transaction which would have been restricted by the lock-up agreement if it had been entered into by the lock-up party during the restricted period or (2) that it will furnish the representatives with the details of any transaction the lock-up party, or any of its affiliates, is a party to as of the date hereof, which transaction would have been restricted by the lock-up agreement if it had been entered into by the lock-up party during the restricted period.

The restrictions described in the immediately preceding paragraph and contained in the lock-up agreements between the underwriters and the lock-up parties do not apply, subject in certain cases to various conditions, to certain transactions, including (a) transfer or dispose of the lock-up party’s lock-up securities: (i) as a bona fide gift or gifts, or for bona fide estate planning purposes, (ii) by will or intestacy or other testamentary document, (iii) to any trust for the direct or indirect benefit of the lock-up party or the immediate family of the lock-up party, or if the lock-up party is a trust, to a trustor or beneficiary of the trust or to the estate of a beneficiary of such trust, (iv) to a

corporation, partnership, limited liability company, investment fund or other entity (A) of which the lock-up party and/or the immediate family of the lock-up party are, directly or indirectly, the legal and beneficial owner of all of the outstanding equity securities or similar interests, or (B) controlled by, or under common control with, the lock-up party or the immediate family of the lock-up party, (v) to a nominee or custodian of a person or entity to whom a disposition or transfer would be permissible under clauses (i) through (iv) above, (vi) if the lock-up party is a corporation, partnership, limited liability company, trust or other business entity, (A) to another corporation, partnership, limited liability company, trust, or other business entity that is an affiliate (as defined in Rule 405 promulgated under the Securities Act) of the lock-up party, or to any investment fund or other entity controlling, controlled by, managing or managed by or under common control or common investment management with the lock-up party or affiliates of the lock-up party (including, for the avoidance of doubt, where the lock-up party is a partnership, to its general partner or a successor partnership or fund, or any other funds managed by such partnership), or to the undersigned's or its affiliates' partners, managers, members, employees, officers, directors or trustees, or (B) as part of a distribution or other transfer to general or limited partners, direct or indirect members, subsidiaries, affiliates or shareholders of the lock-up party, (vii) by operation of law, such as pursuant to a qualified domestic order, divorce settlement, divorce decree or separation agreement, (viii) to us from an employee upon death, disability or termination of employment, in each case, of such employee, (ix) as part of a sale or other transaction involving of the lock-up party's or its direct or indirect affiliates' lock-up securities acquired in this offering, subject to certain exceptions, or in open market transactions after the pricing date for this offering; (x) to us in connection with the vesting, settlement, or exercise of restricted stock units, options, warrants or other rights to purchase shares of common stock (including, in each case, by way of "net" or "cashless" exercise), including for the payment of exercise price and tax and remittance payments due as a result of the vesting, settlement, or exercise of such restricted stock units, options, warrants or rights, provided that any such shares of common stock received upon such exercise, vesting or settlement shall be subject to the terms of the lock-up agreement, and provided further that any such restricted stock units, options, warrants or rights are held by the lock-up party pursuant to an agreement or equity awards granted under a stock incentive plan or other equity award plan, each such agreement or plan which is described in this prospectus, or (xi) pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction that is approved by our board of directors and made to all holders of our capital stock involving a "change of control" (as defined below) (for purposes hereof, "change of control" shall mean the transfer (whether by tender offer, merger, consolidation or other similar transaction), in one transaction or a series of related transactions, to a person or group of affiliated persons, of shares of capital stock if, after such transfer, such person or group of affiliated persons would hold at least a majority of our outstanding voting securities (or the surviving entity)); provided that in the event that such tender offer, merger, consolidation or other similar transaction is not completed, the lock-up party's lock-up securities shall remain subject to the provisions of the lock-up agreement; provided that (A) in the case of any transfer, disposition or distribution pursuant to clause (a)(i), (ii), (iii), (iv), (v) and (vii), such transfer shall not involve a disposition for value and in the case of any transfer, disposition or distribution pursuant to clause (a)(i), (ii), (iii), (iv), (v), (vi) and (vii), each donee, devisee, transferee or distributee shall execute and deliver to the representatives a lock-up letter in the form of the lock-up agreement, (B) in the case of any transfer, disposition or distribution pursuant to clause (a) (i), (ii), (iii), (iv), (v) and (vi) no filing by any party (donor, donee, devisee, transferor, transferee, distributor or distributee) under the Exchange Act or other public announcement shall be required or shall be made voluntarily in connection with such transfer or distribution (other than a filing on a Form 5 or a filing required pursuant to Section 13 of the Exchange Act and the rules and regulations promulgated thereunder subject to certain conditions) and (C) in the case of any transfer or distribution pursuant to clause (a)(vii), (viii) and (x) it shall be a condition to such transfer that no public filing, report or announcement shall be voluntarily made and if any filing under Section 16(a) of the Exchange Act, or other public filing, report or announcement reporting a reduction in beneficial ownership of shares of common stock in connection with such transfer or distribution shall be legally required during the restricted period, such filing, report or announcement shall clearly indicate in the footnotes thereto the nature and conditions of such transfer; (b) exercise outstanding options, settled restricted stock units or other equity awards or exercise warrants pursuant to plans described in this prospectus; provided that any lock-up securities received upon such exercise, vesting or settlement shall be subject to the terms of the lock-up agreement; (c) convert outstanding preferred stock, warrants to acquire preferred stock or convertible securities into shares of common stock or warrants to acquire shares of common stock; provided that any such shares of common stock or warrants received upon such conversion shall be subject to the terms of the lock-up agreement; and (d) establish trading plans pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of lock-up securities; provided that (1) such plans do not provide for the transfer of lock-up securities during the restricted

period and (2) no filing by any party under the Exchange Act or other public announcement shall be required or made voluntarily in connection with such trading plan.

The representatives, in their sole discretion, may release the securities subject to any of the lock-up agreements with the underwriters described above, in whole or in part at any time.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act.

We intend to apply to have our shares of common stock approved for listing on The Nasdaq Global Market under the symbol "PRME".

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the shares of common stock while this offering is in progress. These stabilizing transactions may include making short sales of shares of common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be "covered" shorts, which are short positions in an amount not greater than the underwriters' option to purchase additional shares of common stock referred to above, or may be "naked" shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares of common stock, in whole or in part, or by purchasing shares of common stock in the open market. In making this determination, the underwriters will consider, among other things, the price of shares of common stock available for purchase in the open market compared to the price at which the underwriters may purchase shares of common stock through the option to purchase additional shares of common stock. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares of common stock in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the shares of common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase shares of common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares of common stock as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the shares of common stock or preventing or retarding a decline in the market price of the shares of common stock, and, as a result, the price of the shares of common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on Nasdaq, in the over-the-counter market or otherwise.

Prior to this offering, there has been no public market for our shares of common stock. The initial public offering price will be determined by negotiations between us and the representatives of the underwriters. In determining the initial public offering price, we and the representatives of the underwriters expect to consider a number of factors including:

- the information set forth in this prospectus and otherwise available to the representatives;
- our prospects and the history and prospects for the industry in which we compete;
- an assessment of our management;
- our prospects for future earnings;
- the general condition of the securities markets at the time of this offering;

- the recent market prices of, and demand for, publicly traded common stock of generally comparable companies; and
- other factors deemed relevant by the underwriters and us.

Neither we nor the underwriters can assure investors that an active trading market will develop for our shares of common stock, or that the shares of common stock will trade in the public market at or above the initial public offering price.

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each a “Relevant State”), no shares of our common stock have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the shares of our common stock which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation), except that offers of Shares may be made to the public in that Relevant State at any time under the following exemptions under the Prospectus Regulation:

- a) to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
- b) to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the underwriters for any such offer; or
- c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of shares of common stock shall require the Issuer or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

Each person in a Relevant State who initially acquires any shares of common stock or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with the Company and the underwriters that it is a qualified investor within the meaning of the Prospectus Regulation.

In the case of any shares of common stock being offered to a financial intermediary as that term is used in Article 5(1) of the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares of common stock acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer to the public other than their offer or resale in a Relevant State to

qualified investors, in circumstances in which the prior consent of the underwriters has been obtained to each such proposed offer or resale.

The Company, the underwriters and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

For the purposes of this provision, the expression an “offer to the public” in relation to any shares of common stock in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any Shares to be offered so as to enable an investor to decide to purchase or subscribe for any Shares, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129.

Notice to Prospective Investors in the United Kingdom

In relation to the United Kingdom, or the UK, no shares of our common stock have been offered or will be offered pursuant to the offering to the public in the UK prior to the publication of a prospectus in relation to the shares of common stock which has been approved by the Financial Conduct Authority in the UK in accordance with the UK Prospectus Regulation and the FSMA, except that offers of shares of common stock may be made to the public in the UK at any time under the following exemptions under the UK Prospectus Regulation and the FSMA:

- (a) to any legal entity which is a qualified investor as defined under the UK Prospectus Regulation;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined under the UK Prospectus Regulation), subject to obtaining the prior consent of the underwriters for any such offer; or
- (c) at any time in other circumstances falling within section 86 of the FSMA,

provided that no such offer of shares of common stock shall require the Issuer or any underwriter to publish a prospectus pursuant to Section 85 of the FSMA or Article 3 of the UK Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation.

Each person in the UK who initially acquires any shares of common stock or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with the Company and the underwriters that it is a qualified investor within the meaning of the UK Prospectus Regulation.

In the case of any shares of common stock being offered to a financial intermediary as that term is used in Article 5(1) of the UK Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the Shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer to the public other than their offer or resale in the UK to qualified investors, in circumstances in which the prior consent of the underwriters has been obtained to each such proposed offer or resale.

The Company, the underwriters and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

For the purposes of this provision, the expression an “offer to the public” in relation to any shares of our common stock in the UK means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock to be offered so as to enable an investor to decide to purchase or subscribe for any shares of our common stock, the expression “UK Prospectus Regulation” means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018, and the expression “FSMA” means the Financial Services and Markets Act 2000.

This document is for distribution only to persons who (i) have professional experience in matters relating to investments and who qualify as investment professionals within the meaning of Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (as amended, the “Financial Promotion Order”), (ii) are persons falling within Article 49(2)(a) to (d) (“high net worth companies, unincorporated associations etc.”) of the Financial Promotion Order, (iii) are outside the United Kingdom, or (iv) are persons to whom an invitation or

inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) in connection with the issue or sale of any securities may otherwise lawfully be communicated or caused to be communicated (all such persons together being referred to as “relevant persons”). This document is directed only at relevant persons and must not be acted on or relied on by persons who are not relevant persons. Any investment or investment activity to which this document relates is available only to relevant persons and will be engaged in only with relevant persons.

Notice to Prospective Investors in Canada

The shares of common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares of common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser’s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser’s province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Notice to Prospective Investors in Switzerland

The shares of common stock may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document does not constitute a prospectus within the meaning of, and has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares of common stock or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company, the shares of common stock have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares of common stock will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of shares of common stock has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares of common stock.

Notice to Prospective Investors in Hong Kong

The shares of common stock have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong), or SFO, of Hong Kong and any rules made thereunder; or (b) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong), or CO, or which do not constitute an offer to the public within the meaning of the CO. No advertisement, invitation or document relating to the shares of common stock has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with

respect to shares of common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the SFO and any rules made thereunder.

Notice to Prospective Investors in Singapore

Each joint book-running manager has acknowledged that this prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, each joint book-running manager has represented and agreed that it has not offered or sold any shares of common stock or caused the shares of common stock to be made the subject of an invitation for subscription or purchase and will not offer or sell any shares of common stock or cause the shares of common stock to be made the subject of an invitation for subscription or purchase, and has not circulated or distributed, nor will it circulate or distribute, this prospectus or any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares of common stock, whether directly or indirectly, to any person in Singapore other than:

- (a) to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time, or the SFA) pursuant to Section 274 of the SFA;
- (b) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA; or
- (c) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares of common stock are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries’ rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares of common stock pursuant to an offer made under Section 275 of the SFA except:
 - (i) to an institutional investor or to a relevant person, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
 - (ii) where no consideration is or will be given for the transfer;
 - (iii) where the transfer is by operation of law;
 - (iv) as specified in Section 276(7) of the SFA; or
 - (v) as specified in Regulation 37A of the Securities and Futures (Offers of Investments) (Securities and Securities-based Derivatives Contracts) Regulations 2018.

Singapore SFA Product Classification—In connection with Section 309B of the SFA and the CMP Regulations 2018, unless otherwise specified before an offer of shares of common stock, we have determined, and hereby notify all relevant persons (as defined in Section 309A(1) of the SFA), that the shares of common stock are “prescribed capital markets products” (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Notice to Prospective Investors in Japan

The shares of common stock have not been and will not be registered pursuant to Article 4, Paragraph 1 of the Financial Instruments and Exchange Act. Accordingly, none of the shares of common stock nor any interest therein may be offered or sold, directly or indirectly, in Japan or to, or for the benefit of, any “resident” of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to or for the benefit of a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Act and any other applicable laws, regulations and ministerial guidelines of Japan in effect at the relevant time.

Notice to Prospective Investors in the United Arab Emirates

The shares of common stock have not been, and are not being, publicly offered, sold, promoted or advertised in the United Arab Emirates (including the Dubai International Financial Centre) other than in compliance with the laws of the United Arab Emirates (and the Dubai International Financial Centre) governing the issue, offering and sale of securities. Further, this prospectus does not constitute a public offer of securities in the United Arab Emirates (including the Dubai International Financial Centre) and is not intended to be a public offer. This prospectus has not been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority or the Dubai Financial Services Authority.

Notice to Prospective Investors in Israel

In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728—1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728—1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions, or the Addressed Investors; or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728—1968, subject to certain conditions, or the “Qualified Investors”. The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. We have not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728—1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our shares of common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728—1968. In particular, we may request, as a condition to be offered shares of common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728—1968 and the regulations promulgated thereunder in connection with the offer to be issued shares of common stock; (iv) that the shares of common stock that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728—1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728—1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor’s name, address and passport number or Israeli identification number.

Notice to Prospective Investors in Australia

This prospectus:

- (a) does not constitute a disclosure document or a prospectus under Chapter 6D.2 of the Corporations Act 2001 (Cth), or the Corporations Act;
- (b) has not been, and will not be, lodged with the Australian Securities and Investments Commission, or ASIC, as a disclosure document for the purposes of the Corporations Act and does not purport to include the information required of a disclosure document for the purposes of the Corporations Act; and
- (c) may only be provided in Australia to select investors who are able to demonstrate that they fall within one or more of the categories of investors, available under section 708 of the Corporations Act, or Exempt Investors.

The shares of common stock may not be directly or indirectly offered for subscription or purchased or sold, and no invitations to subscribe for or buy the shares of common stock may be issued, and no draft or definitive offering memorandum, advertisement or other offering material relating to any shares of common stock may be distributed in Australia, except where disclosure to investors is not required under Chapter 6D of the Corporations Act or is otherwise in compliance with all applicable Australian laws and regulations. By submitting an application for the shares of common stock, you represent and warrant to us that you are an Exempt Investor.

As any offer of shares of common stock under this document will be made without disclosure in Australia under Chapter 6D.2 of the Corporations Act, the offer of those securities for resale in Australia within 12 months may, under section 707 of the Corporations Act, require disclosure to investors under Chapter 6D.2 if none of the exemptions in section 708 applies to that resale. By applying for the shares of common stock you undertake to us that you will not, for a period of 12 months from the date of issue of the shares of common stock, offer, transfer, assign or otherwise alienate those shares of common stock to investors in Australia except in circumstances where disclosure to investors is not required under Chapter 6D.2 of the Corporations Act or where a compliant disclosure document is prepared and lodged with ASIC.

Notice to Prospective Investors in China

This prospectus will not be circulated or distributed in the PRC and the shares of common stock will not be offered or sold, and will not be offered or sold to any person for re-offering or resale directly or indirectly to any residents of the PRC except pursuant to any applicable laws and regulations of the PRC. Neither this prospectus nor any advertisement or other offering material may be distributed or published in the PRC, except under circumstances that will result in compliance with applicable laws and regulations.

Notice to Prospective Investors in Korea

The shares of common stock have not been and will not be registered under the Financial Investments Services and Capital Markets Act of Korea and the decrees and regulations thereunder, or the FSCMA, and the shares of common stock have been and will be offered in Korea as a private placement under the FSCMA. None of the shares of common stock may be offered, sold or delivered directly or indirectly, or offered or sold to any person for re-offering or resale, directly or indirectly, in Korea or to any resident of Korea except pursuant to the applicable laws and regulations of Korea, including the FSCMA and the Foreign Exchange Transaction Law of Korea and the decrees and regulations thereunder, or FETL. Furthermore, the purchaser of the shares of common stock shall comply with all applicable regulatory requirements (including but not limited to requirements under the FETL) in connection with the purchase of the shares of common stock. By the purchase of the shares of common stock, the relevant holder thereof will be deemed to represent and warrant that if it is in Korea or is a resident of Korea, it purchased the shares of common stock pursuant to the applicable laws and regulations of Korea.

Notice to Prospective Investors in Saudi Arabia

This document may not be distributed in the Kingdom of Saudi Arabia except to such persons as are permitted under the Offers of Securities Regulations as issued by the board of the Saudi Arabian Capital Market Authority, or CMA, pursuant to resolution number 2-11-2004 dated 4 October 2004 as amended by resolution number 1-28-2008, as amended, or the CMA Regulations. The CMA does not make any representation as to the accuracy or completeness of this document and expressly disclaims any liability whatsoever for any loss arising from, or incurred in reliance upon, any part of this document. Prospective purchasers of the securities offered hereby should conduct their own due diligence on the accuracy of the information relating to the securities. If you do not understand the contents of this document, you should consult an authorized financial adviser.

Notice to Prospective Investors in the Dubai International Financial Centre (DIFC)

This document relates to an Exempt Offer in accordance with the Markets Rules 2012 of the Dubai Financial Services Authority, or DFSA. This document is intended for distribution only to persons of a type specified in the Markets Rules 2012 of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement nor taken steps to verify the information set forth herein and has no responsibility for this document. The securities to which this document relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered should conduct their own due diligence on the securities. If you do not understand the contents of this document, you should consult an authorized financial adviser.

In relation to its use in the DIFC, this document is strictly private and confidential and is being distributed to a limited number of investors and must not be provided to any person other than the original recipient, and may not be reproduced or used for any other purpose. The interests in the securities may not be offered or sold directly or indirectly to the public in the DIFC.

Notice to Prospective Investors in Bermuda

Shares of common stock may be offered or sold in Bermuda only in compliance with the provisions of the Investment Business Act of 2003 of Bermuda which regulates the sale of securities in Bermuda. Additionally, non-Bermudian persons (including companies) may not carry on or engage in any trade or business in Bermuda unless such persons are permitted to do so under applicable Bermuda legislation.

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Certain legal matters relating to this offering will be passed upon for the underwriters by Davis Polk & Wardwell LLP, New York, New York.

EXPERTS

The financial statements as of December 31, 2021 and December 31, 2020 and for the years ended December 31, 2021 and 2020, and for the period from September 13, 2019 (inception) to December 31, 2019, included in this Prospectus have been so included in reliance on the report of PricewaterhouseCoopers LLP (“PwC”), an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

In connection with their engagement, PwC completed an independence assessment to evaluate the services and relationships with Prime Medicine, Inc. (“Prime” or the “Company”) and its affiliates that may bear on PwC’s independence under the SEC and the PCAOB (United States) independence rules. From September 13, 2019 (inception of the Company) through November 24, 2021, a business relationship existed between PwC and a beneficial owner that had significant influence (“BOSI”) over Prime whereby PwC is a cloud services partner of the BOSI and advises clients on their cloud computer strategy and operations. The existence of this business relationship identified is inconsistent with SEC and PCAOB auditor independence rules provided in Rule 2-01 of Regulation S-X. The matter was resolved on November 24, 2021, when the Company determined the beneficial owner no longer demonstrated the ability to exercise significant influence over Prime.

PwC provided an overview of the facts and circumstances surrounding the business arrangement to our board of directors and management, including the entity involved and other relevant facts. The PwC audit engagement team members did not participate in PwC’s activities and engagements with the BOSI or any entity that is part of PwC’s business relationship with the BOSI, and the business relationship was not quantitatively or qualitatively material to PwC or the BOSI.

Considering the facts presented, our board of directors and PwC have concluded that the business relationship would not impair PwC’s application of objective and impartial judgment on any matters encompassed within the audit engagement performed by PwC for our financial statements as of and for the fiscal years ended December 31, 2021 and 2020, and for the period from September 13, 2019 (inception) to December 31, 2019, and that a reasonable investor with knowledge of all relevant facts and circumstances would conclude that PwC is capable of remaining objective and impartial with respect to the audit of Prime’s financial statements.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 (File Number 333-) under the Securities Act with respect to the common stock we are offering by this prospectus. This prospectus, which constitutes part of the registration statement, does not contain all of the information included in the registration statement. For further information pertaining to us and our common stock, you should refer to the registration statement and to its exhibits. Whenever we make reference in this prospectus to any of our contracts, agreements or other documents, the references are not necessarily complete, and you should refer to the exhibits attached to the registration statement for copies of the actual contract, agreement or other document.

Upon the completion of the offering, we will be subject to the informational requirements of the Exchange Act and will file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, at the SEC’s website at www.sec.gov. We also maintain a website at <https://www.primemedicine.com> and upon completion of the offering, you may access, free of charge, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and any amendments to those reports, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this prospectus.

PRIME MEDICINE, INC.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Prime Medicine, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Prime Medicine, Inc., and its subsidiary (the “Company”) as of December 31, 2021 and 2020, and the related consolidated statements of operations and comprehensive loss, of redeemable convertible and convertible preferred stock and stockholders’ equity (deficit) and of cash flows for the years ended December 31, 2021 and 2020 and the period from September 13, 2019 (Inception) to December 31, 2019, including the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for the years ended December 31, 2021 and 2020 and the period from September 13, 2019 (Inception) to December 31, 2019 in conformity with accounting principles generally accepted in the United States of America.

Change in Accounting Principle

As discussed in Note 2 to the consolidated financial statements, the Company changed the manner in which it accounts for leases in 2021.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on the Company’s consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB and in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
February 4, 2022

We have served as the Company's auditor since 2021.

PRIME MEDICINE, INC.
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share amounts)

	December 31,	
	2020	2021
Assets		
Current assets:		
Cash and cash equivalents	\$ 36,975	\$ 185,420
Short-term investments	—	68,238
Related party short-term investment	16,353	15,962
Prepaid expenses and other current assets	74	959
Total current assets	53,402	270,579
Property and equipment, net	596	4,932
Operating lease right-of-use lease assets	—	10,746
Restricted Cash	—	13,125
Other assets	785	2,474
Total assets	\$ 54,783	\$ 301,856
Liabilities, Redeemable Convertible and Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	\$ 250	\$ 1,435
Preferred stock tranche right liability	17,515	—
Anti-dilution obligation	855	—
Accrued expenses and other current liabilities ⁽¹⁾	822	37,192
Related party forward contract liability	—	12,020
Operating lease liability	—	7,336
Total current liabilities	19,442	57,983
Operating lease liability, net of current	—	3,070
Non current deferred tax liability	1,867	1,243
Total liabilities	21,309	62,296
Commitments and contingencies (Note 12)		
Series A redeemable convertible preferred stock, \$0.00001 par value; 115,000,000 and 115,761,842 shares authorized at December 31, 2020 and 2021, respectively; 10,000,001 and 115,761,842 shares issued and outstanding at December 31, 2020 and 2021, respectively; liquidation preference of \$46,388 and \$125,000 at December 31, 2020 and 2021, respectively	31,136	196,157
Series B convertible preferred stock, \$0.00001 par value; No shares authorized, issued or outstanding at December 31, 2020; 45,658,957 shares authorized, issued and outstanding at December 31, 2021; liquidation preference of \$210,814 at December 31, 2021	—	199,643
Stockholders' equity (deficit):		
Common stock, \$0.00001 par value; 220,000,000, 293,258,790 shares authorized at December 31, 2020 and 2021, respectively; 88,568,497 and 100,768,255 shares issued and outstanding at December 31, 2020 and 2021, respectively	1	1
Additional paid-in capital	8,346	15,162
Accumulated other comprehensive loss	—	(27)
Accumulated deficit	(6,009)	(171,376)
Total stockholders' equity (deficit)	2,338	(156,240)
Total liabilities, redeemable convertible and convertible preferred stock and stockholders' equity (deficit)	\$ 54,783	\$ 301,856

(1) Includes related party amount of \$30,000 as of December 31, 2021 (see Note 14).

The accompanying notes are an integral part of these consolidated financial statements.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except share and per share amounts)

	Period from September 13, 2019 (Inception) to December 31, 2019	Year Ended December 31,	
		2020	2021
Related party collaboration revenue	\$ —	\$ 5,210	\$ —
Operating expenses:			
Research and development ⁽¹⁾	920	2,980	70,550
General and administrative	1,252	3,162	13,924
Total operating expenses	2,172	6,142	84,474
Income (loss) from operations	(2,172)	(932)	(84,474)
Other income (expense):			
Change in fair value of preferred stock tranche right liability	(353)	(10,904)	(74,319)
Change in fair value of anti-dilution obligation	—	(700)	(6,681)
Change in fair value of related party short-term investment	—	10,867	(391)
Other income (expense), net ⁽²⁾	—	126	12
Total other expense, net	(353)	(611)	(81,379)
Net loss before income taxes	(2,525)	(1,543)	(165,853)
Provision for (benefit from) income taxes	4	1,867	(486)
Net loss	(2,529)	(3,410)	(165,367)
Accretion of preferred stock to redemption value	(265)	(1,645)	(1,468)
Cumulative dividend on preferred stock	—	—	(17,284)
Net loss attributable to common stockholders	\$ (2,794)	\$ (5,055)	\$ (184,119)
Net loss per share attributable to common stockholders, basic and diluted	\$ (0.60)	\$ (0.62)	\$ (4.57)
Weighted-average common shares outstanding, basic and diluted	4,622,576	8,206,374	40,332,091
Comprehensive Loss:			
Net loss	\$ (2,529)	\$ (3,410)	\$ (165,367)
Change in unrealized gains (losses) on investments, net of tax	—	—	(27)
Total other comprehensive loss	—	—	(27)
Comprehensive Loss	\$ (2,529)	\$ (3,410)	\$ (165,394)

(1) Includes related party amounts of \$45, \$150 and \$42,170 for the period from September 13, 2019 (inception) to December 31, 2019 and for the years ended December 31, 2020 and 2021, respectively (see Note 14).

(2) Includes related party amount of \$126 for the year ended December 31, 2020 (see Note 14).

The accompanying notes are an integral part of these consolidated financial statements.

PRIME MEDICINE, INC.

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE AND CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)

(In thousands, except share amounts)

	Redeemable Convertible Preferred Stock		Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Losses	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount				
Balances at September 13, 2019 (Inception)	—	\$ —	—	\$ —	—	\$ —	\$ —	\$ —	\$ —	\$ —
Issuance of Series A redeemable convertible preferred stock, net of preferred stock tranche right liability of \$6,258 and issuance costs of \$20	10,000,001	3,722	—	—	—	—	—	—	—	—
Accretion of redeemable convertible preferred stock to redemption value	—	265	—	—	—	—	(195)	—	(70)	(265)
Issuance of common stock in exchange for Broad license	—	—	—	—	1,938,429	—	39	—	—	39
Stock-based compensation expense	—	—	—	—	—	—	156	—	—	156
Issuance of restricted common stock	—	—	—	—	64,772,720	1	—	—	—	1
Net loss	—	—	—	—	—	—	—	—	(2,529)	(2,529)
Balances at December 31, 2019	10,000,001	3,987	—	—	66,711,149	1	—	—	(2,599)	(2,598)
Issuance of Series A redeemable convertible preferred stock for the settlement of the second tranche right liability, net of issuance costs of \$46	34,999,999	25,504	—	—	—	—	9,450	—	—	9,450
Accretion of redeemable convertible preferred stock to redemption value	—	1,645	—	—	—	—	(1,645)	—	—	(1,645)
Issuance of common stock as consideration for related party collaboration agreement	—	—	—	—	5,000,000	—	150	—	—	150
Issuance of restricted common stock	—	—	—	—	16,857,348	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	391	—	—	391
Net loss	—	—	—	—	—	—	—	—	(3,410)	(3,410)
Balances at December 31, 2020	45,000,000	31,136	—	—	88,568,497	1	8,346	—	(6,009)	2,338
Balances at December 31, 2020	45,000,000	31,136	—	—	88,568,497	1	8,346	—	(6,009)	2,338
Issuance of Series A redeemable convertible preferred stock, including the settlement of the third and fourth tranche right liability, net of issuance costs of \$41	70,761,842	71,719	—	—	—	—	(998)	—	—	(998)
Reclassification of preferred stock tranche liability upon settlement	—	91,834	—	—	—	—	—	—	—	—
Accretion of redeemable convertible preferred stock to redemption value	—	1,468	—	—	—	—	(1,468)	—	—	(1,468)
Issuance of Series B convertible preferred stock, net of issuance costs of \$356	—	—	45,658,957	199,643	—	—	—	—	—	—
Issuance of restricted common stock	—	—	—	—	4,488,000	—	—	—	—	—
Issuance of common stock and settlement of the anti-dilution obligation	—	—	—	—	7,768,425	—	—	—	—	—
Reclassification of the anti-dilution obligation upon settlement	—	—	—	—	—	—	7,536	—	—	7,536
Repurchase of unvested restricted common stock	—	—	—	—	(56,667)	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	1,746	—	—	1,746
Net loss	—	—	—	—	—	—	—	—	(165,367)	(165,367)
Change in unrealized gain on investments, net of tax	—	—	—	—	—	—	—	(27)	—	(27)
Balances at December 31, 2021	115,761,842	\$ 196,157	45,658,957	\$ 199,643	100,768,255	\$ 1	\$ 15,162	\$ (27)	\$ (171,376)	\$ (156,240)

The accompanying notes are an integral part of these consolidated financial statements.

PRIME MEDICINE, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(In thousands)

	Period from September 13, 2019 (date of (Inception) to December 31, 2019	Year Ended December 31,	
		2020	2021
Cash flows from operating activities:			
Net loss	\$ (2,529)	\$ (3,410)	\$ (165,367)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation and amortization expense	—	43	568
Amortization of premiums and discount on short-term investments	—	—	715
Stock-based compensation expense	156	391	1,746
Non cash research and development expense for licenses	194	—	12,020
Non cash consideration received under related party collaboration arrangement	—	(5,360)	—
Non cash payment to Beam	—	150	—
Non cash lease expense	—	—	4,293
Deferred income taxes	—	1,867	(624)
Change in fair value of preferred stock tranche right liability	353	10,904	74,319
Change in fair value of anti-dilution obligation	—	700	6,681
Change in fair value of related party short-term investment	—	(10,867)	391
Non cash other income (expense)	—	(126)	—
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(50)	(388)	(885)
Accounts payable	—	250	1,185
Accrued expenses and other current liabilities	542	302	35,206
Lease liability	—	—	(4,330)
Net cash used in operating activities	(1,334)	(5,544)	(34,082)
Cash flows from investing activities:			
Purchases of property and equipment	—	(639)	(4,150)
Purchase of short-term investments	—	—	(81,980)
Matured short-term investments	—	—	13,000
Payments of security deposits	—	(423)	(496)
Net cash used in investing activities	—	(1,062)	(73,626)
Cash flows from financing activities:			
Proceeds from the issuance of convertible preferred stock series A, net of issuance costs paid	9,980	34,954	70,721
Proceeds from the issuance of convertible preferred stock series B, net of issuance costs paid	—	—	199,643
Payments of deferred offering costs	—	(20)	(1,086)
Proceeds from the issuance of common stock	1	—	—
Net cash provided by (used in) financing activities	9,981	34,934	269,278
Net increase (decrease) in cash, cash equivalents and restricted cash	8,647	28,328	161,570
Cash and cash equivalents at beginning of period	—	8,647	36,975
Cash and cash equivalents at end of period	\$ 8,647	\$ 36,975	\$ 198,545

PRIME MEDICINE, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(In thousands)

	Period from September 13, 2019 (date of Inception) to December 31, 2019	Year Ended December 31,	
		2020	2021
Supplemental cash flow information:			
Right-of-use assets obtained in exchange for new operating lease liabilities	\$ —	\$ —	\$ 12,264
Supplemental disclosure of non-cash investing and financing activities:			
Initial fair value of preferred stock tranche right liability	\$ 6,258	\$ —	\$ —
Settlement of Series A preferred stock tranche obligation	\$ —	\$ —	\$ 91,834
Issuance of Series A preferred stock at a price below fair value	\$ —	\$ —	\$ 998
Issuance of common stock in exchange for licenses	\$ 39	\$ —	\$ —
Initial fair value of anti-dilution obligation	\$ 155	\$ —	\$ —
Settlement of anti-dilution obligation	\$ —	\$ —	\$ 7,536
Deferred offering costs included in accrued expenses	\$ 20	\$ —	\$ 410
Purchases of property and equipment included in accounts payable and accrued expenses	\$ —	\$ —	\$ 754
Accretion of preferred stock to redemption value	\$ 265	\$ 1,645	\$ 1,468
Short-term investment in connection with related party collaboration arrangement	\$ —	\$ 5,486	\$ —
Unrealized loss on short-term investments	\$ —	\$ —	\$ 27
Reconciliation of cash, cash equivalents and restricted cash:			
Cash and cash equivalents	\$ 8,647	\$ 36,975	\$ 185,420
Restricted cash	—	—	13,125
Total cash, cash equivalents and restricted cash shown in the statement of cash flows	\$ 8,647	\$ 36,975	\$ 198,545

The accompanying notes are an integral part of these consolidated financial statements.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of the Business and Basis of Presentation

Prime Medicine, Inc., together with its consolidated subsidiary (the “Company”) is a biotechnology company committed to deliver genetic therapies to address diseases by deploying gene editing technology, Prime Editing. The Company was incorporated in the State of Delaware in September 2019.

The Company is subject to risks and uncertainties common to early stage companies in the biotechnology industry, including, but not limited to, completing preclinical studies and clinical trials, obtaining regulatory approval for product candidates, market acceptance of products, development by competitors of new technological innovations, dependence on key personnel, the ability to attract and retain qualified employees, reliance on third-party organizations, protection of proprietary technology, compliance with government regulations, the impact of the COVID-19 pandemic, and the ability to raise additional capital to fund operations. The Company’s product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure, and extensive compliance-reporting capabilities. Even if the Company’s development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

The accompanying consolidated financial statements have been prepared on the basis of continuity of operations, realization of assets, and the satisfaction of liabilities and commitments in the ordinary course of business. Through years ended December 31, 2020 and 2021, the Company has funded its operations primarily with proceeds from sales of its convertible preferred stock. The Company has incurred net losses of \$2.5 million, \$3.4 million and \$165.4 million for the period from September 13, 2019 (inception) to December 31, 2019 and for the years ended December 31, 2020 and 2021, respectively. As of December 31, 2020 and 2021, the Company had an accumulated deficit of \$6.0 million and \$171.4 million, respectively. As of February 4, 2022, the issuance date of the annual consolidated financial statements for the year ended December 31, 2021, the Company expects that its cash and cash equivalents and short-term investments will be sufficient to fund its operating expenses and capital expenditure requirements for the next twelve months. The future viability of the Company beyond that point is dependent on its ability to raise additional capital to finance its operations.

The Company is seeking to complete an initial public offering (“IPO”) of its common stock. Upon the completion of a qualifying public offering on specified terms, the Company’s outstanding convertible preferred stock will automatically convert into shares of common stock (see Note 6).

In the event the Company does not complete an IPO, the Company expects to seek additional funding through private and public equity financings, debt financings, additional collaborations, strategic alliances and marketing, distribution or licensing arrangements. The Company may not be able to obtain financing on acceptable terms, or at all, and the Company may not be able to enter into additional collaborations or other arrangements. The terms of any financing may adversely affect the holdings or the rights of the Company’s stockholders.

If the Company is unable to obtain sufficient funding, the Company will be forced to delay, scale back or discontinue some or all of its research and development programs, product portfolio expansion efforts or commercialization efforts, which could adversely affect its business prospects. Although management continues to pursue these plans, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

Impact of the COVID-19 Pandemic

In March 2020, the World Health Organization declared the outbreak of COVID-19 a global pandemic. The Company is subject to a number of risks associated with the COVID-19 global pandemic, including potential delays associated with the Company’s ongoing preclinical studies and anticipated clinical trials. COVID-19 may have an adverse impact on the Company’s operations, supply chains and distribution systems or those of its third-party vendors and collaborators, and increase expenses, including as a result of impacts associated with preventive and precautionary measures that are being taken, such as restrictions on travel and border crossings, quarantine policies and social distancing. For example, the Company’s laboratory-based personnel have been unable to maximize use of its existing laboratory space due to restrictions on density of people and other aspects of its work have been limited

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

by the need for its staff to isolate. The Company and its third-party vendors and collaborators may experience disruptions in supply of items that are essential for its research and development activities. The Company cannot predict the scope and severity of any economic recovery after the COVID-19 pandemic abates, including following any additional “waves” or other intensifying of the pandemic will have on its financial condition, operations, and business plans.

Basis of Presentation

The accompanying consolidated financial statements reflect the operations of the Company and its wholly-owned subsidiary. Intercompany balances and transactions have been eliminated in consolidation. The accompanying consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States of America (“GAAP”). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification (“ASC”) and Accounting Standards Updates (“ASU”) of the Financial Accounting Standards Board (“FASB”).

2. Summary of Significant Accounting Policies***Use of Estimates***

The preparation of the Company’s consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting periods. Significant estimates and assumptions reflected within these consolidated financial statements include, but are not limited to, revenue recognition, the valuation of the Company’s common stock and stock-based awards, the valuation of preferred stock tranche right liability, the valuation of the anti-dilution obligation and the valuation of the related party forward contract liability. The Company bases its estimates on historical experience, known trends and other market-specific or other relevant factors that it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates, as there are changes in circumstances, facts and experience. Actual results may differ materially from those estimates or assumptions.

Concentrations of Credit Risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents and short-term investments. The Company invests in treasury bills and maintains its cash and cash equivalents at high-quality and accredited financial institutions in amounts that could exceed federally insured limits. Cash equivalents are invested in money market funds. However, the Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less at the time of initial purchase to be cash equivalents. As of December 31, 2020 and 2021, the amount of cash equivalents included in cash and cash equivalents totaled \$34.0 million and \$49.5 million, respectively.

Restricted Cash

Restricted cash consists of a letter of credit totaling \$13.1 million that is required to be maintained in connection with the Company’s lease arrangements. The letter of credit is in the name of the Company’s landlords and is required to fulfill lease requirements in the event the Company should default on its lease obligations. As of December 31, 2021, the Company classified its restricted cash as non-current on the consolidated balance sheet based on the release dates of the restrictions.

Short-term Investments and Related Party Short-Term Investment

The Company’s short-term investments consist of investments in debt, including U.S. Treasury securities with remaining maturities beyond three months at the date of purchase and one year or less from the balance sheet date.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

As of December 31, 2021, all of the Company's debt securities were classified as available-for-sale and were carried at fair market value (see Note 3). The unrealized losses on the Company's available-for-sale debt securities are recorded in other comprehensive income in the consolidated statements of operations and comprehensive loss.

Short-term debt securities are considered impaired when a decline in fair value is judged to be other-than-temporary. The Company consults with its investment managers and considers available quantitative and qualitative evidence in evaluating potential impairment of its short-term investments on a quarterly basis. If the cost of an individual investment exceeds its fair value, the Company evaluates, among other factors, general market conditions, the duration and extent to which the fair value is less than cost and its intent and ability to hold the investment. Once a decline in fair value is determined to be other-than-temporary, an impairment charge will be recorded to other income (expense), net, in the consolidated statements of operations and comprehensive loss.

The Company's related party short-term equity investment was obtained from the collaboration agreement with Beam Therapeutics, Inc. ("Beam"), which is a public company trading on the NASDAQ Exchange. At each reporting date, the Company will mark-to-market the Beam common stock to the fair value of the related party short-term investment.

The Company's equity securities with readily determinable fair values are recorded at fair value based upon the market prices of the securities at each reporting date. Unrealized and realized gains and losses on the Company's equity investment is included as a component of other income (expense) in the consolidated statements of operations and comprehensive loss. The costs of debt and equity securities for purposes of computing realized and unrealized gains and losses is based on the specific identification method.

Deferred Offering Costs

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of an equity financing, these costs are recorded as a reduction of the proceeds from the offering, either as a reduction of the carrying value of the preferred stock or in stockholders' equity (deficit) as a reduction of additional paid-in capital generated as a result of the offering. Should the in-process equity financing be abandoned, the deferred offering costs would be expensed immediately as a charge to operating expenses in the statements of operations and comprehensive loss. As of December 31, 2020, there were no deferred offering costs capitalized. As of December 31, 2021, there were \$1.5 million of deferred offering costs capitalized.

Fair Value Measurements

Certain assets and liabilities are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

Level 1 — Quoted prices in active markets for identical assets or liabilities.

Level 2 — Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.

Level 3 — Unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company's cash equivalents, short-term investments, preferred stock tranche right liability, anti-dilution obligation and related party forward contract liability are carried at fair value, determined according to the fair value

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

hierarchy described above (see Note 3). The carrying values of the Company's accounts payable and accrued expenses approximate their fair values due to the short-term nature of these liabilities.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation and amortization expense is recognized using the straight-line method over the estimated useful life of each asset as follows:

	Estimated Useful Life
Laboratory equipment	5 years
Furniture and fixtures	5 years
Leasehold improvements	Shorter of remaining lease term or useful life

Costs for capital assets not yet placed into service are capitalized and are depreciated once placed into service. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation and amortization are removed from the accounts and any resulting gain or loss is included in loss from operations. Expenditures for repairs and maintenance that do not improve or extend the life of the respective assets are charged to expense as incurred.

Impairment of Long-Lived Assets

Long-lived assets consist primarily of property and equipment, and operating lease right-of-use assets. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset group for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset group to its carrying value. An impairment loss would be recognized in loss from operations when estimated undiscounted future cash flows expected to result from the use of an asset group are less than its carrying amount. If such asset group is considered to be impaired, the impairment loss to be recognized is measured based on the excess of the carrying value of the impaired asset group over its fair value.

For the period from September 13, 2019 (inception) to December 31, 2019 and the years ended December 31, 2020 and 2021, the Company did not recognize any impairment losses on long-lived assets.

Leases

Prior to January 1, 2021, the Company accounted for leases in accordance with Accounting Standards Codification ("ASC") ASC 840, *Leases*. At lease inception, the Company determined if an arrangement was an operating or capital lease. For operating leases, the Company recognized rent expense, inclusive of rent escalation, on a straight-line basis over the lease term.

Effective on January 1, 2021, the Company accounts for leases in accordance with ASC 842, *Leases*. In accordance with ASC 842, *Leases*, the Company determines if an arrangement is or contains a lease at inception. A contract is or contains a lease if the contract conveys the right to control the use of an identified asset for a period of time in exchange for consideration. The Company classifies leases at the lease commencement date as operating or finance leases and records a right-of-use asset and a lease liability on the consolidated balance sheet for all leases with an initial lease term of greater than 12 months. Leases with an initial term of 12 months or less are not recorded in the balance sheet, but payments are recognized as expense on a straight-line basis over the lease term. The Company has elected not to recognize leases with terms of 12 months or less.

A lease qualifies as a finance lease if any of the following criteria are met at the inception of the lease: (i) there is a transfer of ownership of the leased asset to the Company by the end of the lease term, (ii) the Company holds an option to purchase the leased asset that it is reasonably certain to exercise, (iii) the lease term is for a major part of

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

the remaining economic life of the leased asset, (iv) the present value of the sum of lease payments equals or exceeds substantially all of the fair value of the leased asset, or (v) the nature of the leased asset is specialized to the point that it is expected to provide the lessor no alternative use at the end of the lease term. All other leases are recorded as operating leases.

The Company enters into contracts that contain both lease and non-lease components. Non-lease components may include maintenance, utilities, and other operating costs. The Company combines the lease and non-lease components of fixed costs in its lease arrangements as a single lease component. Variable costs, such as utilities or maintenance costs, are not included in the measurement of right-of-use assets and lease liabilities, but rather are expensed when the event determining the amount of variable consideration to be paid occurs.

Finance and operating lease assets and liabilities are recognized at the lease commencement date based on the present value of the lease payments over the lease term using the discount rate implicit in the lease. If the rate implicit is not readily determinable, the Company utilizes an estimate of its incremental borrowing rate based upon the available information at the lease commencement date. Operating lease assets are further adjusted for prepaid or accrued lease payments. Operating lease payments are expensed using the straight-line method as an operating expense over the lease term. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Finance lease assets are amortized to depreciation expense using the straight-line method over the shorter of the useful life of the related asset or the lease term. Finance lease payments are bifurcated into (i) a portion that is recorded as imputed interest expense and (ii) a portion that reduces the finance liability associated with the lease.

Certain of the Company's leases include options to extend or terminate the lease. The amounts determined for the Company's right-of-use assets and lease liabilities generally do not assume that renewal options or early-termination provisions, if any, are exercised, unless it is reasonably certain that the Company will exercise such options.

In addition, the Company examines other contracts with suppliers, vendors and outside parties to identify whether such contracts contain an embedded lease and, as applicable, records such embedded leases in accordance with ASC 842.

Segment Information

The Company operates and manages its business as a single segment for the purposes of assessing performance and making operating decisions. The Company's chief executive officer, who is the chief operating decision maker, reviews the Company's financial information on a consolidated basis for purposes of evaluating financial performance and allocating resources. All of the Company's long-lived assets are located in the United States and all of the Company's revenue was derived in the United States.

Classification and Accretion of Redeemable Convertible Preferred Stock

The Company has classified the convertible preferred stock outside of stockholders' equity (deficit) on the Company's consolidated balance sheets because the holders of such stock have redemption features and certain liquidation rights in the event of a deemed liquidation that, in certain situations, are not solely within the control of the Company and would require the redemption of the then-outstanding convertible preferred stock.

The Company's Series A redeemable convertible preferred stock ("Series A Preferred Stock") were redeemable in an amount equal to the original issue price per share plus all declared but unpaid dividends thereon. The Company recorded periodic accretion to the values of its outstanding Series A Preferred Stock such that the carrying value of the Series A Preferred Stock would be equal to the redemption value at the earliest redemption date. Adjustments to the carrying value of the Series A Preferred Stock at each reporting date resulted in an increase to net loss attributable to common stockholders. In April 2021, the redemption rights for Series A Preferred Stock were removed and such shares of preferred stock were no longer redeemable. After the removal of the redemption rights, the Company did not record any further accretion to the carrying value of Series A Preferred Stock (see Note 6).

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The Company's Series B convertible preferred stock is not redeemable, except in the event of a deemed liquidation (see Note 6). Because the occurrence of a deemed liquidation event is not currently probable, the carrying values of the Series B convertible preferred stock are not being accreted to their redemption values. Subsequent adjustments to the carrying values of the convertible preferred stock would be made only when a deemed liquidation event becomes probable.

Revenue Recognition

The Company recognizes revenue in accordance with ASU 2014-09, *Revenue from Contracts with Customers (Topic 606)* and its related amendments, or, collectively, ASC 606.

Under ASC 606, revenue is recognized when a customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. In order to achieve this core principle, the Company applies the following five steps when recording revenue: (1) identify the contract, or contracts, with the customer, (2) identify the performance obligations in the contract, (3) determine the transaction price, (4) allocate the transaction price to the performance obligations in the contract and (5) recognize revenue when, or as, performance obligations are satisfied.

At contract inception, the Company assesses the goods or services promised within each contract, whether each promised good or service is distinct, and determines those that are performance obligations. In assessing whether promised goods or services are distinct, the Company considers factors such as the stage of development of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on their own and whether the required expertise is readily available. In addition, the Company considers whether the collaboration partner can benefit from a promise for its intended purpose without the receipt of the remaining promises, whether the value of the promise is dependent on the unsatisfied promises, whether there are other vendors that could provide the remaining promises, and whether it is separately identifiable from the remaining promises. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when or as the performance obligation is satisfied.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under its arrangements, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the assessment of the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations, and (v) recognition of revenue when, or as, the Company satisfies each performance obligation. As part of the accounting for arrangements under ASC 606, the Company must use significant judgment to determine: a) the performance obligations based on the determination under step (ii) above; b) the transaction price under step (iii) above; and c) the standalone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above. The Company also uses judgment to determine whether milestones or other variable consideration, except for royalties and sales-based milestones where such payments principally relate to a license of intellectual property, should be included in the transaction price as described below. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment. The transaction price is allocated to each performance obligation based on the relative standalone selling price of each performance obligation in the contract, and the Company recognizes revenue based on those amounts when, or as, the performance obligations under the contract are satisfied. The Company utilizes key assumptions to determine the standalone selling price, which may include other comparable transactions, pricing considered in negotiating the transaction, probabilities of technical and regulatory success and the estimated costs. Certain variable consideration is allocated specifically to one or more performance obligations in a contract when the terms of the variable consideration relate to the satisfaction of the performance obligation and the resulting amounts allocated to each performance obligation are consistent with the amounts the Company would expect to receive for each performance obligation.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Research and Development Expenses

Research and development expenses are expensed as incurred. Research and development expenses may consist of costs incurred in connection with acquired in-process research and development and performing research and development activities, including amounts incurred under agreements with external vendors and consultants engaged to perform preclinical studies and to manufacture research and development materials for use in such studies, salaries and related personnel costs, stock-based compensation, consultant fees, and third-party license fees.

Upfront payments under license agreements are expensed upon receipt of the license, and annual maintenance fees under license agreements are expensed over the maintenance period. Milestone payments under license agreements are accrued, with a corresponding expense being recognized, in the period in which the milestone is determined to be probable of achievement and the related amount is reasonably estimable.

Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed.

Acquired In-Process Research and Development

The Company measures and recognizes asset acquisitions or licenses to intellectual property that are not deemed to be business combinations based on the cost to acquire or license the asset or group of assets, which includes transaction costs. Goodwill is not recognized in asset acquisitions or transaction to license intellectual property. In an asset acquisition or license to intellectual property, the cost allocated to acquire in-process research and development (“IPR&D”) with no alternative future use is recognized as research and development expense on the acquisition date.

Upfront and milestone payments made are accrued for and expensed when the achievement of the milestone is probable up to the point of regulatory approval. Milestone payments made upon regulatory approval are capitalized and amortized over the remaining useful life of the related product.

Acquired IPR&D for the period from September 13, 2019 (inception) to December 31, 2019 consisted of (i) \$0.2 million initial recognition of an anti-dilution obligation that obligates the Company to issue shares of common stock equal to 5.0 percent of the Company’s capital stock until the Company has raised \$100.0 million in net cash proceeds from equity financings, (ii) issuance of 1.9 million shares of common stock valued at \$39,000 and (iii) the upfront cash consideration for a license arrangement of \$0.5 million (see Note 11). There were no acquired IPR&D recognized for the year ended December 31, 2020. Acquired IPR&D for the year ended December 31, 2021, consisted of (i) the related party forward contract liability for the issuance of 3.4 million shares of common stock initially valued at \$12.0 million and (ii) upfront cash consideration for a license arrangement of \$30.0 million (see Note 11).

Patent Costs

The Company expenses as incurred all patent-related costs incurred in connection with filing and prosecuting patent applications due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses in the statements of operations and comprehensive loss.

Contingencies

The Company is subject to contingent liabilities, such as legal proceedings and claims, that arise in the ordinary course of business activities. The Company accrues for loss contingencies when losses become probable and are reasonably estimable. If the reasonable estimate of the loss is a range and no amount within the range is a better estimate, the minimum amount of the range is recorded as a liability on the consolidated balance sheets. The Company does not accrue for contingent losses that, in its judgment, are considered to be reasonably possible, but not probable; however, it discloses the range of reasonably possible losses. As of December 31, 2020 and 2021, no liabilities were recorded for loss contingencies (see Note 12).

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Stock-Based Compensation

The Company measures all stock-based awards granted to employees, directors and non-employees based on the fair value of the awards on the date of grant using the Black-Scholes option-pricing model. The Company measures restricted common stock awards using the difference, if any, between the purchase price per share of the award and the fair value of the Company's common stock at the date of grant.

The Company grants stock options and restricted stock awards that are subject to either service or performance-based vesting conditions. Compensation expense for awards to employees and directors with service-based vesting conditions is recognized using the straight-line method over the requisite service period, which is generally the vesting period of the respective award. Compensation expense for awards to non-employees with service-based vesting conditions is recognized in the same manner as if the Company had paid cash in exchange for the goods or services, which is generally over the vesting period of the award. Forfeitures are accounted for as they occur. Compensation expense for awards to employees and non-employees with performance-based vesting conditions is recognized based on the grant-date fair value over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable. As of each reporting date, the Company estimates the probability that specified performance criteria will be met and does not recognize compensation expense until it is probable that the performance-based vesting condition will be achieved.

The Company classifies stock-based compensation expense in its consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

Preferred Stock Tranche Right Liability

The subscription agreements for the Company's Series A Preferred Stock (see Note 6) obligated investors, to participate in subsequent offerings of Series A Preferred Stock upon satisfaction of certain conditions (the "Series A preferred stock tranche right liability").

The Company classified this preferred stock tranche right as a liability on its consolidated balance sheets as each preferred stock tranche right is a freestanding financial instrument that may require the Company to transfer assets upon satisfaction of certain conditions. Each preferred stock tranche right liability was initially recorded at fair value upon the date of issuance of each preferred stock tranche right and is subsequently remeasured to fair value at each reporting date. Changes in the fair value of the preferred stock tranche right liability are recognized as a component of other income (expense), net in the consolidated statement of operations and comprehensive loss. Changes in the fair value of the preferred stock tranche right liability were recognized until the preferred stock tranche right was settled in full upon the satisfaction of certain conditions in April 2021.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. For the period from September 13, 2019 (inception) to December 31, 2019 and year ended December 31, 2020, there was no difference between net loss and comprehensive loss. For the year ended December 31, 2021, comprehensive loss includes net loss and unrealized gains (losses) on investments.

Net Loss per Share Attributable to Common Stockholders

The Company applies the two-class method when computing net income (loss) per share attributable to common stockholders as the Company has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income (loss) available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to share in the undistributed earnings as if all income (loss) for the period had been distributed. The Company considers its convertible preferred stock to be participating securities as, in the event a dividend is paid on common stock, the holders of convertible preferred stock would be

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

entitled to receive dividends on a basis consistent with the common stockholders. There is no allocation required under the two-class method during periods of loss since the participating securities do not have a contractual obligation to share in the losses of the Company.

Basic net income (loss) per share attributable to common stockholders is computed by dividing the net income (loss) attributable to common stockholders by the weighted-average number of common shares outstanding for the period, excluding potentially dilutive common shares and of unvested restricted common stock. Diluted net income (loss) per share attributable to common stockholders is computed by adjusting net loss attributable to common stockholders to reallocate undistributed earnings based on the potential impact of dilutive securities. Diluted net income (loss) per share attributable to common stockholders is computed by dividing the diluted net income (loss) attributable to common stockholders by the weighted-average number of common shares outstanding for the period, including potential dilutive common shares. For purposes of this calculation, the Company's outstanding stock options and convertible preferred stock are considered potential dilutive common shares.

The Company reported net loss and net loss attributable to common stockholders for the period from September 13, 2019 (inception) through December 31, 2019, and for the years ended December 31, 2020 and 2021.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined based on the differences between the financial statement basis and tax basis of assets and liabilities using enacted tax rates in effect for the years in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more likely than not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50 percent likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties. The Company had accrued no amounts for interest or penalties related to uncertain tax positions as of December 31, 2020 and 2021.

Recently Adopted Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases* (Topic 842) ("ASU 2016-02"), as subsequently amended, which sets out the principles for the recognition, measurement, presentation, and disclosure of leases for both parties to a contract (i.e., lessees and lessors), and replaces the existing guidance in ASC 840, *Leases*.

The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine the recognition pattern of lease expense over the term of the lease. In addition, a lessee is required to record (i) a right-of-use asset and a lease liability on its balance sheet for all leases with accounting lease terms of more than 12 months regardless of whether it is an operating or financing lease and (ii) lease expense in its consolidated statement of operations and comprehensive loss for operating leases and amortization and interest expense in its consolidated statement of operations and comprehensive loss for financing leases. Leases with a term of 12 months or less may be accounted for similar to existing guidance for operating leases under ASC 840. In July 2018, the FASB issued ASU No. 2018-11, *Leases* (Topic 842), which added an optional transition method that

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allows companies to adopt the standard as of the beginning of the year of adoption as opposed to the earliest comparative period presented. This guidance is effective for the Company for annual periods beginning after December 15, 2021, including interim periods within that fiscal year. Early adoption is permitted.

The Company adopted the new leasing standard effective January 1, 2021, using the modified retrospective transition approach which uses the effective date, or January 1, 2021, as the date of initial application. As a result, prior periods are presented in accordance with the previous guidance in ASC 840. The Company has elected to apply the package of practical expedients requiring no reassessment of whether any expired or existing contracts are or contain leases, the lease classification of any expired or existing leases, or the capitalization of initial direct costs for any existing leases.

Upon its adoption of ASC 842, the Company recorded lease liabilities and their corresponding right-of-use assets based on the present value of lease payments over the remaining lease term. The adoption of ASC 842 resulted in the recognition of operating lease liabilities of \$2.7 million and right-of-use assets of \$2.8 million and the derecognition of prepaid rent balances recorded in other assets of \$0.1 million on the Company's balance sheet as of January 1, 2021. The adoption impact relates to the Company's existing operating lease for office and laboratory space. The adoption of ASU 2016-02 did not have a material impact on the Company's statements of operations and comprehensive loss or statements of cash flows.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, or ASU 2016-13, which requires the measurement and recognition of expected credit losses for financial assets held at amortized cost. ASU 2016-13 replaces the existing incurred loss impairment model with an expected loss model. It also eliminates the concept of other-than-temporary impairment and requires credit losses related to available-for-sale debt securities to be recorded through an allowance for credit losses rather than as a reduction in the amortized cost basis of the securities. These changes may result in earlier recognition of credit losses. For public entities that are Securities and Exchange Commission filers, excluding entities eligible to be smaller reporting companies, ASU 2016-13 is effective for annual periods beginning after December 15, 2019, including interim periods within those fiscal years. For all other entities, ASU 2016-13 is effective for annual periods beginning after December 15, 2022, including interim periods within those fiscal years. Early adoption is permitted. The Company adopted ASU 2016-13 on January 1, 2021. The adoption of ASU 2016-13 did not have a material impact on the Company's consolidated financial statements.

In July 2017, the FASB issued ASU No. 2017-11, *Earnings Per Share (Topic 260), Distinguishing Liabilities from Equity (Topic 480) and Derivatives and Hedging (Topic 815): I. Accounting for Certain Financial Instruments with Down Round Features and II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception* ("ASU 2017-11"). Part I of this update addresses the complexity of accounting for certain financial instruments with down round features. Down round features are features of certain equity-linked instruments (or embedded features) that result in the strike price being reduced on the basis of the pricing of future equity offerings. Current accounting guidance creates cost and complexity for entities that issue financial instruments (such as warrants and convertible instruments) with down round features that require fair value measurement of the entire instrument or conversion option. Pursuant to the amendments in Part I of this update, when determining whether certain financial instruments should be classified as liabilities or equity instruments, a down round feature no longer precludes equity classification when assessing whether the instrument is indexed to an entity's own stock. Part II of this update replaces the indefinite deferral for certain mandatorily redeemable noncontrolling interests and mandatorily redeemable financial instruments of nonpublic entities contained within ASC No. 480 with a scope exception. The amendments in Part II of this update do not have an accounting effect. For public entities, ASU 2017-11 was required to be adopted for annual periods beginning after December 15, 2018, including interim periods within those fiscal years. For nonpublic entities, ASU 2017-11 is effective for annual periods beginning after December 15, 2019, and interim periods within fiscal years beginning after December 15, 2020. Early adoption was permitted. The Company adopted ASU 2017-11 on January 1, 2020. The adoption of ASU 2017-11 did not have a material impact on the Company's consolidated financial statements.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation-Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07"). The standard largely aligns the

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

accounting for share-based payments to nonemployees by aligning it with the accounting for share-based payments to employees and directors, with certain exceptions. Under ASU 2018-07, an entity should apply the requirements of Topic 718 to nonemployee awards except for specific guidance on inputs to an option pricing model and the attribution of cost. The amendments specify that Topic 718 applies to all share-based payment transactions in which a grantor acquires goods or services to be used or consumed in a grantor's own operations by issuing share-based payment awards. The amendments also clarify that Topic 718 does not apply to share-based payments used to effectively provide (1) financing to the issuer or (2) awards granted in conjunction with selling goods or services to customers as part of a contract accounted for under ASC Topic 606, *Revenue from Contracts with Customers* ("ASC 606"). For public entities, ASU 2018-07 was required to be adopted for annual periods beginning after December 15, 2018, including interim periods within those fiscal years. For nonpublic entities, ASU 2018-07 is effective for annual periods beginning after December 15, 2019, including interim periods within fiscal years beginning after December 15, 2020. Early adoption is permitted for all entities but no earlier than the Company's adoption of ASC 606. The Company early adopted ASU 2018-07 as of January 1, 2020 and the adoption did not have a material impact on its consolidated financial statements.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Requirements for Fair Value Measurement* ("ASU 2018-13"), which modifies the existing disclosure requirements for fair value measurements in Topic 820. The new disclosure requirements include disclosure related to changes in unrealized gains or losses included in other comprehensive loss for recurring Level 3 fair value measurements held at the end of each reporting period and the explicit requirement to disclose the range and weighted-average of significant unobservable inputs used for Level 3 fair value measurements. The other provisions of ASU 2018-13 include eliminated and modified disclosure requirements. For all entities, this guidance is required to be adopted for annual periods beginning after December 15, 2019, including interim periods within those fiscal years. The Company adopted ASU 2018-13 as of January 1, 2020 and the adoption did not have a material impact on its consolidated financial statements.

In November 2018, the FASB issued ASU No. 2018-18, *Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606* ("ASU 2018-18"). ASU 2018-18 makes targeted improvements to GAAP for collaborative arrangements, including (i) clarification that certain transactions between collaborative arrangement participants should be accounted for as revenue under ASC Topic 606 when the collaborative arrangement participant is a customer in the context of a unit of account, (ii) adding unit-of-account guidance in ASC Topic 808, *Collaborative Arrangements*, to align with the guidance in ASC 606 and (iii) a requirement that in a transaction with a collaborative arrangement participant that is not directly related to sales to third parties, presenting the transaction together with revenue recognized under ASC 606 is precluded if the collaborative arrangement participant is not a customer. For public entities, this guidance was effective for annual periods beginning after December 15, 2019, including interim periods within those fiscal years. For nonpublic entities, this guidance is effective for annual periods beginning after December 15, 2020, including interim periods within fiscal years beginning after December 15, 2021. Early adoption is permitted. The Company early adopted ASU 2018-18 as of January 1, 2020 and the adoption did not have a material impact on its consolidated financial statements.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12"). ASU 2019-12 eliminates certain exceptions related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. The update also clarifies and simplifies other aspects of the accounting for income taxes. For public entities, ASU 2019-12 is required to be adopted for annual periods beginning after December 15, 2020, including interim periods within those fiscal years. For nonpublic entities, ASU 2019-12 is effective for annual periods beginning after December 15, 2021, including interim periods within fiscal years beginning after December 15, 2022. Early adoption is permitted, including adoption in any interim period for which financial statements have not yet been issued or made available for issuance. An entity that elects to early adopt the update in an interim period should reflect any adjustments as of the beginning of the annual period that includes that interim period. Additionally, an entity that elects early adoption must adopt all the amendments in the update in the same period. The Company early adopted ASU 2019-12 as of January 1, 2020 and the adoption did not have a material impact on its consolidated financial statements.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Recently Issued Accounting Pronouncements Not Yet Adopted

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies and adopted by the Company as of the specified effective date. The Company qualifies as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012 and has elected not to “opt out” of the extended transition related to complying with new or revised accounting standards, which means that when a standard is issued or revised and it has different application dates for public and nonpublic companies, the Company will adopt the new or revised standard at the time nonpublic companies adopt the new or revised standard and will do so until such time that the Company either (i) irrevocably elects to “opt out” of such extended transition period or (ii) no longer qualifies as an emerging growth company. As a result of this election, the Company’s financial statements may not be comparable to those public companies that comply with new or revised accounting pronouncements as of public company effective dates. The Company may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for nonpublic companies.

In August 2020, the FASB issued ASU 2020-06, *Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity’s Own Equity (Subtopic 815-40)*. This standard eliminates the beneficial conversion and cash conversion accounting models for convertible instruments. It also amends the accounting for certain contracts in an entity’s own equity that are currently accounted for as derivatives because of specific settlement provisions. In addition, the new guidance modifies how particular convertible instruments and certain contracts that may be settled in cash or shares impact the diluted earnings per share (“EPS”) computation. Additionally, the amended guidance requires the application of the if-converted method for calculating diluted EPS and the treasury stock method will no longer be available. For public business entities, it is effective for fiscal years beginning after December 15, 2021, including interim periods within those fiscal years using the fully retrospective or modified retrospective method. For all other entities, the amendments are effective for fiscal years beginning after December 15, 2023, including interim periods within those fiscal years. Early adoption is permitted but no earlier than fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. The Company is currently evaluating the potential impact of ASU 2020-06 will have on its consolidated financial statements and related disclosures but does not currently expect that the adoption of ASU 2020-06 will have a material impact.

3. Fair Value Measurements

The following tables present the Company’s fair value hierarchy for its assets and liabilities that are measured at fair value on a recurring basis and indicate the level within the fair value hierarchy of the valuation techniques the Company utilized to determine such fair value (in thousands):

	Fair Value Measurements at December 31, 2020 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	\$ —	\$ 34,000	\$ —	\$ 34,000
Related party short-term investment:				
Beam equity securities	16,353	—	—	16,353
	<u>\$ 16,353</u>	<u>\$ 34,000</u>	<u>\$ —</u>	<u>\$ 50,353</u>
Liabilities:				
Preferred stock tranche right liability	\$ —	\$ —	\$ 17,515	\$ 17,515
Anti-dilution obligation	—	—	855	855
	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 18,370</u>	<u>\$ 18,370</u>

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

	Fair Value Measurements at December 31, 2021 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	\$ —	\$ 49,450	\$ —	\$ 49,450
Short-term investment:				
U.S. Treasury Bonds	—	68,238	—	68,238
Related party short-term investment:				
Beam equity securities	15,962	—	—	15,962
	<u>\$ 15,962</u>	<u>\$ 117,688</u>	<u>\$ —</u>	<u>\$ 133,650</u>
Liabilities:				
Related party forward contract liability	—	—	12,020	12,020
	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 12,020</u>	<u>\$ 12,020</u>

Money market funds were valued by the Company based on observable inputs, which represent a Level 2 measurement within the fair value hierarchy. For the years ended December 31, 2020 and 2021, there were no transfers between Level 1, Level 2 and Level 3.

The Company classifies its U.S. Treasury as short-term based on each instrument's underlying contractual maturity date. The fair value of the Company's U.S. Treasury securities and money market funds are classified as Level 2 because they are valued using observable inputs to quoted market prices, benchmark yields, reported trades, broker/dealer quotes or alternative pricing sources with reasonable levels of price transparency and U.S. Treasury securities.

The underlying securities held in the money market funds held by the Company are all government backed securities.

Short-term investments consisted of the following (in thousands):

	December 31, 2020			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Related party short-term investment:				
Beam equity securities	\$ 5,486	\$ 10,867	\$ —	\$ 16,353
	<u>\$ 5,486</u>	<u>\$ 10,867</u>	<u>\$ —</u>	<u>\$ 16,353</u>
	December 31, 2021			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Short-term investments:				
U.S. Treasury Bonds	\$ 68,265	\$ —	\$ (27)	\$ 68,238
Related party short-term investment:				
Beam equity securities	5,486	10,476	—	15,962
	<u>\$ 73,751</u>	<u>\$ 10,476</u>	<u>\$ (27)</u>	<u>\$ 84,200</u>

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The contractual maturities of the Company's short-term investments in available-for-sale debt securities held were as follows:

	December 31, 2021
Due within one year	\$ 68,238
	<u>\$ 68,238</u>

Valuation of Preferred Stock Tranche Right Liability

The preferred stock tranche right liability in the table above is composed of the fair value of rights to purchase Series A Preferred Stock (see Note 6). The fair value of the preferred stock tranche right liability was determined based on significant inputs not observable in the market, which represented a Level 3 measurement within the fair value hierarchy. The fair value of the preferred stock tranche right liability was determined using a Black Scholes option pricing model, which considered as inputs the estimated fair value of the preferred stocks as of each valuation date, the risk-free interest rate, volatility and estimated time to each tranche closing.

The most significant assumption in the Black Scholes option pricing model impacting the fair value of the preferred stock tranche right liability is the fair value of the Company's convertible preferred stock as of each measurement date. The Company determines the fair value per share of the underlying convertible preferred stock by taking into consideration the most recent sales of its convertible preferred stock, results obtained from third-party valuations and additional factors the Company deems relevant. In November 2020, the second tranche of the Series A Preferred Stock closed and in April 2021, the third and fourth tranches of the Series A Preferred Stock closed. Upon satisfaction of certain conditions and the closing date of the third and fourth tranches, the associated Series A preferred stock tranche right liability was settled. The fair value of each Series A Preferred Stock was \$0.73 per share upon the closing of the second tranche. The fair value of Series A Preferred Stock was \$2.31 per share upon the closing of the third and fourth tranches. As of December 31, 2020, the fair value of Series A Preferred Stock was \$0.76 per share. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining estimated time to each tranche closing. The volatility is based on the historical volatility of publicly traded peer companies. Changes in the estimated fair value of the Company's convertible preferred stock can have a significant impact on the fair value of the preferred stock tranche right liability.

The preferred stock tranche right liability was initially recorded at fair value upon the date of issuance of the preferred stock tranche right and is subsequently remeasured to fair value at each reporting date, and immediately prior to the closing dates of Series A preferred stock tranches. Changes in the fair value of the preferred stock tranche right liability are recognized as a component of other income (expense), net in the consolidated statement of operations and comprehensive loss. Changes in the fair value of the preferred stock tranche right liability were recognized until the preferred stock tranche right liability was settled in full upon the satisfaction of certain conditions in April 2021.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The following table provides a roll-forward of the aggregate fair value of the Company's preferred stock tranche right liability, for which fair value is determined using Level 3 inputs (in thousands):

	Preferred Stock Tranche Right
Balances at September 13, 2019 (Inception)	\$ —
Initial fair value of Series A preferred stock tranche right liability	6,258
Change in fair value of Series A preferred stock tranche right liability	353
Balance as of December 31, 2019	6,611
Change in fair value of Series A preferred stock tranche right liability	10,904
Balance as of December 31, 2020	17,515
Change in fair value of Series A preferred stock tranche right liability	74,319
Reclassification of Series A preferred stock tranche right liability upon settlement	(91,834)
Balance as of December 31, 2021	\$ —

Valuation of Anti-dilution Obligation

The fair value of the anti-dilution obligation recognized in connection with the anti-dilution provisions set forth in the Company's license agreement with Broad Institute (see Note 11) was determined based on significant inputs not observable in the market, which represented a Level 3 measurement within the fair value hierarchy.

The fair value of the anti-dilution obligation was estimated using a probability-weighted scenario which considered as inputs the probability of occurrence of events that would trigger the issuance of shares, including (i) the closing of Series A Preferred Stock, (ii) the Company's initial public offering, and (iii) no future sale of equity securities. The weighted-average fair value of all scenarios was calculated utilizing the fair value per share of the underlying common stock. Changes in the estimated fair value of common stock and the probability of achieving different financing scenarios can have a significant impact on the fair value of the anti-dilution obligation. The most significant assumption impacting the fair value of the anti-dilution obligation was the fair value of the Company's common stock as of each measurement date. The Company determined the fair value per share of the underlying common stock by taking into consideration the most recent sales of its convertible preferred stock, results obtained from third-party valuations and additional factors the Company deems relevant. The per share fair value of the Company's common stock was \$0.11 as of December 31, 2020. Immediately prior to the settlement of the anti-dilution obligation, the fair value of the Company's common stock was \$0.97 per share.

The anti-dilution obligation was initially recorded at fair value upon entering into the license agreement with Broad Institute and was subsequently remeasured to fair value at each reporting date. Changes in fair value of the anti-dilution obligation were recognized as a component of other income (expense), net in the consolidated statements of operations and comprehensive loss. Changes in the fair value of the anti-dilution obligation were recognized until achievement of \$100.0 million in cumulative equity financing is raised by the Company, which was achieved in connection with the fourth Series A Preferred Stock closing, resulting in the issuance of 7,768,425 shares of common stock to Broad Institute with a fair value of \$7.5 million.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The following table provides a roll-forward of the aggregate fair value of the Company's anti-dilution obligation, for which fair value was determined using Level 3 inputs (in thousands):

	Anti-dilution Obligation
Balances at September 13, 2019 (Inception)	\$ —
Initial fair value of anti-dilution obligation	155
Balance as of December 31, 2019	155
Change in fair value of anti-dilution obligation	700
Balance as of December 31, 2020	855
Change in fair value of anti-dilution obligation	6,681
Reclassification of anti-dilution obligation upon settlement	(7,536)
Balance as of December 31, 2021	\$ —

Valuation of the Related Party Forward Contract Liability

The Company measured its related party forward contract liability, which was established in connection with its obligation to issue shares of its common stock to Myeloid Therapeutics, Inc. ("Myeloid") under a stock subscription agreement (see Note 11), at fair value based on significant inputs not observable in the market, which represented a Level 3 measurement within the fair value hierarchy. The initial fair value of the related party forward contract liability was determined based on the number of shares to be issued by the Company and the then per share fair value of the Company's common stock, which was determined based, in part, on a third-party valuation that utilized methodologies and assumptions consistent with the Company's most recent common stock valuations, including on a minority, nonmarketable interest basis.

Changes in the fair value of the related party forward contract liability will be recognized as other income (expense), net in the consolidated statements of operations through the settlement date. There was no change in the fair value of the Company's common stock from the initial date of the related party forward contract liability and December 31, 2021. The Company assessed these assumptions and estimates until settlement of the forward contract in January 2022 (see Note 15).

A reconciliation of the related party forward contract liability measured and recorded at fair value on a recurring basis is as follows (in thousands):

	Forward Contract
Balance at December 31, 2020	\$ —
Initial fair value of related party forward contract liability	12,020
Balance as of December 31, 2021	\$ 12,020

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4. Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2020	2021
Laboratory equipment	\$ 639	\$ 5,274
Leasehold improvement	—	125
Furniture and Fixture	—	144
	639	5,543
Less: Accumulated depreciation and amortization	(43)	(611)
	<u>\$ 596</u>	<u>\$ 4,932</u>

Depreciation and amortization expense of property and equipment for the years ended December 31, 2020 and 2021 was \$43,000 and \$0.6 million, respectively.

5. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31,	
	2020	2021
Accrued Myeloid license fee–related party	\$ —	\$ 30,000
Accrued employee compensation and benefits	627	2,364
Accrued professional fees	116	3,830
Deferred rent	46	—
Lab-related supplies	—	719
Other	33	279
	<u>\$ 822</u>	<u>\$ 37,192</u>

6. Convertible Preferred Stock

The Company has issued Series A Preferred Stock and Series B convertible preferred stock (the “Series B Preferred Stock” and, together with the Series A Preferred Stock, the “Preferred Stock”).

In September 2019, the Company completed its first closing of its Series A Preferred Stock and issued and sold 10,000,001 shares of Series A Preferred Stock at a price of \$1.00 per share for gross proceeds of \$10.0 million (the “2019 Preferred Stock Financing”). The Company incurred issuance costs of \$20,000 in connection with this transaction.

The purchase agreement for the Series A Preferred Stock obligates the investors of the 2019 Preferred Stock Financing to purchase an additional 104,999,997 Series A Preferred Stock at a price of \$1.00 per share in the subsequent closings upon certain conditions (“Series A Subsequent Closings”). The investors’ obligation to purchase shares in the subsequent closing will terminate upon occurrence of a Deemed Liquidation Event (as defined below), the Company’s initial public offering, or bankruptcy by the Company. If an investor does not participate in the subsequent closing when obligated to do so, then any existing Series A Preferred Stock held by that investor will be converted into common shares of the Company on a ten-for-one basis.

The Company concluded that these obligations of investors to participate in the subsequent closing of Series A Preferred Stock met the definition of a freestanding financial instrument that was required to be recorded as a liability at fair value as (i) the instruments are legally detachable and separately exercisable from the Series A

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Preferred Stock and (ii) the rights will require the Company to transfer assets upon future closings of the Series A Preferred Stock. Upon the first closing of the Series A Preferred Stock in September 2019, the Company recorded a preferred stock tranche right liability of \$6.3 million and a corresponding reduction to the carrying value of the Series A Preferred Stock (see Note 3).

In November 2020, the Company completed the second closing of its Series A Preferred Stock, in which the Company issued and sold 34,999,999 shares of Series A Preferred Stock, at a price of \$1.00 per share, for gross proceeds of \$35.0 million and incurred \$46,000 of issuance costs. As the fair value of the Series A Preferred Stock was \$0.73 at the time of the second closing, the Company recorded a capital contribution of \$9.5 million for the difference between the fair value per share and the \$1.00 per share paid by the holders of the Series A Preferred Stock participating in the second closing, which included members of the Company's board of directors.

In April 2021, the Company completed the third and fourth closings of its Series A Preferred Stock, in which the Company issued and sold an aggregate of 70,761,842 shares of Series A Preferred Stock, at a price of \$1.00 per share, for gross proceeds of \$70.8 million and incurred \$41,000 of issuance costs. As a result of this issuance, the Series A preferred stock tranche right liability with a then fair value of \$91.8 million, based on a fair value of \$2.31 per share of Series A Preferred Stock immediately prior to the closings, was settled in full and reclassified as an increase to the carrying value of Series A Preferred Stock.

In April 2021, the Company issued and sold 45,658,957 shares of Series B Preferred Stock, at a price of \$4.3803 per share, for gross proceeds of \$200.0 million and incurred \$0.4 million of issuance costs.

Upon issuance of each series of Preferred Stock, the Company assessed the embedded conversion and liquidation features of the securities and determined that such features did not require the Company to separately account for these features. The Company also concluded that no beneficial conversion feature existed on the issuance date of each series of Preferred Stock.

As of each balance sheet date, the Preferred Stock consisted of the following (in thousands, except share amounts):

December 31, 2020						
	Preferred Stock Authorized	Preferred Stock Issued and Outstanding	Carrying Value	Liquidation Preference	Conversion price per share	Common Stock Issuable Upon Conversion
Series A Preferred Stock	115,000,000	45,000,000	31,136	\$ 46,388	\$ 1.00	45,000,000
	115,000,000	45,000,000	31,136	\$ 46,388		45,000,000
December 31, 2021						
	Preferred Stock Authorized	Preferred Stock Issued and Outstanding	Carrying Value	Liquidation Preference	Conversion price per share	Common Stock Issuable Upon Conversion
Series A Preferred Stock	115,761,842	115,761,842	\$ 196,157	\$ 125,000	\$ 1.00	115,761,842
Series B Preferred Stock	45,658,957	45,658,957	199,643	210,814	\$ 4.3803	45,658,957
	161,420,799	161,420,799	\$ 395,800	\$ 335,814		161,420,799

The holders of the Preferred Stock have the following rights and preferences:

Voting

The holders of the Preferred Stock are entitled to vote, together with the holders of common stock, as a single class, on all matters submitted to the shareholders for a vote and are entitled to the number of votes equal to the number of common stock into which the Preferred Stock could convert on the record date for determination of shareholders entitled to vote. A majority vote of the holders of Preferred Stock is required to, among others, liquidate or dissolve the Company, amend the certificate of incorporation or bylaws, reclassify common stock or

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establish another class of capital stock, create shares that would rank senior to or authorize additional shares of Preferred Stock, declare a dividend or make a distribution, or change the authorized number of directors constituting the board of directors.

In addition, the holders of shares of Series A Preferred Stock, voting exclusively and as a separate class, are entitled to elect three directors of the Company. The holders of shares of common stock and any other class or series of voting stock (including the Series B Preferred Stock), exclusively and voting together as a single class, are entitled to elect the balance of the total number of directors of the Company.

Conversion

Each Preferred Stock is convertible into voting common stock, at any time, at the option of the holder, and without the payment of additional consideration, at the applicable conversion ratio then in effect. In addition, each share of Preferred Stock will be automatically converted into shares of common stock at the then-effective applicable conversion ratio upon either (i) the closing of a firm-commitment underwritten public offering of its common stock resulting in at least \$50.0 million of gross proceeds, net of underwriting discount and commissions, to the Company, or (ii) the date specified by vote or written consent of the holders of a majority in voting power of the outstanding shares of Preferred Stock, voting as a single class.

The conversion ratio of each class of Preferred Stock is determined by dividing the Original Issue Price of each class of Preferred Stock by the Conversion Price of each class. As of December 31, 2020, and 2021, the Conversion Price was \$1.00 per share for Series A Preferred Stock and \$4.3803 per share for Series B Preferred Stock, each subject to appropriate adjustment in the event of any share dividend, share split, combination or other similar recapitalization with respect to the Preferred Stock.

There shall be no adjustment in the conversion price of the Series A Preferred Stock as the result of the issuance or deemed issuance of additional shares of Company's common stock if the Company receives written notice from the holders of at least 65 percent of the then outstanding shares of Series A Preferred Stock agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of additional shares of the Company's common stock. There shall be no adjustment in the conversion price of the Series B Preferred Stock as the result of the issuance or deemed issuance of additional shares of the Company's common stock if the Company receives written notice from the holders of at least a majority of the then outstanding shares of Series B Preferred Stock agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such additional shares of the Company's common stock.

In the event that any holder of shares of Series A Preferred Stock is required to participate in a Series A Subsequent Closing pursuant to the purchase agreement does not purchase the aggregate number of subsequent closing shares, then each share of Series A Preferred Stock held by such holder shall automatically be converted into shares of common stock at a ratio of one share of common stock for every ten shares of Series A Preferred Stock held immediately prior to the consummation of such Series A Subsequent Closing.

Dividends

The holders of the Series A Preferred Stock are entitled to receive cumulative dividends at a rate of \$0.08 per share per annum of the Original Issue Price when, as and if declared by the board of directors (the "Series A Preferred Dividend"). The holders of the series B Preferred Stock are entitled to receive cumulative dividends at a rate of \$0.35 per share per annum of the Original Issue Price when, as and if declared by the board of directors (the "Series B Preferred Dividend", and together with Series A Preferred Dividend, the "Preferred Dividend").

The Company may not declare, pay or set aside any dividends on common shares of the Company unless the holders of Preferred Stock then outstanding first receive, or simultaneously receive, the Preferred Dividend on each outstanding Preferred Stock and a dividend on each outstanding Preferred Stock in an amount at least equal to the greater of (i) the amount of the aggregate Preferred Dividend then accrued on such share of Preferred Stock and not previously paid and (ii) (a) in the case of a dividend on common stock or any class or series that is convertible into common stock, that dividend per share of Preferred Stock as would equal to the product of (1) the dividend payable on each share of such class or series determined, as if all shares of such class or series had been converted into

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common stock and (2) the number of shares of common stock issuable upon conversion of a share of such series of Preferred Stock, in each case calculated on the record date for determination of the holders entitled to receive such dividend or the dividend payable on each share of such class or series determined, if applicable, as if all shares of such class or series had been converted into common shares or (b) in the case of a dividend on any class or series that is not convertible into common stock, at a rate per share of Preferred Stock determined by (1) dividing the amount of dividend payable on each share of such class or series of capital stock by the original issuance price of such class or series of capital stock and (2) multiplying such fraction by an amount equal to the Original Issue Price for such series of Preferred Stock. If the Company declares, pays, or sets aside, on the same date, a dividend on shares of more than one class or series of shares in the capital of the Company (other than the Preferred Stock), the dividend payable to the holders of Preferred Stock shall be calculated based upon the dividend on the class or series of shares in the capital of the Company that would result in the highest dividend on the Preferred Stock. Through December 31, 2020 and December 31, 2021, no cash dividends have been declared or paid.

Liquidation

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, or upon the occurrence of a Deemed Liquidation Event (as defined below), the holders of shares of Preferred Stock then outstanding are entitled, on a *pari passu* basis, to be paid out of the assets or funds of the Company available for distribution to stockholders before any payment is made to the holders of common stock. The holders of Preferred Stock are entitled to an amount per share equal to (i) in the case of Series A Preferred Stock, the Original Issue Price plus any accruing dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon, and (ii) in the case of Series B Preferred Stock, the greater of (a) the applicable Original Issue Price plus any accruing dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared, or not declared, but unpaid thereon (the "Series B Preference Amount") or (b) the amount that would have been payable had all shares of each series of Preferred Stock been converted into common stock immediately prior to such liquidation, dissolution, winding up or Deemed Liquidation Event (as defined below). After the payment in full of the Series A Preferred Stock preference amount and if applicable, the Series B Preference Amount, the remaining assets of the Company available for distribution to stockholders shall be distributed among the holders of Series A Preferred Stock and common stock on a pro rata basis provided that such distribution includes holders of Series B Preferred Stock if such distribution is greater than the Series B Preference Amount.

Unless at least the holders of a majority in voting power of the outstanding shares of Preferred Stock, elect otherwise, a Deemed Liquidation Event shall include a merger, consolidation, or share exchange (other than one in which stockholders of the Company own a majority by voting power of the outstanding shares of the surviving or acquiring corporation) or a sale, lease, transfer, exclusive license or other disposition of all or substantially all of the assets of the Company.

Redemption

As of December 31, 2020, at the written election of at least 65 percent of the holders of the outstanding shares of Series A Preferred Stock, voting together as a single class and on an as-converted to common stock basis, the shares of Series A Preferred Stock outstanding were redeemable, at any time on or after the fifth anniversary of issuance, in three equal annual installments commencing 60 days after receipt of the required vote. Shares of Series A Preferred Stock were redeemable in an amount equal to the Original Issue Price per share plus any accruing dividends accrued but unpaid thereon, whether or not declared.

In April 2021, in connection with the Series B Preferred Stock closing, the Company adopted an amended and restated certificate of incorporation, which removed the redemptions rights of the holders of Series A Preferred Stock. As a result of this amendment, Series A Preferred Stock was no longer redeemable at the option of the holders. The Company determined that the changes to the rights underlying the Series A Preferred Stock was not substantive and did not materially modify the rights and preferences of the holders of Series A Preferred Stock.

Prior to the amendment, the Company recognized changes in the redemption values of its Series A Preferred Stock over the period from the date of issuance to the earliest redemption date and adjusted the carrying value of the

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instrument to equal the redemption value at the redemption date. During the period from September 19, 2019 (inception) to December 31, 2019, the years ended December 31, 2020 and 2021, the Company recorded adjustments to increase the carrying values of the Series A Preferred Stock by an aggregate of \$0.3 million, \$1.6 million, and \$1.5 million, respectively, which resulted in an increase in redeemable convertible preferred stock by those amounts, offset by charges against additional paid-in-capital, if any, and then in the absence of additional paid-in capital the accretion is charged to the accumulated deficit.

The Company's articles of the corporation, as amended and restated, does not provide redemption rights to the holders of Series B Preferred Stock.

7. Common Stock

The voting, dividend and liquidation rights of the holders of the Company's common stock are subject to and qualified by the rights, powers and preferences of the holders of the Preferred Stock set forth above. Each share of common stock entitles the holder to one vote, together with the holders of the Preferred Stock, on all matters submitted to the stockholders for a vote. The holders of common stock are entitled to receive dividends, if any, as declared by the Company's board of directors, subject to the preferential dividend rights of Preferred Stock.

As of December 31, 2020, and 2021, the Company had reserved 127,257,387 and 181,602,866 shares, respectively, of common stock for the potential conversion of shares of Preferred Stock into common stock (including committed but unissued shares under future tranche obligations for the Series A Preferred Stock), common stock for the settlement of the Company's anti-dilution obligation and related party forward contract liability, the exercise of outstanding stock options for common stock, and the issuance of common stock options and restricted stock awards remaining available for grant under the 2019 Equity Incentive Plan.

8. Stock-Based Compensation

2019 Equity Incentive Plan

The Company's 2019 Stock Option and Grant Plan (the "2019 Plan") provides for the Company to grant incentive stock options ("ISO"), non-qualified stock options, unrestricted stock awards, restricted stock awards ("RSA") and other stock-based awards (collectively, the "Awards") to the officers, employees, consultants and other key persons of the Company. The 2019 Plan is administered by the board of directors, or at the discretion of the board of directors, by a committee of the board of directors. The exercise prices, vesting and other restrictions are determined at the discretion of the board of directors, or its committee if so delegated.

The total number of shares of common stock issuable under the 2019 Plan was 19,186,379. In April 2021, the Company's board of directors further increased the number of shares of common stock reserved for issuance under the plan from 19,186,379 shares to 35,943,372 shares. As of December 31, 2019, 2020, and 2021, there were 19,186,379 shares, 4,488,652 shares, and 7,479,092 shares, respectively, remaining available for future grants under the 2019 Plan. Shares of unused common stock underlying any Awards that are forfeited, canceled or reacquired by the Company prior to vesting will again be available for the grant of awards under the 2019 Plan.

The exercise price for stock options granted may not be less than the fair market value of the Company's common stock on the date of grant, as determined by the board of directors, or at least 110 percent of the fair market value of the Company's common stock on the date of grant in the case of an ISO granted to an employee who owns stock representing more than 10 percent of the voting power of all classes of stock ("10% Owner") as determined by the board of directors as of the date of grant. The Company's board of directors determines the fair market value of the Company's common stock, taking into consideration its most recently available valuation of common stock performed by third parties as well as additional factors which may have changed since the date of the most recent contemporaneous valuation through the date of grant. Unless otherwise provided, at the time of grant, the options granted pursuant to the 2019 Plan expire ten years from the date of grant, or five years from the date of grant in the case of an ISO that is granted to a 10% Owner. Awards typically vest over four years, with the first 25 percent vesting on the first anniversary of the vesting commencement date and the remainder vesting in 36 equal monthly installments thereafter, contingent on the recipient's continued employment, service or relationship with the Company.

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Stock Option Valuation

The fair value of each stock option grant is estimated on the grant date using the Black-Scholes option-pricing model. The Company historically has been a private company and lacks company-specific historical and implied volatility information. Therefore, it estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. For options with service-based vesting conditions, the expected term of the Company's options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. The expected dividend yield is based on the fact that the Company has never paid cash dividends on common stock and does not expect to pay any cash dividends in the foreseeable future.

The following table presents, on a weighted-average basis, the assumptions used in the Black-Scholes option-pricing model to determine the fair value of stock options granted:

	December 31, 2021
Fair value per share of underlying common stock	\$ 2.43
Risk-free interest rate	1.2 %
Expected term (in years)	6.0
Expected volatility	75.27 %
Expected dividend yield	— %

Performance-Based Stock Options

During the year ended December 31, 2021, the Company granted performance-based stock options to purchase 750,000 shares of common stock. The performance-based options commence vesting upon the achievement of (i) IND acceptance, (ii) consummation of the Company's IPO and (iii) a research milestone to be mutually agreed upon and vest over three equal installments. The performance-based vesting conditions for stock options to purchase 500,000 shares of common stock granted were established by the board of directors on October 27, 2021. The grant date of these awards for accounting purposes is the date on which the performance conditions of the award were established by the board of directors and all terms of the award were known by the recipient. As a result, the grant-date fair value of each such award for accounting purposes was determined on October 27, 2021 and such awards are reflected in the Company's total stock options outstanding as of December 31, 2021. The performance-based vesting condition for stock options to purchase 250,000 shares of common stock granted on October 27, 2021 has not been established by the Company's board of directors as of December 31, 2021 and therefore a grant date for accounting purposes has not been established for those stock options although such stock options are included in the Company's total stock options outstanding as of December 31, 2021. As of December 31, 2021, the Company concluded that the achievement of the IND acceptance and consummation of the Company's IPO performance conditions for such awards was not probable. Once the performance condition for the research milestone to be mutually agreed upon is established, and therefore establishing a grant date for accounting purposes, the Company will assess whether such performance condition is probable of achievement at each reporting date.

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Stock Options

The following table summarizes the Company's stock option activity since December 31, 2020:

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Balance at December 31, 2020	—	—	—	—
Granted	9,335,220	\$ 1.27	—	\$ —
Exercised	—	—	—	—
Forfeited	—	—	—	—
Balance at December 31, 2021	9,335,220	\$ 1.27	9.73	\$ 19,763
Options vested and exercisable at December 31, 2021	57,618	1.18	9.83	127
Options vested and expected to vest at December 31, 2021	9,335,220	\$ 1.27	9.73	\$ 19,763

All stock options granted have time-based vesting conditions and vest over a four year period. The weighted-average grant-date fair value of stock options granted for year ended December 31, 2021 was \$1.89 per share. As of December 31, 2021, there was \$14.2 million of total unrecognized compensation cost related to time-based unvested stock options the Company expects to recognize such amount over a remaining weighted-average period of 3.3 years. As of December 31, 2021, there was \$1.4 million of total unrecognized compensation cost related to performance-based stock options.

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the options and the fair value of the Company's common stock for those stock options that had an exercise price lower than the fair value of the Company's common stock.

Restricted Common Stock Awards

The Company awards restricted common stock to employees and non-employees under its 2019 Plan. The fair value of each share of restricted common stock is based on the market price of the Company's common stock on the date of grant.

For a period of up to six months from a grantee's termination, the Company has the right and option to repurchase unvested restricted common stock at the lower of (i) the original purchase price per share (\$0.00001) or (ii) the fair market value per share as of the date of the Company elects to exercise its repurchase right. In August 2021, the Company repurchased 56,667 unvested shares of the restricted common stock at a price of \$0.00001 per share, the original sale price, and the repurchased common shares were restored to the amount of unissued, authorized shares of common stock as of December 31, 2021.

During the period from September 13, 2019 (inception) to December 31, 2019, the years ended December 31, 2020 and 2021, the Company issued time-based restricted common stock and performance-based restricted common stock with vesting subject to certain performance conditions. Shares of restricted common stock granted to employees and directors are not deemed, for accounting purposes, to be outstanding until those shares have vested.

Each award type is discussed below.

Time-Based Restricted Common Stocks

The majority of the restricted common stock have time-based vesting conditions and vest over a four-year period, subject to the employee's continued employment with, or service to, the Company on such vesting date. Compensation expense is recognized on a straight-line basis over the vesting period.

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Time-Based Restricted Common Stock: Founder Shares

In September 2019, a co-founder of the Company was granted a total of 64,772,720 shares of restricted common stock, of which 10,795,453 shares are performance-based restricted common stock as described below. The remaining 53,977,267 shares are subject to service conditions. In February 2020, another co-founder of the Company was granted 2,159,621 shares of restricted common stock that are subject to service conditions. These awards vest over a four-year period and provide for accelerated vesting of a portion of the unvested awards, as determined in the award agreement, upon the initial or subsequent closings of the Series A Preferred Stock. Upon the grant date, the Company determined the initial and subsequent closings of the Series A Preferred Stock were probable to occur and recognized the compensation expense over the expected service period.

The following table summarizes the Company's time-based restricted common stock activity since December 31, 2020:

	Number of Shares	Weighted-Average Grant-Date Fair Value
Unvested restricted common stock at December 31, 2020	59,287,638	0.02
Issued	3,288,000	0.11
Vested	(28,939,657)	0.02
Repurchased	(56,667)	0.03
Unvested restricted common stock at December 31, 2021	<u>33,579,314</u>	<u>\$ 0.03</u>

The aggregate fair value of restricted common stock that vested during the period from September 13, 2019 (inception) to December 31, 2019 and the years ended December 31, 2020 and 2021 was \$0.1 million, \$0.1 million, and \$0.6 million, respectively.

As of December 31, 2021, there was \$0.8 million of total unrecognized compensation cost related to unvested time-based restricted common stock which the Company expects to recognize over a weighted-average period of 2.6 years.

Performance-Based Restricted Common Stock

The Company has also granted performance-based restricted common stock to certain executive officers and key persons of the Company with terms that allow the grantees to vest in a specific number of shares based upon the achievement of performance-based milestones. The Company granted 10,795,453 shares of performance-based restricted common stock to a co-founder of the Company in 2019, which will vest upon on the dosing of first patient in a Phase II or later-stage clinical trial or FDA approval of compound. The Company granted 2,159,621 and 1,200,000 shares of performance-based restricted common stock to certain executive officers in the years ended December 31, 2020 and 2021, respectively. These awards vest in three equal installments upon the achievements of (i) proof of concept in lead indication, (ii) IND acceptance and (iii) consummation of the Company's IPO.

Share-based compensation expense associated with the performance-based restricted common stock is recognized if the performance condition is considered probable of achievement using the Company's best estimates of the time to vesting for the achievement of the performance-based milestones. Each reporting period, the Company updates its assessment of the probability that the performance-based milestones will be achieved. As of December 31, 2020 and 2021, the Company has concluded it was not probable that these performance conditions related to performance-based restricted common stock would be achieved, and as a result no compensation expense related to the performance-based restricted common stock has been recorded. The fair value of the restricted common stock was based on the fair market value of the Company's common stock on the date of grant.

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The following table summarizes the Company's performance-based restricted common stock activity since December 31, 2020:

	Number of Shares	Weighted-Average Grant-Date Fair Value
Unvested restricted common stock at December 31, 2020	12,955,074	0.02
Issued	1,200,000	0.11
Vested	—	—
Repurchased	—	—
Unvested restricted common stock at December 31, 2021	<u>14,155,074</u>	<u>\$ 0.03</u>

As of December 31, 2021, there was \$0.4 million of total unrecognized compensation cost related to unvested performance-based restricted common stock.

Stock-Based Compensation

The following table below summarizes the classification of the Company's stock-based compensation expense related to stock options and restricted common stock awards in the consolidated statements of operations and comprehensive loss (in thousands):

	Period from September 13, (Inception) to December 31,		
	2019	Year Ended December 31,	
		2020	2021
General and administrative	\$ —	\$ 40	\$ 459
Research and development	156	351	1,287
	<u>\$ 156</u>	<u>\$ 391</u>	<u>\$ 1,746</u>

9. Income Taxes

For the period from September 13, 2019 (inception) to December 31, 2019, the years ended December 31, 2020 and 2021, the Company recorded a tax provision (benefit) of \$4,000, \$1.9 million and \$(0.5) million, respectively. The deferred provision for the year ended December 31, 2021 was attributable to the Company recording a valuation allowance on its deferred tax assets and liabilities due to the Company being in a net deferred tax asset position.

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The components of income tax provision are as follows (in thousands):

	Period from September 13, 2019 (Inception) to December 31,		Year Ended December 31,	
	2019	2020	2021	
Components of income tax provision				
Current provision:				
Federal	\$ —	\$ —	\$ —	
State	4	—	138	
Total current provision	4	—	138	
Deferred income tax provision (benefit):				
Federal	—	1,332	(928)	
State	—	535	304	
Total deferred income tax provision (benefit)	—	1,867	(624)	
Total provision for (benefit from) income taxes	\$ 4	\$ 1,867	\$ (486)	

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Period from September 13, 2019 (Inception) to December 31,		Year Ended December 31,	
	2019	2020	2021	
Rate Reconciliation				
Federal income tax expense at statutory rate	21.0 %	21.0 %	21.0 %	
State income taxes, net of federal benefit	5.3 %	(38.5)%	3.5 %	
Permanent differences	(2.9)%	(148.5)% ⁽¹⁾	(9.6)% ⁽¹⁾	
Tax credits	— %	9.5 %	0.7 %	
Other	(1.7)%	(0.3)%	(0.1)%	
Change in valuation allowance	(21.8)%	35.8 %	(15.2)%	
Effective income tax rate	(0.1)%	(121.0)%	0.3 %	

(1) Permanent differences for the years ended December 31, 2020 and 2021 related to the change in fair value of Series A Preferred Stock tranche rights

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Net deferred tax assets (liabilities) consisted of the following (in thousands):

	Year Ended December 31,	
	2020	2021
Deferred Tax Summary		
Deferred tax assets:		
U.S. and state net operating loss carryforwards	\$ 431	\$ 11,365
Tax credits	144	1,547
Depreciation and amortization	486	13,584
Accrual	138	639
Deferred Rent	13	—
Lease Liability	—	2,843
Total deferred tax assets	1,212	29,978
Deferred tax liabilities:		
Stock compensation	(76)	(136)
Mark to market adjustments	(34)	(34)
Unrealized gain/loss	(2,969)	(2,862)
Right of Use Asset	—	(2,936)
Total deferred tax liabilities	(3,079)	(5,968)
Valuation allowance	—	(25,253)
Net deferred tax assets (liabilities)	\$ (1,867)	\$ (1,243)

As of December 31, 2021, the Company had U.S. federal net operating loss carryforwards of \$41.8 million, which may be available to reduce future taxable income, which do not expire. In addition, as of December 31, 2021, the Company had state net operating loss carryforwards of \$40.9 million, which may be available to reduce future taxable income and expire at various times beginning in 2039. As of December 31, 2021, the Company also had federal and state research and development tax credit carryforwards of \$1.3 million and \$0.4 million, respectively, which may be available to reduce future tax liabilities and begin to expire in 2040 and 2035, respectively.

Utilization of the U.S. federal and state net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, and corresponding provisions of state law, due to certain ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income and tax liabilities. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50 percent over a three-year period. The Company has not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined by Section 382, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards would be subject to an annual limitation, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before their utilization. Further, until a study is completed by the Company and any limitation is known, no amounts are being presented as an uncertain tax position.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. Management has considered the Company's history of cumulative net losses incurred since inception, expectation of future losses and lack of other positive evidence. For the year ended December 31, 2019, the Company has concluded that it is more likely than not it will not realize the benefits of the net deferred tax assets. Accordingly, a full valuation allowance has been established against the net deferred tax assets. As of December 31,

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2020, the Company was in a deferred tax liability position due to the unrealized gain and therefore had released the valuation allowance and recorded an ending deferred tax liability balance. For the year ended December 31, 2021, the Company was in a net deferred tax asset position and therefore recorded a valuation allowance against the portion of its deferred tax assets that cannot be fully supported by the future reversal of existing deferred tax liabilities. The Company has determined that the indefinite nature of the deferred tax liability related to its unrealized gain on its related party short-term investment can only support 80 percent of the federal deferred tax assets and none of the state deferred tax assets, resulting in a net deferred tax liability position at December 31, 2021 of \$1.2 million.

For the year ended December 31, 2021, the valuation allowance increased primarily due to the increases in net operating loss carryforwards and research and development tax credit carryforwards. The changes in the valuation allowance were as follows (in thousands):

	Year Ended December 31,	
	2020	2021
Valuation allowance at beginning of year	\$ 552	\$ —
Increases (decreases) recorded to income tax provision	(552)	25,253
Valuation allowance at end of year	\$ —	\$ 25,253

The Company assesses the uncertainty in its income tax positions to determine whether a tax position of the Company is more likely than not to be sustained upon examination, including resolution of any related appeals or litigation processes, based on the technical merits of the position. For tax positions meeting the more-likely-than-not threshold, the tax amount recognized in the financial statements is reduced by the largest benefit that has a greater than 50 percent likelihood of being realized upon the ultimate settlement with the relevant taxing authority. As of December 31, 2021, the Company had not recorded any reserves for uncertain tax positions or related interest and penalties.

The Company files income tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. Since the Company is in a loss carryforward position, the Company is generally subject to examination by the U.S. federal, state and local income tax authorities for all years in which a loss carryforward is available. As of December 31, 2021, there were no pending tax examinations. The Company is open to future tax examination under statute from 2019 to the present.

10. Leases

21 Erie Street, Cambridge, Massachusetts Lease

In March 2020, the Company entered into an operating lease to sublease office and laboratory space located at 21 Erie Street, Cambridge, Massachusetts. The lease commenced in March 2020 and expires in March 2022. The lease agreement provides for escalating monthly rental payments with fixed costs for expenses and property taxes included in each payment. Upon the execution of the lease agreement the Company paid \$0.1 million for the rental fee for the last month of the term and \$0.1 million as a security deposit on the space, which is classified as other assets on the consolidated balance sheet as of December 31, 2020. Effective August 2020, the Company amended the sublease for additional office and laboratory space (the “1st Amendment”) with the lease commencement date in February 2021, and to extend the maturity of the sublease through June 2023. Upon the execution of the 1st Amendment, the Company paid a rental fee of \$0.3 million to lease additional office space in addition to the last month’s rent of the lease and \$0.3 million security deposit, which is classified as other assets on the consolidated balance sheet as of December 31, 2020. The lease was subsequently amended in October 2020 (the “2nd Amendment”) to shorten the maturity of the sublease through March 2023.

In May 2021, the Company amended (the “3rd Amendment”) the sublease for additional office and laboratory space (“Expanded Premises”). The lease commenced in December 2021 and expires in March 2023. Upon the execution of the 3rd Amendment the Company paid \$0.2 million for the rental fee for the last month of the term and \$0.2 million as a security deposit on the space, which is classified as other assets on the consolidated balance sheet

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as of December 31, 2021. In July 2021, the Company amended (the “4th Amendment”) the sublease for additional laboratory space (“Lab Space”) with a term of less than one year. The Lab Space lease is classified as a short-term lease and the Company will recognize lease payments as an expense on a straight-line basis over the term.

38 Sidney Street, Cambridge, Massachusetts Lease

In July 2021, the Company entered into a non-cancelable operating lease to sublease office space in Cambridge, Massachusetts. The lease commenced in August 2021 and expires in December 2024. The Company has a right to extend the lease for one additional six-month period at a market rate as determined by the sublandlord and agreed to by the Company. The option to extend the lease term is not included in the right-of-use asset and lease liability as it is not reasonably certain of being exercised. The lease requires the Company to share in prorated expenses and property taxes based on actual amounts incurred; those amounts are not fixed for future periods and, therefore, are not included in the measurement of the lease.

64 Sidney Street, Cambridge, Massachusetts Lease

In July 2021, the Company entered into a non-cancelable operating lease to sublease office space located at 64 Sidney Street, Cambridge, Massachusetts. The lease is expected to commence in April 2022 and expire in April 2025. The Company has a right to extend the lease for one additional six-month period at a market rate as determined by the sublandlord and agreed to by the Company. The lease requires the Company to share in prorated expenses and property taxes based on actual amounts incurred; those amounts are not fixed for future periods and, therefore, these amounts will not be included in the measurement of the lease.

60 First Street, Cambridge, Massachusetts Lease

In November 2021, the Company entered into a lease for office and laboratory space in Cambridge, Massachusetts. The Landlord is required to perform certain base building work prior to turning over the space to the Company to perform certain additional improvements, which is not currently expected until the second half of 2022. The lease will then commence when the Company obtains control over the space with rental payments commencing 11 months later. The initial non-cancelable term of the lease is ten years, and the Company has an option to extend the lease for an additional period of ten years with the rent during the option period being the then fair market rent. The Company secured the lease with a \$13.1 million security deposit, which was recorded as restricted cash on the consolidated balance sheet as of December 31, 2021.

Summary of lease costs recognized under ASC 842

The following tables contains a summary of the lease costs recognized under ASC 842 and other information pertaining to the Company’s operating leases for the year ended December 31, 2021.

The components of lease cost under ASC 842 were as follows (in thousands):

	Year Ended December 31, 2021
Operating lease cost	\$ 4,457
Variable lease cost	222
Short-term lease cost	432
Total lease cost	<u>\$ 5,111</u>

The weighted-average remaining lease term and discount rate were as follows:

Weighted average remaining lease term (in years)	1.8 years
Weighted average discount rate	2.10 %

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Future annual lease payments under non-cancelable operating leases as of December 31, 2021 were as follows (in thousands):

2022	7,404
2023	1,936
2024	1,262
Total future minimum lease payments	\$ 10,602
Less: imputed interest	(196)
	<u>\$ 10,406</u>

The lease for office space at 64 Sidney Street, Cambridge, Massachusetts, is expected to commence in April 2022 and the Company expects to pay approximately \$9.8 million in total lease payments over the lease term. As the lease has not commenced as of December 31, 2021, the operating lease liabilities on the consolidated balance sheet as of December 31, 2021 and the table above excludes any amounts related to this lease.

The lease for office space at 60 First Street, Cambridge, Massachusetts has not yet commenced and the expected date for which the Company obtains control of the space is currently uncertain but not expected to occur until the second half of 2022. The Company currently expects rent to commence 11 months after taking possession of the space, with full occupancy expected in 2024, for which the Company will pay approximately \$208.7 million over the ten-year lease term. As the lease has not commenced as of December 31, 2021, the operating lease liabilities on the consolidated balance sheet as of December 31, 2021 and the table above excludes any amounts related to this lease.

Disclosures under ASC 840

The Company did not enter into any lease agreements for the period from September 13, 2019 (inception) to December 31, 2019.

The Company recognizes rent expense on a straight-line basis over the respective lease period. During the year ended December 31, 2020, rent expense was \$1.0 million.

Future minimum rental commitments to be paid by the Company at December 31, 2020 is as follows (in thousands):

Year Ended December 31:	
2021	\$ 2,669
2022	111
Total future minimum lease payments	<u>\$ 2,780</u>

11. License and Collaboration Agreements

License Agreement with Broad Institute

In September 2019, the Company entered into a license agreement with Broad Institute, Inc. (“Broad Institute”), and in May 2020 and February 2021, the Company entered into amendments to the license agreement, for certain patents related to delivery or targeting of DNA (the “Broad License Agreement”). Under the Broad License Agreement, Broad Institute granted the Company (i) an exclusive, worldwide license under the licensed patent rights solely to offer for sale, sell, have sold and import products covered by such licensed patent rights, or licensed products, solely for use within the Prime Broad Field (subject to certain specified limitations and exclusions with respect to certain applications), (ii) a non-exclusive, worldwide license under the licensed patent rights solely to make, have made, offer for sale, sell, have sold, and import licensed products solely for use in the Prime Broad Field, (iii) a non-exclusive, worldwide license under the licensed patent rights solely to make, have made, offer for sale, sell, have sold and import other products that are enabled by (a) the licensed patent rights or (b) the use of certain materials transferred to the Company by Broad Institute, solely for the prevention or treatment of human

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diseases and (iv) a non-exclusive, worldwide license solely for internal research. Further, with respect to DNA delivery or targeting applications covered by the licensed patent rights, the exclusive license granted to the Company by Broad Institute is limited only to “prime editor” products and specifically excludes applications relating to the production or processing of small or large molecules, including for the prevention or treatment of human disease. Under the Broad License Agreement, the Company also has the right to grant sublicenses to its affiliates and third parties, subject to certain requirements. The Company is obligated to use commercially reasonable efforts to develop, seek marketing approval for, and commercialize licensed products in the field. As partial consideration for the license, the Company made a upfront payment of \$0.5 million to Broad Institute.

Concurrently with the Broad License Agreement, the Company entered into a subscription agreement with Broad Institute (the “Broad Subscription Agreement”). Under the Broad Subscription Agreement, as additional consideration for the license, the Company issued 1,938,429 shares of common stock, with a fair value of \$39,000, to Broad Institute, representing 5.0 percent of its then outstanding capital stock on a fully-diluted basis. The Broad Subscription Agreement also obligated the Company to issue additional shares of common stock to Broad Institute without additional consideration to maintain Broad Institute’s ownership of the Company at 5.0 percent on a fully-diluted basis, if at any time prior to the achievement of an equity financing up to \$100.0 million, the Company issues additional securities that would cause Broad Institute shares of common stock to be less than 5.0 percent of the Company’s outstanding capital stock on a fully-diluted basis (the “Anti-Dilution Obligation”). In connection with the fourth Series A Preferred Stock closing, the Anti-Dilution Obligation was settled in full (see Note 3).

The Company also granted certain preemptive rights to Broad Institute, under which if after the Company has reached the financing threshold of \$100.0 million, the Company proposes to offer or sell any new securities, then Broad Institute shall have the right to purchase from the Company the portion of such new securities that would allow Broad Institute to maintain its 5.0 percent ownership in the Company. The Company determined that the Anti-Dilution Obligation was required to be recorded as a liability because it was a freestanding instrument that would require the Company to transfer assets to settle the obligation and it is indexed to an obligation to contingently redeem the Company’s equity shares. Accordingly, the Company recorded a liability of \$0.2 million equal to the Anti-Dilution Obligation fair value upon entering into the Broad Subscription Agreement. In April 2021, the Company exceeded the financing threshold with the fourth issuance of the Series A Preferred Stock (Note 6). In connection with the fourth closing of Series A Preferred Stock, Broad Institute purchased an additional 761,844 shares of Series A preferred stock, at a price of \$1.00 per share for gross proceeds of \$0.8 million, to maintain its 5.0 percent ownership in the Company. At the time of purchase, the Company’s Series A Preferred Stock had a fair value of \$2.31 per share. Therefore, the Company recorded the difference between the purchase price and the fair value per share as additional paid-in capital as it represented a transaction with a stockholder due to Broad Institute’s existing ownership of the Company’s common stock.

Under the Broad License Agreement, the Company is also required to use commercially reasonable efforts to develop licensed products in the Prime Broad Field in accordance with a development plan that the Company prepared and submitted to Broad Institute. The Company is also obligated to pay Broad Institute an annual license maintenance fee ranging from the low to mid five-figures dollar amount through the end of 2020 to a low six-figures dollar amount beginning in 2021. In addition, the Company is obligated to reimburse Broad Institute for its documented, out-of-pocket costs incurred while prosecuting and maintaining its licensed patent rights.

Broad Institute is also entitled to receive clinical and regulatory milestone payments up to a total of \$20.0 million per licensed product, depending on the patient population to be treated by the licensed product achieving the applicable milestone. If the Company undergoes a change of control at any time during the term of the Broad License Agreement, certain of the clinical and regulatory milestone payments will increase by a specified percentage. Broad Institute is also entitled to sales-based milestone payments up to a total of \$54.0 million per licensed product, depending on the patient population to be treated by the licensed product achieving the applicable milestone. Broad Institute is entitled to lower payments to the extent the clinical and regulatory milestones or sales-based milestones are achieved by enabled products, rather than licensed products.

Broad Institute is entitled to receive mid-single digit percentage royalties on net sales of licensed products, and low single-digit percentage royalties of enabled products. Royalties payable to Broad Institute are subject to customary offsets and reductions with respect to a product in a given country, to a floor. Royalties are due on a

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country-by-country and product-by-product basis beginning upon the first commercial sale of each product and ending on the latest of (i) the expiration of the last valid claim of a patent covering such product in such country, (ii) the period of regulatory exclusivity associated with such product in such country or (iii) 10 years after the first commercial sale of such product in such.

Unless earlier terminated, the Broad License Agreement will remain in effect until the later of (i) the last to expire valid claim of an issued patent or pending patent application within the licensed patent rights covering the Company's licensed products or (ii) the expiration of the last royalty term for a licensed product in a country. The Company can terminate the Broad License Agreement for convenience after a certain period of time following prior written notice to Broad Institute. Each party may terminate the Broad License Agreement for the other party's uncured material breach within a specified time period following notice of such breach. Broad Institute may also immediately terminate the Broad License Agreement (i) to the extent the Company (or its affiliates or sublicensees) challenges a licensed patent right, (ii) upon the Company's bankruptcy or insolvency or (iii) if the Company fails to procure and maintain insurance.

The Company determined that the Broad License Agreement represented an asset acquisition of IPR&D assets with no alternative future use and recognized the aggregate acquisition cost as acquired IPR&D within research and development expense in the consolidated statement of operations and comprehensive loss. The acquisition did not qualify as a business combination as the acquisition did not include both an input and substantive processes, including an assembled workforce, that together contribute to the ability to create outputs. For the period from September 13, 2019 (inception) to December 31, 2019, the Company recorded \$0.7 million of research and development expense related to the acquired IPR&D from Broad Institute, which consisted of the initial upfront payment of \$0.5 million, the \$39,000 fair value of common stock issued to Broad Institute and the initial fair value of the Anti-Dilution Obligation of \$0.2 million. For the period from September 13, 2019 (inception) to December 31, 2019, and for the years ended December 31, 2020 and 2021, the Company recognized \$0.5 million, \$0.1 million, and \$0.3 million, respectively, of research and development expense (in addition to the IPR&D above) related to annual license maintenance fees. For the period from September 13, 2019 (inception) to December 31, 2019, and for the years ended December 31, 2020 and 2021, the Company recognized \$0.4 million, \$0.6 million and \$1.3 million, respectively, of general and administrative expenses related to its payment obligation with respect to out-of-pocket patent costs incurred by Broad Institute under the Broad License Agreement. As of December 31, 2019, 2020 and 2021, no milestone payments or royalties under the agreement had been paid or were due, and no specified milestones were deemed to be probable of achievement.

In May 2020 and February 2021, the Company amended the Broad License Agreement, in each case, to update or include additional licensed patent rights. Under the February 2021 amendment, as partial consideration for the addition of licensed patent rights relating to prime editing improvements, the Company paid Broad Institute an amendment fee of \$0.1 million.

Option Agreement with Broad Institute

In May 2021, the Company entered into an exclusive option agreement with Broad Institute (the "Broad Option Agreement), pursuant to which, Broad Institute granted to the Company an exclusive option to negotiate an amendment to the Broad License Agreement to include certain additional patent rights relating to prime editing improvements to the Company's license thereunder (subject to certain specific limitations and exclusions with respect to certain applications) (the "Exclusive Option"). In connection with the Broad Option Agreement, Broad Institute also granted the Company, during the option period, a limited, non-exclusive license under the new patent rights solely for research purposes to evaluate whether to exercise its option (subject to certain specified exceptions). The Company paid a upfront fee of \$0.1 million to Broad Institute under the agreement upon execution of the agreement.

The Company may terminate the Broad Option Agreement for convenience by giving advance written notice of termination to Broad Institute. Broad Institute has the right to terminate the agreement if the Company (i) fails to pay its obligations, (ii) materially breaches the agreement and fails to cure such nonpayment or breach within specified cure periods or (iii) becomes insolvent.

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The Company's option expires in November 2022, unless it mutually agrees in writing with Broad Institute to extend such expiration date. As of December 31, 2021, the Company has not exercised its Exclusive Option.

Other than the expense for the upfront payment made in May 2021 of \$0.1 million, the Company did not recognize any research and development expense for the period from September 13, 2019 (inception) to December 31, 2019, and for the years ended December 31, 2020 and 2021 in connection with its payment obligations under the Broad Option Agreement.

Broad Pledge

In February 2021, the Company committed to donate \$5.0 million to Broad Institute and Harvard University annually for 14 years, commencing in 2021 (the "Pledge"). The Pledge is intended to be used for research and development related to new genome editing technologies, for example Prime Editing, improve on existing genome-editing technologies, identify delivery mechanisms for these technologies and apply these technologies to the understanding and treatment of rare genetic diseases. The Company can terminate the Pledge at its discretion, subject to providing one year of funding from the date of termination.

The Company accounts for this Pledge as research and development expenses as it has access to certain data generated as a result of the Pledge. For the year ended December 31, 2021, the Company recognized \$5.0 million of research and development expense in connection with the Pledge.

Related Party Beam Collaboration Agreement

In September 2019, the Company entered into a collaboration agreement with Beam (the "Beam Collaboration Agreement") to collaborate on the research, development, manufacture and commercialization of certain prime editing products within a specified field and provide each other with access and licenses to certain proprietary technology to advance the other's progress. Under the Beam Collaboration Agreement, each party agreed to provide each other with access to, and licenses under, certain technology, know-how and patent rights controlled by each party for a limited number of years after the effective date, known as the initial term, and certain improvements thereto. Under the Beam Collaboration Agreement, the Company granted Beam an exclusive (even as to the Company and its affiliates), worldwide license under (i) certain prime editing technology, know-how and patent rights that the Company controls during the initial term, and improvements thereto that the Company controls for a specified number of years following the initial term, and (ii) the Company's interest in certain jointly-owned collaboration technology, in each case, solely to develop, make, have made, use, offer for sale, sell, import and commercialize licensed products only in the Beam field. Beam also granted to the Company certain non-exclusive, worldwide licenses under certain technology, know-how and patent rights, including under certain CRISPR or delivery-related technology, know-how and patent rights, that it controls during the initial term, and improvements thereto that Beam controls for a specified number of years following the initial term, solely to develop, make, have made, use, offer for sale, sell, import and commercialize products only in the Company's field. As partial consideration for the Beam Collaboration Agreement, Beam agreed to pay the Company, upon its election to continue its collaboration with the Company on the first anniversary of the Beam Collaboration Agreement, \$5.0 million worth of its own shares of common stock.

Before and within a short period of time after the filing of an IND for a development candidate being developed under the Beam Collaboration Agreement, Beam has the option to designate up to a mid-single digit number of licensed products for which the Company is not permitted to exercise the profit share right (described below) (the "Beam Option"). Under the Beam Collaboration Agreement, a licensed product for which the Company has not exercised its profit share option or for which Beam has exercised the Beam Option is collectively referred to as "protected product." Beam must exercise its option within 30 days following the filing of an IND for such product. Unless the Company exercises its profit sharing option for a licensed product, Beam is solely responsible for the development and commercialization of licensed products in the Beam field under the Beam Collaboration Agreement. If Beam exercises its option for a protected product, Beam will owe Prime a payment of \$5.0 million if the product is developed for non-sickle cell disease or \$10.0 million if the product is developed for sickle cell disease.

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On a licensed product-by-licensed product basis, the Company has the right to elect to share equally with Beam in the profits and losses in the United States for Beam's licensed products. The Company may exercise such right for each licensed product within a specified period of time. Any such licensed product for which the Company exercises its right is referred to as a collaboration product. If the Company exercises such right, the Company agrees to share equally in the costs, profits and losses of each such collaboration product in the United States, rather than receiving milestones and royalties based on development and sales thereof by Beam in the United States. For clarity, the Company is still entitled to receive milestones and royalties on the development and sale of each such collaboration product outside the United States. The Company also has the right to elect, within a specified time period, at least one year prior to the expected filing of an NDA, to co-promote with Beam each collaboration product in the United States, in addition to sharing in the profits and losses. To the extent the Company exercises its co-promote option with respect to a given collaboration product, the Company and Beam must use commercially reasonable efforts to commercialize such collaboration product, in each case, in the Beam field in the major markets in which marketing authorization has been obtained. After the Company has exercised its right to profit share on a collaboration product, the Company is able to, at any time during the term of the Beam Collaboration Agreement, on a collaboration product-by-collaboration product basis, opt-out of the profit and loss share and co-promotion activities with respect to any collaboration product with prior written notice to Beam within a certain time period.

The Company is entitled to receive development milestone payments from Beam on Beam's development of protected products (which, for clarity, includes any licensed product for which the Company has not exercised its profit share option) and collaboration products. For protected products, the Company is entitled to receive up to a total of \$35.5 million on a protected product-by-protected product basis based on Beam's development of such protected product and, for collaboration products, up to a total of \$17.8 million on a collaboration product-by-collaboration product basis based on Beam's development of such collaboration product outside of the United States, in each case, with such amounts lowered if such licensed product achieves a given milestone for use in treating an orphan disease. The Company is also entitled to receive sales-based milestone payments from Beam based on net sales of licensed products. For protected products, the Company is entitled to receive up to a total of \$84.5 million on a protected product-by-protected product basis based on net sales of such protected product worldwide, and, for collaboration products, up to a total of \$42.3 million on a collaboration product-by-collaboration product basis based on net sales of collaboration products outside of the United States.

The sickle cell disease product partnered with Beam is a licensed product under the Beam Collaboration Agreement. Beam has not designated this product as a protected product and the Company has not received any development or sales-based milestones with respect to Beam's exploitation thereof.

Beam is obligated to pay the Company tiered royalties ranging from a high-single digit percentage to a low double-digit percentage, but less than teens on net sales of protected products worldwide on a protected product-by-protected product basis and net sales of collaboration products outside of the United States on a collaboration product-by-collaboration product basis. The Company's royalties are subject to customary offsets and reductions, to a floor that takes into account any royalties the Company is obligated to pay to its third-party licensors, including Broad Institute. In addition, certain of the rights licensed under the Beam Collaboration Agreement are sublicensed from third parties, and Beam agrees to reimburse the Company for certain payments the Company is required to make to its third-party licensors attributable to Beam's exercise of any sublicense the Company grants to Beam, including payments it makes to Broad Institute under the Broad License Agreement.

If the Company develops a product that is covered by the technology, know-how or patent rights that Beam licenses to the Company under the Beam Collaboration Agreement, which it refers to as a Prime product, the Company is obligated to pay to Beam a low single digit royalty on its worldwide net sales of such any product on a Prime product-by-Prime product and country-by-country basis, subject to certain customary reductions, to a floor.

Unless earlier terminated in accordance with its terms, the Beam Collaboration Agreement will expire on the later of (a) expiration of the last royalty term for a product on which a party is obligated to pay royalties to the other party or (b) with respect to any collaboration product, the date on which neither party is developing or commercializing any such collaboration product in the United States.

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After expiration of the initial term, Beam can terminate the Beam Collaboration Agreement for convenience in its entirety, or on a licensed product-by-licensed product or subfield-by-subfield basis, with prior written notice to the Company. Each party may terminate the Beam Collaboration Agreement for (a) the other party's uncured material breach, (b) upon the insolvency or bankruptcy of the other party or (c) immediately to the extent the other party (or its affiliates or sublicensees) challenges a patent right licensed to such party.

In connection with the Beam Collaboration Agreement, concurrently in September 2019, Beam and the Company also entered into a mutual subscription agreement ("Beam Mutual Subscription Agreement"). Under the Beam Mutual Subscription Agreement, if Beam elected to continue its collaboration with the Company, on the first anniversary of the agreement the Company was obligated to grant Beam 5,000,000 shares of the Company's common stock which represented 5.0 percent of the 100 million shares of Series A Preferred Stock that the Company had issued or committed to issue as of the effective date of the Beam Mutual Subscription Agreement. In September 2020, Beam elected to continue its collaboration with the Company and, in October 2020, as required by the terms under the Beam Mutual Subscription Agreement, the Company issued 5,000,000 shares of the Company's common stock to Beam with a fair value of \$0.2 million. For the year ended December 31, 2020, the Company recognized \$5.2 million of collaboration revenue, which represents the net of the fair value of Beam's common stock of \$5.4 million as of the first anniversary of the Beam Collaboration Agreement, which was when the Company was entitled to the Beam shares, offset by the fair value of \$0.2 million related to the 5,000,000 shares of the Company's common stock required to be issued to Beam, which reflect a payment to the Company's customer.

The Company concluded that the Beam Collaboration Agreement and the Beam Mutual Subscription Agreement should be combined and treated as a single arrangement for accounting purposes as the agreements were entered into contemporaneously and in contemplation of one another. The Company determined that the combined agreements are accounted for under Topic 606, *Revenue recognition*. The Company identified the following performance obligations: (i) exclusive, worldwide license to certain Prime patents, (ii) non-exclusive, worldwide licenses to CRISPR technology and (iii) joint research committee participation. The Company also evaluated whether the Beam Option and the Company's right to elect collaboration products in the Beam Collaboration Agreement represented material rights that would give rise to a performance obligation and concluded that neither the Beam Option nor the Company's right to elect collaboration products convey a material right to Beam and therefore are not considered separate performance obligations within the Beam Collaboration Agreement. There have been no protected product or collaboration products to date. Under the Beam Collaboration Agreement, the Company is eligible to receive certain milestones and royalties regardless of whether any options are exercised, which are considered variable consideration. At each reporting period, the Company evaluates whether milestones are considered probable of being reached and, to the extent that a significant reversal would not occur in future periods, estimates the amount to be included in the transaction price. During the years ended December 31, 2020 and 2021, the Company did not receive any milestone payments and all variable consideration related to the Beam Collaboration Agreement remained fully constrained.

The Company assessed the above promises and determined that the exclusive license for certain Prime products and non-exclusive licenses to CRISPR technology represent performance obligations within the scope of Topic 606. The exclusive license for certain Prime products and non-exclusive licenses to CRISPR technology are considered functional intellectual property and distinct from other promises under the contract. The exclusive license for certain Prime products and non-exclusive licenses to CRISPR technology are considered functional licenses that are distinct in the context of the Beam Collaboration Agreement as Beam can benefit from the licenses on its own or together with other readily available resources. As the exclusive license for certain Prime products and non-exclusive licenses to CRISPR technology are delivered at the same time, they are considered one performance obligation at contract inception. The joint research committee performance promise is immaterial in the context of the contract.

The Company determined the transaction price under Topic 606 at the inception of the Beam Collaboration Agreement to be \$5.2 million, consisting of the value of the Beam equity investment under the Beam Mutual Subscription Agreement, when measured at fair value, less the value of the Prime shares issued to Beam of \$0.2 million. The shares Prime issued to Beam represents a payment to a customer and is therefore a reduction of the transaction price.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The Company recognizes revenue for the license performance obligations at a point in time, that is upon the first anniversary of the effective date when Beam elected to continue its collaboration with the Company. As control of these licenses was transferred on this date, Beam could begin to use and benefit from the licenses, the Company recognized \$5.2 million of license revenue during the year ended December 31, 2020 under the Beam Collaboration Agreement. There was no revenue recognized during the year ended December 31, 2021.

In September 2020, on the first anniversary of the Beam Collaboration Agreement, the Company was entitled to receive 200,307 shares of Beam common stock, which had a fair value of \$5.4 million and which was recorded as related party collaboration revenue in the consolidated statements of operations and comprehensive loss at that time. In October 2020, Beam issued the shares of common stock to the Company at which time the common shares had a fair value of \$5.5 million and which the Company recorded as related party short-term investments on the consolidated balance sheet. For the year ended December 31, 2020, the Company recognized a net gain of \$0.1 million for the change in fair value of the Beam shares the Company was entitled to receive, which was recorded to other income (expense), net in the consolidated statements of operations and comprehensive loss. There was no change in fair value of \$0.2 million related to the 5,000,000 shares of common stock issued by the Company to Beam, between the first anniversary date of the Beam Collaboration Agreement, in September 2020 and the issuance date of the shares of common stock in October 2020.

For the years ended December 31, 2020 and 2021, the Company recognized an unrealized gain (loss) of \$10.9 million and \$(0.4) million, respectively, for the change in fair value of the related party short-term investment consisting of Beam shares, which was recorded to other income (expense), net in the consolidated statements of operations and comprehensive loss.

Additionally, in September 2019, in connection with the Beam Collaboration Agreement, the Company executed a letter agreement, as amended, to receive certain interim management and startup services from Beam through March 2021. The Company is obligated to reimburse Beam for out-of-pocket costs incurred in connection with performing the services. The Company concluded this does not represent a payment to a customer because it is a distinct service at standalone selling price. For the years ended December 31, 2020 and 2021, the Company paid \$0.1 million and \$0.1 million, respectively, for such services. As of December 31, 2020, there was \$30,000 included within accounts payable and no amounts as of December 31, 2021.

Beam Sub-license Agreement

On January 25, 2021, the Company entered into a sub-license agreement with Beam (the "Beam Sub-license Agreement"), under which Beam granted to the Company a non-exclusive, non-transferable, fully paid-up and royalty-free license to certain intellectual property that Beam has licensed from the Ohio State Innovation Foundation (the "OSIF") for internal research purposes only. The patent rights and other proprietary rights in or related to the patent rights are and will remain the exclusive property of the OSIF. There was no accounting impact of this amendment.

Research Collaboration, Option and License Agreement with Myeloid

In December 2021, the Company entered into a research collaboration and exclusive option agreement with Myeloid (the "Myeloid Agreement"). Under the Myeloid Agreement, the Company collaborates with Myeloid, a related party, on the research and development of LINE-1 retrotransposon technology. In connection with the Myeloid Agreement, the Company also entered into a subscription agreement with Myeloid under which the Company was obligated to issue an aggregate of 3,424,422 shares of its common stock as additional consideration for the license.

Myeloid grants to the Company an exclusive option, exercisable during the research term and for 60 days thereafter, to obtain ownership of certain patent rights and know-how owned by Myeloid that relate to LINE-1 retrotransposon technology. If the Company exercises its option, in addition to assigning the Company ownership of the applicable patent rights and know-how, Myeloid also agrees to grant the Company certain exclusive and non-exclusive licenses, including to certain improvements and other enabling technology.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Following the exercise of the Company's option, the Company agrees to grant Myeloid, in addition to certain other licenses, an exclusive, worldwide license under the assigned patent rights and know-how to develop and commercialize products in the field of myeloid cells and myeloid cell engineering, or the Myeloid Field. As of December 31, 2021, the Company has not exercised its option.

Upon entering into the Myeloid Agreement, Myeloid was entitled to receive an upfront payment of \$30.0 million in cash and an aggregate of 3,424,422 shares of the Company's common stock, with a then fair value of \$12.0 million, both of which Myeloid received in January 2022. If the research agreement meets its goals, then (i) during the research term, Myeloid is entitled to cash payments of up to \$35.0 million in the aggregate upon the achievement of certain milestones reflecting the technology's development; and (ii) if the Company exercises its option, the Company agrees to pay to Myeloid an option exercise fee of \$80.0 million in cash, and shares of the Company's common stock with a then fair value of \$30.0 million. Additionally, if the research collaboration meets its goal and the Company exercises its option, and the Company is able to proceed with the development and commercialization of a product that is covered by (a) the patent rights or know-how subject to the Company's option or (b) the patent rights or know-how developed by one or both of the parties during the research term related to LINE-1 retrotransposon technology, or, collectively, a Prime Product, Myeloid would be eligible to receive, for the first five Prime Products, development and regulatory milestone payments of up to \$120.0 million on a Prime Product-by-Prime Product basis and sales-based milestone payments of up to \$210.0 million on a Prime Product-by-Prime Product basis.

Myeloid is also eligible to receive tiered low to mid single-digit percentage royalties on the Company's annual aggregate global net sales of Prime Products on a Prime Product-by-Prime Product and country-by-country basis, subject to customary offsets and reductions to a floor. On a country-by-country and Prime Product-by-Prime Product basis, the period during which royalties will be paid will continue until the latest of (i) the expiration date of the last to expire valid claim of an issued patent or pending patent application within the patent rights subject to the Company's option or the patent rights developed by one or both of the parties during the research term related to LINE-1 retrotransposon technology, in each case, covering the applicable Prime Product, (ii) loss of regulatory exclusivity for such Prime Product in such country, or (iii) ten (10) years after the first commercial sale of such Prime Product in such country.

Following the exercise of the Company's option and for a period of two years thereafter, Myeloid will have the right to select up to three targets, subject to certain exclusions, for the development and commercialization of products directed at such targets in all fields and the Company will be eligible to receive the development, regulatory and sales-based milestone payments and royalty payments as set forth above from Myeloid with respect to such products.

Unless earlier terminated based on customary termination rights, the Myeloid Agreement will continue on a Prime Product-by-Prime Product and country-by-country basis until the expiration of the royalty term for such Prime Product in such country. If the Company exercises its option, neither party will have the right to terminate the Myeloid Agreement for any reason.

The Company determined that the Myeloid Collaboration Agreement represented an asset acquisition of IPR&D assets with no alternative future use and recognized the aggregate acquisition cost as acquired IPR&D within research and development expense in the consolidated statement of operations and comprehensive loss. The acquisition did not qualify as a business combination as the acquisition did not include both an input and substantive processes, including an assembled workforce, that together contribute to the ability to create outputs. For the year ended December 31, 2021, the Company recorded \$42.0 million of research and development expense related to the acquired IPR&D from Myeloid, which consisted of the initial upfront payment of \$30.0 million and the \$12.0 million fair value of common stock to be issued to Myeloid. As of December 31, 2021, no milestone payments under the agreement had been paid or were due, and no specified milestones were deemed to be probable of achievement.

In connection with the Company's obligation to issue Myeloid shares of its common stock, the Company determined the fair value of the common stock to be issued based, in part, on the results obtained from a third-party valuation of the Company's equity securities prepared as of December 24, 2021. As the Company had not issued the shares to Myeloid as of December 31, 2021, the Company recorded a \$12.0 million related party forward contract

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

liability based on the common stock fair value as of the date of the Myeloid Subscription Agreement. Further, there was no change in fair value of the shares from the date of the Myeloid Subscription Agreement to December 31, 2021. As such, the Company will recognize any future changes in fair value of the shares as other income (expense) through the date such shares are issued to Myeloid. In addition, as the upfront payment was not made as of December 31, 2021, the Company recorded the \$30.0 million payment obligation within accrued expenses and other current liabilities on its consolidated balance sheet as of December 31, 2021. In January 2022, the Company made the \$30.0 million payment and also issued the shares of its common stock to Myeloid.

12. Commitments and Contingencies***Leases***

The Company's commitments under its operating leases are described in Note 10.

License and Collaboration Agreements

The Company entered into various license and collaboration agreements under which it is obligated to make fixed and contingent payments (see Note 11).

401(k) Plan

The Company maintains a defined-contribution plan under Section 401(k) of the Internal Revenue Code of 1986 (the "401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. Matching contributions to the 401(k) Plan may be made at the discretion of management. The Company is not required to make, and to date has not made, any matching contributions to the 401(k) Plan through December 31, 2020 or 2021.

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with all board of directors that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company is not aware of any indemnification arrangements that could have a material effect on its financial position, results of operations or cash flows, and it has not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2020 and 2021.

Legal Proceedings

From time to time, the Company may become involved in legal proceedings or other litigation relating to claims arising in the ordinary course of business. The Company accrues a liability for such matters when it is probable that future expenditures will be made and that such expenditures can be reasonably estimated. Significant judgment is required to determine both probability and estimated exposure amount. Legal fees and other costs associated with such proceedings are expensed as incurred. As of December 31, 2020 and 2021, the Company was not a party to any material legal proceedings or claims.

13. Net Loss per Share

The Company calculated basic and diluted net loss per share attributable to common stockholders using the two-class method required for companies with participating securities. The Company considers Series A Preferred Stock and Series B Preferred Stock to be participating securities as the holders are entitled to receive cumulative dividends as well as residuals in liquidation.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Under the two-class method, basic net loss per share available to common shareholders was calculated by dividing the net loss available to common shareholders by the weighted-average number of shares of common stock outstanding during the period. The net loss available to common shareholders was not allocated to the Series A Preferred Stock and Series B Preferred Stock as the holders of preferred stock did not have a contractual obligation to share in losses. Diluted net loss per share available to common shareholders was computed by giving effect to all potentially dilutive common stock equivalents outstanding for the period. For purposes of this calculation, preferred stock, unvested restricted stock and stock options to purchase common stock were considered common stock equivalents but had been excluded from the calculation of diluted net loss per share available to common shareholders as their effect was anti-dilutive. In periods in which the Company reports a net loss available to common shareholders, diluted net loss per share available to common shareholders is the same as basic net loss per share available to common shareholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

Net Loss Per Share

	Period from September 13, 2019 (Inception) to December 31, 2019			Year Ended December 31,		
	2019	2020	2021	2020	2021	
Numerator:						
Net loss	\$ (2,529)	\$ (3,410)	\$ (165,367)			
Accretion of preferred stock to redemption value	(265)	(1,645)	(1,468)			
Cumulative dividend on preferred stock	—	—	(17,284)			
Net loss attributable to common stockholders	\$ (2,794)	\$ (5,055)	\$ (184,119)			
Denominator:						
Weighted-average common shares outstanding, basic and diluted	4,622,576	8,206,374	40,332,091			
Net loss per share attributable to common stockholders, basic and diluted	\$ (0.60)	\$ (0.62)	\$ (4.57)			

For accounting purposes, the computation of basic net loss per share attributable to common stockholders, the amount of weighted-average common shares outstanding includes the impact of the 3,424,422 shares the Company was obligated to issue to Myeloid as of December 24, 2021 (see Note 11) and excludes all shares of unvested restricted common stock as such shares are not considered outstanding (see Note 8).

	Period from September 13, 2019 (Inception) to December 31, 2019			Year Ended December 31,		
	2019	2020	2021	2020	2021	
Convertible preferred stock (as converted to common stock) ⁽¹⁾	10,000,001	45,000,000	161,420,799			
Stock Options to purchase common stock	—	—	9,335,220			
Unvested restricted common stock	61,702,273	72,242,712	47,734,388			
	71,702,274	117,242,712	218,490,407			

(1) Under the "If converted" method, the results of basic and diluted EPS are presented as the same calculation. Due to the Company being in a net loss position for all periods, preferred stock and all other securities will have anti-dilutive effect under the "if converted" method and thus all potentially dilutive securities are excluded from the diluted EPS calculation.

14. Related Party Transactions***Founder Consulting Services***

For the period from September 13, 2019 (inception) to December 31, 2019 and the years ended December 31, 2020 and 2021, the Company made payments of \$45,000, \$0.2 million and \$0.2 million, respectively, to one of the Co-founder shareholders for scientific consulting and other expenses. As of December 31, 2020 and 2021, there were no amounts included within accounts payable.

Beam Therapeutics

The Company and Beam are parties to the Beam Collaboration Agreement and the Beam Mutual Subscription Agreement and have a common founder and one common board member (see Note 11). For the year ended December 31, 2020, the Company recognized a net gain of \$0.1 million, related to change in the fair value of the Beam shares the Company was entitled to receive for the period from the first anniversary date of the Beam Collaboration agreement through the date on which the Beam shares were received in October 2020. Such unrealized gain (loss) was recorded as other income (expense), net within the consolidated statements of operations and comprehensive loss. For the years ended December 31, 2020 and 2021, the Company made payments of \$0.1 million and \$0.1 million, respectively, to Beam for general and administrative services. As of December 31, 2020, the Company recorded \$30,000 due to Beam within accounts payable and no amount was due to Beam as of December 31, 2021.

Newpath Partners

In connection with the Series A and B Preferred Stock closings (see Note 6), the Company issued and sold 9,999,999 and 5,250,781 shares of Series A and B Preferred Stock, respectively, to Newpath Partners L.P. ("Newpath"), which is an affiliate to one of the Company's board members, for an aggregate purchase price of \$10.0 million and \$23.0 million, respectively.

Myeloid Therapeutics

In December 2021, the Company and Myeloid entered into the Myeloid Collaboration Agreement and Myeloid Subscription Agreement (see Note 11 and 15). The Company and Myeloid have one common board member, who is also an affiliate of Newpath, one of the Company's holders of Series A and B Preferred Stock.

15. Subsequent Events

For its consolidated financial statements as of December 31, 2021 and for the year then ended, the Company has evaluated subsequent events through February 4, 2022, the date on which these consolidated financial statements were issued.

In January 2022, the Company made the upfront payment of \$30.0 million and issued 3,424,422 shares of its common stock, with a fair value of \$12.0 million, to Myeloid pursuant to the terms of the Myeloid Collaboration Agreement (see Note 11 and 14). As there was no material change in the fair value of the Company's common stock from the date of the Myeloid Subscription Agreement to the date on which the shares were issued, there was no other income (expense) recorded in connection with the issuance of the shares.

In January 2022, the Company granted options for the purchase of an aggregate of 475,500 shares of common stock, at an exercise price of \$3.51 per share. The aggregate grant-date fair value of the options granted is \$1.1 million, which is expected to be recognized as stock-based compensation expense over a period of 3.0 to 4.0 years.

16. Subsequent Events (unaudited)

On February 9, 2022, the Company increased the number of shares of common stock authorized for issuance from 293,258,790 shares to 775,000,000 shares contingent upon the closing of its IPO.

On February 9, 2022, the Company granted options for the purchase of an aggregate of 57,000 shares of common stock, at an exercise price of \$3.51 per share. The aggregate grant-date fair value of the options granted is \$0.1 million, which is expected to be recognized as stock-based compensation expense over a period of 4.0 years. In addition, the Company's board of directors approved the third performance-based vesting milestone, which requires the building of a chemistry facility, initiation of pegRNA piloting operations, and production of a GLP toxicology lot suitable for *in vivo* non-human primate studies, for stock options to purchase 250,000 shares of common stock granted on October 27, 2021 to the Company's CTO (see Note 8).

shares

prime_
medicine

**Common Stock
Prospectus**

J.P. Morgan

Goldman Sachs & Co. LLC

Morgan Stanley

Jefferies

, 2022

Through and including , 2022 (the 25th day after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

Part II

Information Not Required in Prospectus

Item 13. Other Expenses of Issuance and Distribution

The following table sets forth the costs and expenses, other than underwriting discounts and commissions, to be paid by us in connection with the sale of the shares of common stock being registered hereby. All amounts shown are estimates except for the SEC registration fee, the FINRA filing fee and the Nasdaq Global Market initial listing fee.

SEC registration fee	\$	*
FINRA filing fee		*
Nasdaq listing fee		*
Printing and engraving expenses		*
Legal fees and expenses		*
Accounting fees and expenses		*
Transfer agent and registrar fees and expenses		*
Miscellaneous		*
Total	\$	*

* To be provided by amendment.

Item 14. Indemnification of Directors and Officers

Section 145 of the Delaware General Corporation Law (the DGCL) authorizes a corporation to indemnify its directors and officers against liabilities arising out of actions, suits and proceedings to which they are made or threatened to be made a party by reason of the fact that they have served or are currently serving as a director or officer to a corporation. The indemnity may cover expenses (including attorneys' fees) judgments, fines and amounts paid in settlement actually and reasonably incurred by the director or officer in connection with any such action, suit or proceeding. Section 145 permits corporations to pay expenses (including attorneys' fees) incurred by directors and officers in advance of the final disposition of such action, suit or proceeding. In addition, Section 145 provides that a corporation has the power to purchase and maintain insurance on behalf of its directors and officers against any liability asserted against them and incurred by them in their capacity as a director or officer, or arising out of their status as such, whether or not the corporation would have the power to indemnify the director or officer against such liability under Section 145.

We have adopted provisions in our certificate of incorporation and bylaws to be in effect upon the effectiveness of this registration statement that limit or eliminate the personal liability of our directors to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended. Consequently, a director will not be personally liable to us or our stockholders for monetary damages or breach of fiduciary duty as a director, except for liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any unlawful payments related to dividends or unlawful stock purchases, redemptions or other distributions; or
- any transaction from which the director derived an improper personal benefit.

These limitations of liability do not alter director liability under the federal securities laws and do not affect the availability of equitable remedies such as an injunction or rescission.

In addition, our bylaws to be in effect upon the effectiveness of this registration statement provide that:

- we will indemnify our directors, officers and, in the discretion of our board of directors, certain employees to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended; and
- we will advance reasonable expenses, including attorneys' fees, to our directors and, in the discretion of our board of directors, to our officers and certain employees, in connection with legal proceedings relating to their service for or on behalf of us, subject to limited exceptions.

We intend to enter into indemnification agreements with each of our directors and executive officers. These agreements provide that we will indemnify each of our directors, certain of our executive officers and, at times, their affiliates to the fullest extent permitted by Delaware law. We will advance expenses, including attorneys' fees (but excluding judgments, fines and settlement amounts), to each indemnified director or executive officer in connection with any proceeding in which indemnification is available and we will indemnify our directors and officers for any action or proceeding arising out of that person's services as a director or officer brought on behalf of us or in furtherance of our rights. Additionally, certain of our directors or officers may have certain rights to indemnification, advancement of expenses or insurance provided by their affiliates or other third parties, which indemnification relates to and might apply to the same proceedings arising out of such director's or officer's services as a director referenced herein. Nonetheless, we have agreed in the indemnification agreements that our obligations to those same directors or officers are primary and any obligation of such affiliates or other third parties to advance expenses or to provide indemnification for the expenses or liabilities incurred by those directors are secondary.

We also maintain general liability insurance which covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers, including liabilities under the Securities Act.

The underwriting agreement filed as Exhibit 1.1 to this registration statement provides for indemnification of us and our directors and officers by the underwriters against certain liabilities under the Securities Act and the Exchange Act.

Item 15. Recent Sales of Unregistered Securities

Since our inception in September 2019, we have issued the following securities that were not registered under the Securities Act:

(a) Issuances of Capital Stock

In September 2019, in connection with, and as partial consideration for the entry by The Broad Institute, Inc., or the Broad Institute, into, a License and Subscription Agreement, or the Broad License Agreement, we issued 1,938,429 shares of our common stock to the Broad Institute.

In September 2020, in connection with, and as partial consideration for the entry by Beam Therapeutics, Inc. into, a License and Subscription Agreement, or the Beam License Agreement, we issued an aggregate of 5,000,000 shares of our common stock.

In March 2021, we issued an additional 7,768,425 shares of our common stock pursuant to the Broad Institute's anti-dilution rights under the Broad License Agreement.

In September 2019, November 2020 and April 2021, accredited investors and the Broad Institute purchased an aggregate of 115,761,842 shares of our Series A redeemable convertible preferred stock at a price per share of \$1.00, for an aggregate purchase price of approximately \$115,761,842.

In April 2021, accredited investors purchased an aggregate of 45,658,957 shares of our Series B convertible preferred stock at a price per share of \$4.3803, for an aggregate purchase price of approximately \$199,999,929.

In January 2022, in connection with, and as partial consideration for the entry by Myeloid Therapeutics, Inc. into, a Research, Collaboration, Option and License Agreement and a Subscription Agreement, we issued 3,424,422 shares of our common stock.

No underwriters were involved in the foregoing sales of securities. The sales of securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act, including Regulation D and Rule 506 promulgated thereunder, as transactions by an issuer not involving a public offering. All of the purchasers in these transactions represented to us in connection with their purchase that they were acquiring the securities for investment and not distribution, that they could bear the risks of the investment and could hold the securities for an indefinite period of time. Such purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration or an available exemption from such registration. All of the foregoing securities are deemed restricted securities for the purposes of the Securities Act.

(c) Grants and Exercises of Stock Options and Restricted Stock

As of the date hereof, we have granted stock options to purchase an aggregate of 9,867,720 shares of our common stock, with exercise prices ranging from \$1.18 to \$3.51 per share, to employees, directors and consultants pursuant to 2019 Plan. No shares of common stock have been issued upon the exercise of stock options pursuant to the 2019 Plan.

As of the date hereof, we have granted an aggregate of 19,185,727 shares of restricted stock to employees and consultants under the 2019 Plan and an additional 66,932,341 shares to our co-founders outside of the 2019 Plan. In August 2021, we repurchased 56,667 shares of restricted stock previously granted under the 2019 plan.

The issuances of the securities under the 2019 Plan described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act or Rule 701 promulgated under the Securities Act as transactions pursuant to compensatory benefit plans. The shares of common stock issued upon the exercise of options are deemed to be restricted securities for purposes of the Securities Act.

The issuance of securities described above to employees and consultants outside of the 2019 Plan were deemed exempt from registration pursuant to Section 4(a)(2) of the Securities Act as transactions by an issuer not involving a public offering.

Item 16. Exhibits and Financial Statement Schedules

(a) Exhibits.

Exhibit number	Exhibit table
1.1*	Form of Underwriting Agreement
3.1**	Second Amended and Restated Certificate of Incorporation of the Registrant, as currently in effect
3.2	Form of Third Amended and Restated Certificate of Incorporation of the Registrant (to be effective upon the closing of this offering)
3.3**	By-laws of the Registrant, as currently in effect
3.4	Form of Amended and Restated By-laws (to be effective upon the closing of this offering)
4.1**+	Amended and Restated Investors' Rights Agreement among the Registrant and certain of its stockholders, dated April 20, 2021
4.2**	Form of Common Stock Certificate
5.1*	Opinion of Goodwin Procter LLP
10.1**#	2019 Stock Option and Grant Plan, as amended, and forms of award agreements thereunder
10.2*#	2022 Stock Option and Incentive Plan and forms of award agreements thereunder

10.3*#	2022 Employee Stock Purchase Plan
10.4**#	Senior Executive Cash Incentive Bonus Plan
10.5*#	Non-Employee Director Compensation Policy
10.6**#	Form of Officer Indemnification Agreement
10.7**#	Form of Director Indemnification Agreement
10.8*#	Employment Agreement between the Registrant and Keith Gottesdiener, to be in effect upon the closing of this offering
10.9*#	Employment Agreement between the Registrant and Jeremy Duffield, to be in effect upon the closing of this offering
10.10*#	Employment Agreement between the Registrant and Ann Lee, to be in effect upon the closing of this offering
10.11*#	Employment Agreement between the Registrant and Carman Alenson, to be in effect upon the closing of this offering
10.12*#	Employment Agreement between the Registrant and Meredith Goldwasser, to be in effect upon the closing of this offering
10.13**†	Collaboration and License Agreement, dated September 26, 2019, between Beam Therapeutics, Inc. and the Registrant
10.14**†	License Agreement, dated September 26, 2019, between The Broad Institute, Inc. and the Registrant, as amended
10.15**†	Amendment No. 1 to License Agreement, dated May 5, 2020, between The Broad Institute, Inc. and the Registrant
10.16**†	Amendment No. 2 to License Agreement, dated February 18, 2021, between The Broad Institute, Inc. and the Registrant
10.17**	Pledge from Prime Medicine, dated March 2021, between The Broad Institute, Inc. and the Registrant
10.18**+	License Agreement, dated March 16, 2020, between MIL 21E, LLC and the Registrant, as amended
10.19**+	Consulting Agreement between the Registrant and David Liu, dated September 13, 2019
10.20**	Amendment No. 1 to the Consulting Agreement between the Registrant and David Liu, dated October 22, 2021
10.21**+	Andrew Anzalone Offer Letter, dated December 20, 2019
10.22**	Andrew Anzalone Confidentiality, Assignment and Nonsolicitation Agreement, dated October 16, 2020
21.1**	Subsidiaries of the Registrant
23.1*	Consent of PricewaterhouseCoopers, LLP, Independent Registered Public Accounting Firm
23.2*	Consent of Goodwin Procter LLP (included in Exhibit 5.1)
24.1	Power of Attorney (included on signature page to this registration statement)

* To be filed by amendment.

** Previously filed.

Indicates a management contract or any compensatory plan, contract or arrangement.

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to Item 601(b)(10) of Regulation S-K.

+ Certain exhibits and schedules to these agreements have been omitted pursuant to Item 601(a)(5) and (6) of Regulation S-K. The registrant will furnish copies of any of the exhibits and schedules to the Securities and Exchange Commission upon request.

(b) Financial Statement Schedules.

None.

Item 17. Undertakings

The undersigned Registrant hereby undertakes to provide to the underwriters at the closing specified in the Underwriting Agreement certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that:

- (i) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
- (ii) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Signatures

Pursuant to the requirements of the Securities Act, Prime Medicine, Inc. has duly caused this registration statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on the _____ day of _____, 2022.

Prime Medicine, Inc.

By: _____
Keith Gottesdiener
President and Chief Executive Officer

Signatures and Power of Attorney

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Keith Gottesdiener and Carman Alenson, and each of them, either of whom may act without the joinder of the other, as his true and lawful attorneys-in-fact and agents with full power of substitution and re-substitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement, and to sign any registration statement for the same offering covered by the registration statement that is to be effective upon filing pursuant to Rule 462(b) promulgated under the Securities Act, and all post-effective amendments thereto, and to file the same, with all exhibits thereto and all documents in connection therewith, with the SEC, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or his or her or their substitute or substitutes, may lawfully do or cause to be done or by virtue hereof.

Pursuant to the requirements of the Securities Act, this registration statement has been signed by the following persons in the capacities indicated on the _____ day of _____, 2022.

Signature	Title
_____	_____
Keith Gottesdiener	President, Chief Executive Officer and Director (Principal Executive Officer)
_____	_____
Carman Alenson	Chief Accounting Officer (Principal Financial Officer and Principal Accounting Officer)
_____	_____
John Evans	Director
_____	_____
Stephen Knight	Director
_____	_____
Robert Nelsen	Director
_____	_____
David Schenkein	Director
_____	_____
Thomas Cahill	Director
_____	_____
Michael Kelly	Director
_____	_____
Wendy Chung	Director
_____	_____
Kaye Foster	Director

**THIRD AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION
OF
PRIME MEDICINE, INC.**

Prime Medicine, Inc., a corporation organized and existing under the laws of the State of Delaware (the “Corporation”), hereby certifies as follows:

1. The name of the Corporation is Prime Medicine, Inc. The date of the filing of its original Certificate of Incorporation with the Secretary of State of the State of Delaware was September 13, 2019 (the “Original Certificate”).

2. This Third Amended and Restated Certificate of Incorporation (the “Certificate”) amends, restates and integrates the provisions of the Second Amended and Restated Certificate of Incorporation that was filed with the Secretary of State of the State of Delaware on April 19, 2021 (the “Amended and Restated Certificate”), and was duly adopted in accordance with the provisions of Sections 228, 242 and 245 of the General Corporation Law of the State of Delaware (the “DGCL”).

3. The text of the Amended and Restated Certificate is hereby amended and restated in its entirety to provide as herein set forth in full.

ARTICLE I

The name of the Corporation is Prime Medicine, Inc.

ARTICLE II

The address of the registered office of the Corporation in the State of Delaware is 1209 Orange Street, in the City of Wilmington, County of New Castle, 19801. The name of its registered agent at such address is The Corporation Trust Company.

ARTICLE III

The purpose of the Corporation is to engage in any lawful act or activity for which corporations may be organized under the DGCL.

ARTICLE IV

CAPITAL STOCK

The total number of shares of capital stock which the Corporation shall have authority to issue is Five Hundred and Ten Million (510,000,000), of which (i) Five Hundred Million (500,000,000) shares shall be a class designated as common stock, par value \$0.00001 per share (the “Common Stock”), and (ii) Ten Million (10,000,000) shares shall be a class designated as undesignated preferred stock, par value \$0.00001 per share (the “Undesignated Preferred Stock”).

Except as otherwise provided in any certificate of designations of any series of Undesignated Preferred Stock, the number of authorized shares of the class of Common Stock or Undesignated Preferred Stock may from time to time be increased or decreased (but not below the number of shares of such class outstanding) by the affirmative vote of the holders of a majority in voting power of the outstanding shares of capital stock of the Corporation irrespective of the provisions of Section 242(b)(2) of the DGCL.

The powers, preferences and rights of, and the qualifications, limitations and restrictions upon, each class or series of stock shall be determined in accordance with, or as set forth below in, this Article IV.

A. COMMON STOCK

Subject to all the rights, powers and preferences of the Undesignated Preferred Stock and except as provided by law or in this Certificate (or in any certificate of designations of any series of Undesignated Preferred Stock):

(a) the holders of the Common Stock shall have the exclusive right to vote for the election of directors of the Corporation (the "Directors") and on all other matters requiring stockholder action, each outstanding share entitling the holder thereof to one vote on each matter properly submitted to the stockholders of the Corporation for their vote; provided, however, that, except as otherwise required by law, holders of Common Stock, as such, shall not be entitled to vote on any amendment to this Certificate (or on any amendment to a certificate of designations of any series of Undesignated Preferred Stock) that alters or changes the powers, preferences, rights or other terms of one or more outstanding series of Undesignated Preferred Stock if the holders of such affected series of Undesignated Preferred Stock are entitled to vote, either separately or together with the holders of one or more other such series, on such amendment pursuant to this Certificate (or pursuant to a certificate of designations of any series of Undesignated Preferred Stock) or pursuant to the DGCL;

(b) dividends may be declared and paid or set apart for payment upon the Common Stock out of any assets or funds of the Corporation legally available for the payment of dividends, but only when and as declared by the Board of Directors or any authorized committee thereof; and

(c) upon the voluntary or involuntary liquidation, dissolution or winding up of the Corporation, the net assets of the Corporation shall be distributed pro rata to the holders of the Common Stock.

B. UNDESIGNATED PREFERRED STOCK

The Board of Directors or any authorized committee thereof is expressly authorized, to the fullest extent permitted by law, to provide by resolution or resolutions for, out of the unissued shares of Undesignated Preferred Stock, the issuance of the shares of Undesignated Preferred Stock in one or more series of such stock, and by filing a certificate of designations pursuant to applicable law of the State of Delaware, to establish or change from

time to time the number of shares of each such series, and to fix the designations, powers, including voting powers, full or limited, or no voting powers, preferences and the relative, participating, optional or other special rights of the shares of each series and any qualifications, limitations and restrictions thereof.

ARTICLE V

STOCKHOLDER ACTION

1. Action without Meeting. Any action required or permitted to be taken by the stockholders of the Corporation at any annual or special meeting of stockholders of the Corporation must be effected at a duly called annual or special meeting of stockholders and may not be taken or effected by a written consent of stockholders in lieu thereof. Notwithstanding anything herein to the contrary, the affirmative vote of not less than two-thirds (2/3) of the outstanding shares of capital stock entitled to vote thereon, and the affirmative vote of not less than two-thirds (2/3) of the outstanding shares of each class entitled to vote thereon as a class, shall be required to amend or repeal any provision of this Article V, Section 1.

2. Special Meetings. Except as otherwise required by statute and subject to the rights, if any, of the holders of any series of Undesignated Preferred Stock, special meetings of the stockholders of the Corporation may be called only by the Board of Directors acting pursuant to a resolution approved by the affirmative vote of a majority of the Directors then in office, and special meetings of stockholders may not be called by any other person or persons. Only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders of the Corporation.

ARTICLE VI

DIRECTORS

1. General. The business and affairs of the Corporation shall be managed by or under the direction of the Board of Directors except as otherwise provided herein or required by law.

2. Election of Directors. Election of Directors need not be by written ballot unless the By-laws of the Corporation (the "By-laws") shall so provide.

3. Number of Directors; Term of Office. The number of Directors of the Corporation shall be fixed solely and exclusively by resolution duly adopted from time to time by the Board of Directors. The Directors, other than those who may be elected by the holders of any series of Undesignated Preferred Stock, shall be classified, with respect to the term for which they severally hold office, into three classes. The initial Class I Directors of the Corporation shall be John Evans, Michael Kelly and David Schenkein; the initial Class II Directors of the Corporation shall be Kaye Foster, Wendy Chung and Keith Gottesdiener; and the initial Class III Directors of the Corporation shall be Thomas Cahill and Robert Nelsen. The mailing address of each person who is to serve initially as a director is c/o Prime Medicine, Inc., 21 Erie Street,

Cambridge, MA 02139. The initial Class I Directors shall serve for a term expiring at the annual meeting of stockholders to be held in 2023, the initial Class II Directors shall serve for a term expiring at the annual meeting of stockholders to be held in 2024, and the initial Class III Directors shall serve for a term expiring at the annual meeting of stockholders to be held in 2025. At each annual meeting of stockholders, Directors elected to succeed those Directors whose terms expire shall be elected for a term of office to expire at the third succeeding annual meeting of stockholders after their election. Notwithstanding the foregoing, the Directors elected to each class shall hold office until their successors are duly elected and qualified or until their earlier resignation, death or removal.

Notwithstanding the foregoing, whenever, pursuant to the provisions of Article IV of this Certificate, the holders of any one or more series of Undesignated Preferred Stock shall have the right, voting separately as a series or together with holders of other such series, to elect Directors at an annual or special meeting of stockholders, the election, term of office, filling of vacancies and other features of such directorships shall be governed by the terms of this Certificate and any certificate of designations applicable to such series.

Notwithstanding anything herein to the contrary, the affirmative vote of not less than two-thirds (2/3) of the outstanding shares of capital stock entitled to vote thereon, and the affirmative vote of not less than two-thirds (2/3) of the outstanding shares of each class entitled to vote thereon as a class, shall be required to amend or repeal any provision of this Article VI, Section 3.

4. Vacancies. Subject to the rights, if any, of the holders of any series of Undesignated Preferred Stock to elect Directors and to fill vacancies in the Board of Directors relating thereto, any and all vacancies in the Board of Directors, however occurring, including, without limitation, by reason of an increase in the size of the Board of Directors, or the death, resignation, disqualification or removal of a Director, shall be filled solely and exclusively by the affirmative vote of a majority of the remaining Directors then in office, even if less than a quorum of the Board of Directors, and not by the stockholders. Any Director appointed in accordance with the preceding sentence shall hold office for the remainder of the full term of the class of Directors in which the new directorship was created or the vacancy occurred and until such Director's successor shall have been duly elected and qualified or until his or her earlier resignation, death or removal. Subject to the rights, if any, of the holders of any series of Undesignated Preferred Stock to elect Directors, when the number of Directors is increased or decreased, the Board of Directors shall, subject to Article VI.3 hereof, determine the class or classes to which the increased or decreased number of Directors shall be apportioned; provided, however, that no decrease in the number of Directors shall shorten the term of any incumbent Director. In the event of a vacancy in the Board of Directors, the remaining Directors, except as otherwise provided by law, shall exercise the powers of the full Board of Directors until the vacancy is filled.

5. Removal. Subject to the rights, if any, of any series of Undesignated Preferred Stock to elect Directors and to remove any Director whom the holders of any such series have the right to elect, any Director (including persons elected by Directors to fill vacancies in the

Board of Directors) may be removed from office (i) only with cause and (ii) only by the affirmative vote of the holders of not less than two-thirds (2/3) of the outstanding shares of capital stock then entitled to vote at an election of Directors. At least forty-five (45) days prior to any annual or special meeting of stockholders at which it is proposed that any Director be removed from office, written notice of such proposed removal and the alleged grounds thereof shall be sent to the Director whose removal will be considered at the meeting.

ARTICLE VII

LIMITATION OF LIABILITY

A Director of the Corporation shall not be personally liable to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a Director, except for liability (a) for any breach of the Director's duty of loyalty to the Corporation or its stockholders, (b) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (c) under Section 174 of the DGCL or (d) for any transaction from which the Director derived an improper personal benefit. If the DGCL is amended after the effective date of this Certificate to authorize corporate action further eliminating or limiting the personal liability of Directors, then the liability of a Director of the Corporation shall be eliminated or limited to the fullest extent permitted by the DGCL, as so amended.

Any amendment, repeal or modification of this Article VII by either of (i) the stockholders of the Corporation or (ii) an amendment to the DGCL, shall not adversely affect any right or protection existing at the time of such amendment, repeal or modification with respect to any acts or omissions occurring before such amendment, repeal or modification of a person serving as a Director at the time of such amendment, repeal or modification.

Notwithstanding anything herein to the contrary, the affirmative vote of not less than two-thirds (2/3) of the outstanding shares of capital stock entitled to vote thereon, and the affirmative vote of not less than two-thirds (2/3) of the outstanding shares of each class entitled to vote thereon as a class, shall be required to amend or repeal any provision of this Article VII.

ARTICLE VIII

AMENDMENT OF BY-LAWS

1. Amendment by Directors. Except as otherwise provided by law, the By-laws of the Corporation may be amended or repealed by the Board of Directors by the affirmative vote of a majority of the Directors then in office.

2. Amendment by Stockholders. Except as otherwise provided therein, the By-laws of the Corporation may be amended or repealed at any annual meeting of stockholders, or special meeting of stockholders called for such purpose, by the affirmative vote of not less than two-thirds (2/3) of the outstanding shares of capital stock entitled to vote on such amendment or repeal, voting together as a single class; provided, however, that if the Board of Directors recommends that stockholders approve such amendment or repeal at such meeting of

stockholders, such amendment or repeal shall only require the affirmative vote of the majority of the outstanding shares of capital stock entitled to vote on such amendment or repeal, voting together as a single class.

ARTICLE IX

AMENDMENT OF CERTIFICATE OF INCORPORATION

The Corporation reserves the right to amend or repeal this Certificate in the manner now or hereafter prescribed by statute and this Certificate, and all rights conferred upon stockholders herein are granted subject to this reservation. Whenever any vote of the holders of capital stock of the Corporation is required to amend or repeal any provision of this Certificate, and in addition to any other vote of holders of capital stock that is required by this Certificate or by law, such amendment or repeal shall require the affirmative vote of the majority of the outstanding shares of capital stock entitled to vote on such amendment or repeal, and the affirmative vote of the majority of the outstanding shares of each class entitled to vote thereon as a class, at a duly constituted meeting of stockholders called expressly for such purpose; provided, however, that the affirmative vote of not less than two-thirds (2/3) of the outstanding shares of capital stock entitled to vote on such amendment or repeal, and the affirmative vote of not less than two-thirds (2/3) of the outstanding shares of each class entitled to vote thereon as a class, shall be required to amend or repeal any provision of Article V, Article VI, Article VII, Article VIII or Article IX of this Certificate.

[End of Text]

THIS THIRD AMENDED AND RESTATED CERTIFICATE OF INCORPORATION is executed as of this _____ day
of _____, 2022.

PRIME MEDICINE, INC.

By: _____

Name: Keith Gottesdiener

Title: President and Chief Executive Officer

AMENDED AND RESTATED
BY-LAWS
OF
PRIME MEDICINE, INC.

(the “Corporation”)

ARTICLE I

Stockholders

SECTION 1. Annual Meeting. The annual meeting of stockholders (any such meeting being referred to in these By-laws as an “Annual Meeting”) shall be held at the hour, date and place within or without the United States which is fixed by the Board of Directors, which time, date and place may subsequently be changed at any time by vote of the Board of Directors. If no Annual Meeting has been held for a period of thirteen (13) months after the Corporation’s last Annual Meeting, a special meeting in lieu thereof may be held, and such special meeting shall have, for the purposes of these By-laws or otherwise, all the force and effect of an Annual Meeting. Any and all references hereafter in these By-laws to an Annual Meeting or Annual Meetings also shall be deemed to refer to any special meeting(s) in lieu thereof.

SECTION 2. Notice of Stockholder Business and Nominations.

(a) Annual Meetings of Stockholders.

(1) Nominations of persons for election to the Board of Directors of the Corporation and the proposal of other business to be considered by the stockholders may be brought before an Annual Meeting (i) by or at the direction of the Board of Directors or (ii) by any stockholder of the Corporation who was a stockholder of record at the time of giving of notice provided for in this By-law, who is entitled to vote at the meeting, who is present (in person or by proxy) at the meeting and who complies with the notice procedures set forth in this By-law as to such nomination or business. For the avoidance of doubt, the foregoing clause (ii) shall be the exclusive means for a stockholder to bring nominations or business properly before an Annual Meeting (other than matters properly brought under Rule 14a-8 (or any successor rule) under the Securities Exchange Act of 1934, as amended (the “Exchange Act”)), and such stockholder must comply with the notice and other procedures set forth in Article I, Section 2(a)(2) and (3) of this By-law to bring such nominations or business properly before an Annual Meeting. In addition to the other requirements set forth in this By-law, for any proposal of business to be considered at an Annual Meeting, it must be a proper subject for action by stockholders of the Corporation under Delaware law.

(2) For nominations or other business to be properly brought before an Annual Meeting by a stockholder pursuant to clause (ii) of Article I, Section 2(a)(1) of

this By-law, the stockholder must (i) have given Timely Notice (as defined below) thereof in writing to the Secretary of the Corporation, (ii) have provided any updates or supplements to such notice at the times and in the forms required by this By-law and (iii) together with the beneficial owner(s), if any, on whose behalf the nomination or business proposal is made, have acted in accordance with the representations set forth in the Solicitation Statement (as defined below) required by this By-law. To be timely, a stockholder's written notice shall be received by the Secretary at the principal executive offices of the Corporation not later than the close of business on the ninetieth (90th) day nor earlier than the close of business on the one hundred twentieth (120th) day prior to the one-year anniversary of the preceding year's Annual Meeting; provided, however, that in the event the Annual Meeting is first convened more than thirty (30) days before or more than sixty (60) days after such anniversary date, or if no Annual Meeting were held in the preceding year, notice by the stockholder to be timely must be received by the Secretary of the Corporation not later than the close of business on the later of the ninetieth (90th) day prior to the scheduled date of such Annual Meeting or the tenth (10th) day following the day on which public announcement of the date of such meeting is first made (such notice within such time periods shall be referred to as "Timely Notice"). Notwithstanding anything to the contrary provided herein, for the first Annual Meeting following the initial public offering of common stock of the Corporation, a stockholder's notice shall be timely if received by the Secretary at the principal executive offices of the Corporation not later than the close of business on the later of the ninetieth (90th) day prior to the scheduled date of such Annual Meeting or the tenth (10th) day following the day on which public announcement of the date of such Annual Meeting is first made or sent by the Corporation. Such stockholder's Timely Notice shall set forth:

(A) as to each person whom the stockholder proposes to nominate for election or reelection as a director, (i) the name, age, business address and residence address of the nominee, (ii) the principal occupation or employment of the nominee, (iii) the class and number of shares of the corporation that are held of record or are beneficially owned by the nominee and any derivative positions held or beneficially held by the nominee, (iv) whether and the extent to which any hedging or other transaction or series of transactions has been entered into by or on behalf of the nominee with respect to any securities of the corporation, and a description of any other agreement, arrangement or understanding (including any short position or any borrowing or lending of shares), the effect or intent of which is to mitigate loss to, or to manage the risk or benefit of share price changes for, or to increase or decrease the voting power of the nominee, (v) a description of all arrangements or understandings between or among the stockholder and each nominee and any other person or persons (naming such person or persons) pursuant to which the nominations are to be made by the stockholder or concerning the nominee's potential service on the Board of Directors, (vi) a written statement executed by the nominee acknowledging that as a director of the corporation, the nominee will owe fiduciary duties under Delaware law with respect to the corporation and its stockholders, and (vii) all information relating to such person that is required to be disclosed in solicitations of proxies for election

of directors in an election contest, or is otherwise required, in each case pursuant to Regulation 14A under the Exchange Act (including such person's written consent to being named in the proxy statement as a nominee and to serving as a director if elected);

(B) as to any other business that the stockholder proposes to bring before the meeting, a brief description of the business desired to be brought before the meeting, the reasons for conducting such business at the meeting, the text, if any, of any resolutions or By-law amendment proposed for adoption, and any material interest in such business of each Proposing Person (as defined below);

(C) (i) the name and address of the stockholder giving the notice, as they appear on the Corporation's books, and the names and addresses of the other Proposing Persons (if any) and (ii) as to each Proposing Person, the following information: (a) the class or series and number of all shares of capital stock of the Corporation which are, directly or indirectly, owned beneficially or of record by such Proposing Person or any of its affiliates or associates (as such terms are defined in Rule 12b-2 promulgated under the Exchange Act), including any shares of any class or series of capital stock of the Corporation as to which such Proposing Person or any of its affiliates or associates has a right to acquire beneficial ownership at any time in the future, (b) all Synthetic Equity Interests (as defined below) in which such Proposing Person or any of its affiliates or associates, directly or indirectly, holds an interest including a description of the material terms of each such Synthetic Equity Interest, including without limitation, identification of the counterparty to each such Synthetic Equity Interest and disclosure, for each such Synthetic Equity Interest, as to (x) whether or not such Synthetic Equity Interest conveys any voting rights, directly or indirectly, in such shares to such Proposing Person, (y) whether or not such Synthetic Equity Interest is required to be, or is capable of being, settled through delivery of such shares and (z) whether or not such Proposing Person and/or, to the extent known, the counterparty to such Synthetic Equity Interest has entered into other transactions that hedge or mitigate the economic effect of such Synthetic Equity Interest, (c) any proxy (other than a revocable proxy given in response to a public proxy solicitation made pursuant to, and in accordance with, the Exchange Act), agreement, arrangement, understanding or relationship pursuant to which such Proposing Person has or shares a right to, directly or indirectly, vote any shares of any class or series of capital stock of the Corporation, (d) any rights to dividends or other distributions on the shares of any class or series of capital stock of the Corporation, directly or indirectly, owned beneficially by such Proposing Person that are separated or separable from the underlying shares of the Corporation, and (e) any performance-related fees (other than an asset based fee) that such Proposing Person, directly or indirectly, is entitled to based on any increase or decrease in the value of shares of any class or series of capital stock of the Corporation or any Synthetic Equity Interests (the disclosures to be made pursuant to the foregoing clauses (a) through (e) are referred to, collectively, as "Material

Ownership Interests”) and (iii) a description of the material terms of all agreements, arrangements or understandings (whether or not in writing) entered into by any Proposing Person or any of its affiliates or associates with any other person for the purpose of acquiring, holding, disposing or voting of any shares of any class or series of capital stock of the Corporation;

(D) (i) a description of all agreements, arrangements or understandings by and among any of the Proposing Persons, or by and among any Proposing Persons and any other person (including with any proposed nominee(s)), pertaining to the nomination(s), or other business proposed to be brought before the meeting of stockholders (which description shall identify the name of each other person who is party to such an agreement, arrangement or understanding), and (ii) identification of the names and addresses of other stockholders (including beneficial owners) known by any of the Proposing Persons to support such nominations or other business proposal(s), and to the extent known the class and number of all shares of the Corporation’s capital stock owned beneficially or of record by such other stockholder(s) or other beneficial owner(s); and

(E) a statement whether or not the stockholder giving the notice and/or the other Proposing Person(s), if any, will deliver a proxy statement and form of proxy to holders of, in the case of a business proposal, at least the percentage of voting power of all of the shares of capital stock of the Corporation required under applicable law to approve the proposal or, in the case of a nomination or nominations, at least the percentage of voting power of all of the shares of capital stock of the Corporation reasonably believed by such Proposing Person to be sufficient to elect the nominee or nominees proposed to be nominated by such stockholder (such statement, the “Solicitation Statement”).

For purposes of this Article I of these By-laws, the term “Proposing Person” shall mean the following persons: (i) the stockholder of record providing the notice of nominations or business proposed to be brought before a stockholders’ meeting, and (ii) the beneficial owner(s), if different, on whose behalf the nominations or business proposed to be brought before a stockholders’ meeting is made. For purposes of this Section 2 of Article I of these By-laws, the term “Synthetic Equity Interest” shall mean any transaction, agreement or arrangement (or series of transactions, agreements or arrangements), including, without limitation, any derivative, swap, hedge, repurchase or so-called “stock borrowing” agreement or arrangement, the purpose or effect of which is to, directly or indirectly: (a) give a person or entity economic benefit and/or risk similar to ownership of shares of any class or series of capital stock of the Corporation, in whole or in part, including due to the fact that such transaction, agreement or arrangement provides, directly or indirectly, the opportunity to profit or avoid a loss from any increase or decrease in the value of any shares of any class or series of capital stock of the Corporation, (b) mitigate loss to, reduce the economic risk of or manage the risk of share price changes for, any person or entity with respect to any shares of any class or series of capital stock of the Corporation, (c) otherwise provide in any manner the opportunity to

profit or avoid a loss from any decrease in the value of any shares of any class or series of capital stock of the Corporation, or (d) increase or decrease the voting power of any person or entity with respect to any shares of any class or series of capital stock of the Corporation.

(3) A stockholder providing Timely Notice of nominations or business proposed to be brought before an Annual Meeting shall further update and supplement such notice, if necessary, so that the information (including, without limitation, the Material Ownership Interests information) provided or required to be provided in such notice pursuant to this By-law shall be true and correct as of the record date for the meeting and as of the date that is ten (10) business days prior to such Annual Meeting, and such update and supplement shall be received by the Secretary at the principal executive offices of the Corporation not later than the close of business on the fifth (5th) business day after the record date for the Annual Meeting (in the case of the update and supplement required to be made as of the record date), and not later than the close of business on the eighth (8th) business day prior to the date of the Annual Meeting (in the case of the update and supplement required to be made as of ten (10) business days prior to the meeting).

(4) Notwithstanding anything in the second sentence of Article I, Section 2(a)(2) of this By-law to the contrary, in the event that the number of directors to be elected to the Board of Directors of the Corporation is increased and there is no public announcement naming all of the nominees for director or specifying the size of the increased Board of Directors made by the Corporation at least ten (10) days before the last day a stockholder may deliver a notice of nomination in accordance with the second sentence of Article I, Section 2(a)(2), a stockholder's notice required by this By-law shall also be considered timely, but only with respect to nominees for any new positions created by such increase, if it shall be received by the Secretary of the Corporation not later than the close of business on the tenth (10th) day following the day on which such public announcement is first made by the Corporation.

(b) General.

(1) Only such persons who are nominated in accordance with the provisions of this By-law shall be eligible for election and to serve as directors and only such business shall be conducted at an Annual Meeting as shall have been brought before the meeting in accordance with the provisions of this By-law or in accordance with Rule 14a-8 under the Exchange Act. The Board of Directors or a designated committee thereof shall have the power to determine whether a nomination or any business proposed to be brought before the meeting was made in accordance with the provisions of this By-law. If neither the Board of Directors nor such designated committee makes a determination as to whether any stockholder proposal or nomination was made in accordance with the provisions of this By-law, the presiding officer of the Annual Meeting shall have the power and duty to determine whether the stockholder proposal or nomination was made in accordance with the provisions of this By-law. If the Board of

Directors or a designated committee thereof or the presiding officer, as applicable, determines that any stockholder proposal or nomination was not made in accordance with the provisions of this By-law, such proposal or nomination shall be disregarded and shall not be presented for action at the Annual Meeting.

(2) Except as otherwise required by law, nothing in this Article I, Section 2 shall obligate the Corporation or the Board of Directors to include in any proxy statement or other stockholder communication distributed on behalf of the Corporation or the Board of Directors information with respect to any nominee for director or any other matter of business submitted by a stockholder.

(3) Notwithstanding the foregoing provisions of this Article I, Section 2, if the nominating or proposing stockholder (or a qualified representative of the stockholder) does not appear at the Annual Meeting to present a nomination or any business, such nomination or business shall be disregarded, notwithstanding that proxies in respect of such vote may have been received by the Corporation. For purposes of this Article I, Section 2, to be considered a qualified representative of the proposing stockholder, a person must be authorized by a written instrument executed by such stockholder or an electronic transmission delivered by such stockholder to act for such stockholder as proxy at the meeting of stockholders and such person must produce such written instrument or electronic transmission, or a reliable reproduction of the written instrument or electronic transmission, to the presiding officer at the meeting of stockholders.

(4) For purposes of this By-law, “public announcement” shall mean disclosure in a press release reported by the Dow Jones News Service, Associated Press or comparable national news service or in a document publicly filed by the Corporation with the Securities and Exchange Commission pursuant to Section 13, 14 or 15(d) of the Exchange Act.

(5) Notwithstanding the foregoing provisions of this By-law, a stockholder shall also comply with all applicable requirements of the Exchange Act and the rules and regulations thereunder with respect to the matters set forth in this By-law. Nothing in this By-law shall be deemed to affect any rights of (i) stockholders to have proposals included in the Corporation’s proxy statement pursuant to Rule 14a-8 (or any successor rule), as applicable, under the Exchange Act and, to the extent required by such rule, have such proposals considered and voted on at an Annual Meeting or (ii) the holders of any series of Undesignated Preferred Stock to elect directors under specified circumstances.

(c) Notwithstanding anything herein to the contrary, the affirmative vote of not less than two thirds (2/3) of the outstanding shares of capital stock entitled to vote thereon, and the affirmative vote of not less than two thirds (2/3) of the outstanding shares of each class entitled to vote thereon as a class, shall be required to amend or repeal any provision of this Article I, Section 2; provided, however, that if the Board of Directors recommends that stockholders approve such amendment or repeal at such meeting of stockholders, such amendment or repeal shall only require the affirmative vote of a majority of the outstanding shares entitled to vote on such amendment or repeal, voting together as a single class.

SECTION 3. Special Meetings. Except as otherwise required by statute and subject to the rights, if any, of the holders of any series of Undesignated Preferred Stock, special meetings of the stockholders of the Corporation may be called only by the Board of Directors acting pursuant to a resolution approved by the affirmative vote of a majority of the Directors then in office. The Board of Directors may postpone or reschedule any previously scheduled special meeting of stockholders. Only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders of the Corporation. Nominations of persons for election to the Board of Directors of the Corporation and stockholder proposals of other business shall not be brought before a special meeting of stockholders to be considered by the stockholders unless such special meeting is held in lieu of an annual meeting of stockholders in accordance with Article I, Section 1 of these By-laws, in which case such special meeting in lieu thereof shall be deemed an Annual Meeting for purposes of these By-laws and the provisions of Article I, Section 2 of these By-laws shall govern such special meeting.

Notwithstanding anything herein to the contrary, the affirmative vote of not less than two thirds (2/3) of the outstanding shares of capital stock entitled to vote thereon, and the affirmative vote of not less than two thirds (2/3) of the outstanding shares of each class entitled to vote thereon as a class, shall be required to amend or repeal any provision of this Article I, Section 3; provided, however, that if the Board of Directors recommends that stockholders approve such amendment or repeal at such meeting of stockholders, such amendment or repeal shall only require the affirmative vote of a majority of the outstanding shares entitled to vote on such amendment or repeal, voting together as a single class.

SECTION 4. Notice of Meetings; Adjournments.

(a) A notice of each Annual Meeting stating the hour, date and place, if any, of such Annual Meeting and the means of remote communication, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such meeting, shall be given not less than ten (10) days nor more than sixty (60) days before the Annual Meeting, to each stockholder entitled to vote thereat by delivering such notice to such stockholder or by mailing it, postage prepaid, addressed to such stockholder at the address of such stockholder as it appears on the Corporation's stock transfer books. Without limiting the manner by which notice may otherwise be given to stockholders, any notice to stockholders may be given by electronic transmission in the manner provided in Section 232 of the Delaware General Corporation Law ("DGCL").

(b) Unless otherwise required by the DGCL, notice of all special meetings of stockholders shall be given in the same manner as provided for Annual Meetings, except that the notice of all special meetings shall state the purpose or purposes for which the meeting has been called.

(c) Notice of an Annual Meeting or special meeting of stockholders need not be given to a stockholder if a waiver of notice is executed, or waiver of notice by electronic transmission is provided, before or after such meeting by such stockholder or if such stockholder attends such meeting, unless such attendance is for the express purpose of objecting at the beginning of the

meeting to the transaction of any business because the meeting was not lawfully called or convened.

(d) The Board of Directors may postpone and reschedule any previously scheduled Annual Meeting or special meeting of stockholders and any record date with respect thereto, regardless of whether any notice or public disclosure with respect to any such meeting has been sent or made pursuant to Section 2 of this Article I of these By-laws or otherwise. In no event shall the public announcement of an adjournment, postponement or rescheduling of any previously scheduled meeting of stockholders commence a new time period for the giving of a stockholder's notice under this Article I of these By-laws.

(e) When any meeting is convened, the presiding officer may adjourn the meeting if (i) no quorum is present for the transaction of business, (ii) the Board of Directors determines that adjournment is necessary or appropriate to enable the stockholders to consider fully information which the Board of Directors determines has not been made sufficiently or timely available to stockholders, or (iii) the Board of Directors determines that adjournment is otherwise in the best interests of the Corporation. When any Annual Meeting or special meeting of stockholders is adjourned to another hour, date or place, notice need not be given of the adjourned meeting other than an announcement at the meeting at which the adjournment is taken of the hour, date and place, if any, to which the meeting is adjourned and the means of remote communications, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such adjourned meeting; provided, however, that if the adjournment is for more than thirty (30) days from the meeting date, or if after the adjournment a new record date is fixed for the adjourned meeting, notice of the adjourned meeting and the means of remote communications, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such adjourned meeting shall be given to each stockholder of record entitled to vote thereat and each stockholder who, by law or under the Third Amended and Restated Certificate of Incorporation of the Corporation (as the same may hereafter be amended and/or restated, the "Certificate") or these By-laws, is entitled to such notice.

SECTION 5. Quorum. A majority of the outstanding shares entitled to vote, present in person or represented by proxy, shall constitute a quorum at any meeting of stockholders. If less than a quorum is present at a meeting, the holders of voting stock representing a majority of the voting power present at the meeting or the presiding officer may adjourn the meeting from time to time, and the meeting may be held as adjourned without further notice, except as provided in Section 4 of this Article I. At such adjourned meeting at which a quorum is present, any business may be transacted which might have been transacted at the original meeting. The stockholders present at a duly constituted meeting may continue to transact business until adjournment, notwithstanding the withdrawal of enough stockholders to leave less than a quorum.

SECTION 6. Voting and Proxies. Stockholders shall have one vote for each share of stock entitled to vote owned by them of record according to the stock ledger of the Corporation as of the record date, unless otherwise provided by law or by the Certificate. Stockholders may vote either (i) in person, (ii) by written proxy or (iii) by a transmission permitted by

Section 212(c) of the DGCL. Any copy, facsimile telecommunication or other reliable reproduction of the writing or transmission permitted by Section 212(c) of the DGCL may be substituted for or used in lieu of the original writing or transmission for any and all purposes for which the original writing or transmission could be used, provided that such copy, facsimile telecommunication or other reproduction shall be a complete reproduction of the entire original writing or transmission. Proxies shall be filed in accordance with the procedures established for the meeting of stockholders. Except as otherwise limited therein or as otherwise provided by law, proxies authorizing a person to vote at a specific meeting shall entitle the persons authorized thereby to vote at any adjournment of such meeting, but they shall not be valid after final adjournment of such meeting. A proxy with respect to stock held in the name of two or more persons shall be valid if executed by or on behalf of any one of them unless at or prior to the exercise of the proxy the Corporation receives a specific written notice to the contrary from any one of them.

SECTION 7. Action at Meeting. When a quorum is present at any meeting of stockholders, any matter before any such meeting (other than an election of a director or directors) shall be decided by a majority of the votes properly cast for and against such matter, except where a larger vote is required by law, by the Certificate or by these By-laws. Any election of directors by stockholders shall be determined by a plurality of the votes properly cast on the election of directors.

SECTION 8. Stockholder Lists. The Secretary or an Assistant Secretary (or the Corporation's transfer agent or other person authorized by these By-laws or by law) shall prepare and make, at least ten (10) days before every Annual Meeting or special meeting of stockholders, a complete list of the stockholders entitled to vote at the meeting, arranged in alphabetical order, and showing the address of each stockholder and the number of shares registered in the name of each stockholder. Such list shall be open to the examination of any stockholder, for a period of at least ten (10) days prior to the meeting as provided in the manner, and subject to the terms, set forth in Section 219 of the DGCL (or any successor provision). The list shall also be open to the examination of any stockholder during the whole time of the meeting as provided by law.

SECTION 9. Presiding Officer. The Board of Directors shall designate a representative to preside over all Annual Meetings or special meetings of stockholders, provided that if the Board of Directors does not so designate such a presiding officer, then the Chairman of the Board, if one is elected, shall preside over such meetings. If the Board of Directors does not so designate such a presiding officer and there is no Chairman of the Board or the Chairman of the Board is unable to so preside or is absent, then the Chief Executive Officer, if one is elected, shall preside over such meetings, provided further that if there is no Chief Executive Officer or the Chief Executive Officer is unable to so preside or is absent, then the President shall preside over such meetings. The presiding officer at any Annual Meeting or special meeting of stockholders shall have the power, among other things, to adjourn such meeting at any time and from time to time, subject to Sections 4 and 5 of this Article I. The order of business and all other matters of procedure at any meeting of the stockholders shall be determined by the presiding officer.

SECTION 10. Inspectors of Elections. The Corporation shall, in advance of any meeting of stockholders, appoint one or more inspectors to act at the meeting and make a written report thereof. The Corporation may designate one or more persons as alternate inspectors to replace any inspector who fails to act. If no inspector or alternate is able to act at a meeting of stockholders, the presiding officer shall appoint one or more inspectors to act at the meeting. Any inspector may, but need not, be an officer, employee or agent of the Corporation. Each inspector, before entering upon the discharge of his or her duties, shall take and sign an oath faithfully to execute the duties of inspector with strict impartiality and according to the best of his or her ability. The inspectors shall perform such duties as are required by the DGCL, including the counting of all votes and ballots. The inspectors may appoint or retain other persons or entities to assist the inspectors in the performance of the duties of the inspectors. The presiding officer may review all determinations made by the inspectors, and in so doing the presiding officer shall be entitled to exercise his or her sole judgment and discretion and he or she shall not be bound by any determinations made by the inspectors. All determinations by the inspectors and, if applicable, the presiding officer, shall be subject to further review by any court of competent jurisdiction.

ARTICLE II

Directors

SECTION 1. Powers. The business and affairs of the Corporation shall be managed by or under the direction of the Board of Directors except as otherwise provided by the Certificate or required by law.

SECTION 2. Number and Terms. The number of directors of the Corporation shall be fixed solely and exclusively by resolution duly adopted from time to time by the Board of Directors. The directors shall hold office in the manner provided in the Certificate.

SECTION 3. Qualification. No director need be a stockholder of the Corporation.

SECTION 4. Vacancies. Vacancies in the Board of Directors shall be filled in the manner provided in the Certificate.

SECTION 5. Removal. Directors may be removed from office only in the manner provided in the Certificate.

SECTION 6. Resignation. A director may resign at any time by electronic transmission or by giving written notice to the Chairman of the Board, if one is elected, the President or the Secretary. A resignation shall be effective upon receipt, unless the resignation otherwise provides.

SECTION 7. Regular Meetings. The regular annual meeting and other regular meetings of the Board of Directors may be held at such hour, date and place as the Board of Directors may by resolution from time to time determine and publicize by means of reasonable notice given to any director who is not present at the meeting at which such resolution is adopted.

SECTION 8. Special Meetings. Special meetings of the Board of Directors may be called, orally or in writing, by or at the request of a majority of the directors, the Chairman of the Board, if one is elected, or the President. The person calling any such special meeting of the Board of Directors may fix the hour, date and place thereof.

SECTION 9. Notice of Meetings. Notice of the hour, date and place of all special meetings of the Board of Directors shall be given to each director by the Secretary or an Assistant Secretary, or in case of the death, absence, incapacity or refusal of such persons, by the Chairman of the Board, if one is elected, or the President or such other officer designated by the Chairman of the Board, if one is elected, or the President. Notice of any special meeting of the Board of Directors shall be given to each director in person, by telephone, or by facsimile, electronic mail or other form of electronic communication, sent to his or her business or home address, at least twenty-four (24) hours in advance of the meeting, or by written notice mailed to his or her business or home address, at least forty-eight (48) hours in advance of the meeting. Such notice shall be deemed to be delivered when hand-delivered to such address, read to such director by telephone, deposited in the mail so addressed, with postage thereon prepaid if mailed, dispatched or transmitted if sent by facsimile transmission or by electronic mail or other form of electronic communications. A written waiver of notice signed or electronically transmitted before or after a meeting by a director and filed with the records of the meeting shall be deemed to be equivalent to notice of the meeting. The attendance of a director at a meeting shall constitute a waiver of notice of such meeting, except where a director attends a meeting for the express purpose of objecting at the beginning of the meeting to the transaction of any business because such meeting is not lawfully called or convened. Except as otherwise required by law, by the Certificate or by these By-laws, neither the business to be transacted at, nor the purpose of, any meeting of the Board of Directors need be specified in the notice or waiver of notice of such meeting.

SECTION 10. Quorum. At any meeting of the Board of Directors, a majority of the total number of directors shall constitute a quorum for the transaction of business, but if less than a quorum is present at a meeting, a majority of the directors present may adjourn the meeting from time to time, and the meeting may be held as adjourned without further notice. Any business which might have been transacted at the meeting as originally noticed may be transacted at such adjourned meeting at which a quorum is present. For purposes of this section, the total number of directors includes any unfilled vacancies on the Board of Directors.

SECTION 11. Action at Meeting. At any meeting of the Board of Directors at which a quorum is present, the vote of a majority of the directors present shall constitute action by the Board of Directors, unless otherwise required by law, by the Certificate or by these By-laws.

SECTION 12. Action by Consent. Any action required or permitted to be taken at any meeting of the Board of Directors may be taken without a meeting if all members of the Board of Directors consent thereto in writing or by electronic transmission and the writing or writings or electronic transmission or transmissions are filed with the records of the meetings of the Board of Directors. Such filing shall be in paper form if the minutes are maintained in paper form and

shall be in electronic form if the minutes are maintained in electronic form. Such consent shall be treated as a resolution of the Board of Directors for all purposes.

SECTION 13. Manner of Participation. Directors may participate in meetings of the Board of Directors by means of conference telephone or other communications equipment by means of which all directors participating in the meeting can hear each other, and participation in a meeting in accordance herewith shall constitute presence in person at such meeting for purposes of these By-laws.

SECTION 14. Presiding Director. The Board of Directors shall designate a representative to preside over all meetings of the Board of Directors, provided that if the Board of Directors does not so designate such a presiding director or such designated presiding director is unable to so preside or is absent, then the Chairman of the Board, if one is elected, shall preside over all meetings of the Board of Directors. If both the designated presiding director, if one is so designated, and the Chairman of the Board, if one is elected, are unable to preside or are absent, the Board of Directors shall designate an alternate representative to preside over a meeting of the Board of Directors.

SECTION 15. Committees. The Board of Directors, by vote of a majority of the directors then in office, may elect one or more committees, including, without limitation, a Compensation Committee, a Nominating & Corporate Governance Committee and an Audit Committee, and may delegate thereto some or all of its powers except those which by law, by the Certificate or by these By-laws may not be delegated. Except as the Board of Directors may otherwise determine, any such committee may make rules for the conduct of its business, but unless otherwise provided by the Board of Directors or in such rules, its business shall be conducted so far as possible in the same manner as is provided by these By-laws for the Board of Directors. All members of such committees shall hold such offices at the pleasure of the Board of Directors. The Board of Directors may abolish any such committee at any time. Any committee to which the Board of Directors delegates any of its powers or duties shall keep records of its meetings and shall report its action to the Board of Directors.

SECTION 16. Compensation of Directors. Directors shall receive such compensation for their services as shall be determined by a majority of the Board of Directors, or a designated committee thereof, provided that directors who are serving the Corporation as employees and who receive compensation for their services as such, shall not receive any salary or other compensation for their services as directors of the Corporation.

ARTICLE III

Officers

SECTION 1. Enumeration. The officers of the Corporation shall consist of a President, a Treasurer, a Secretary and such other officers, including, without limitation, a Chairman of the Board of Directors, a Chief Executive Officer and one or more Vice Presidents (including Executive Vice Presidents or Senior Vice Presidents), Assistant Vice Presidents, Assistant Treasurers and Assistant Secretaries, as the Board of Directors may determine.

SECTION 2. Election. At the regular annual meeting of the Board of Directors following the Annual Meeting, the Board of Directors shall elect the President, the Treasurer and the Secretary. Other officers may be elected by the Board of Directors at such regular annual meeting of the Board of Directors or at any other regular or special meeting.

SECTION 3. Qualification. No officer need be a stockholder or a director. Any person may occupy more than one office of the Corporation at any time.

SECTION 4. Tenure. Except as otherwise provided by the Certificate or by these By-laws, each of the officers of the Corporation shall hold office until the regular annual meeting of the Board of Directors following the next Annual Meeting or until his or her successor is elected and qualified or until his or her earlier resignation or removal.

SECTION 5. Resignation. Any officer may resign by delivering his or her written or electronically transmitted resignation to the Corporation addressed to the President or the Secretary, and such resignation shall be effective upon receipt, unless the resignation otherwise provides.

SECTION 6. Removal. Except as otherwise provided by law or by resolution of the Board of Directors, the Board of Directors may remove any officer with or without cause by the affirmative vote of a majority of the directors then in office.

SECTION 7. Absence or Disability. In the event of the absence or disability of any officer, the Board of Directors may designate another officer to act temporarily in place of such absent or disabled officer.

SECTION 8. Vacancies. Any vacancy in any office may be filled for the unexpired portion of the term by the Board of Directors.

SECTION 9. President. The President shall, subject to the direction of the Board of Directors, have such powers and shall perform such duties as the Board of Directors may from time to time designate.

SECTION 10. Chairman of the Board. The Chairman of the Board, if one is elected, shall have such powers and shall perform such duties as the Board of Directors may from time to time designate.

SECTION 11. Chief Executive Officer. The Chief Executive Officer, if one is elected, shall have such powers and shall perform such duties as the Board of Directors may from time to time designate.

SECTION 12. Vice Presidents and Assistant Vice Presidents. Any Vice President (including any Executive Vice President or Senior Vice President) and any Assistant Vice President shall have such powers and shall perform such duties as the Board of Directors or the Chief Executive Officer may from time to time designate.

SECTION 13. Treasurer and Assistant Treasurers. The Treasurer shall, subject to the direction of the Board of Directors and except as the Board of Directors or the Chief Executive Officer may otherwise provide, have general charge of the financial affairs of the Corporation and shall cause to be kept accurate books of account. The Treasurer shall have custody of all funds, securities, and valuable documents of the Corporation. He or she shall have such other duties and powers as may be designated from time to time by the Board of Directors or the Chief Executive Officer. Any Assistant Treasurer shall have such powers and perform such duties as the Board of Directors or the Chief Executive Officer may from time to time designate.

SECTION 14. Secretary and Assistant Secretaries. The Secretary shall record all the proceedings of the meetings of the stockholders and the Board of Directors (including committees of the Board of Directors) in books kept for that purpose. In his or her absence from any such meeting, a temporary secretary chosen at the meeting shall record the proceedings thereof. The Secretary shall have charge of the stock ledger (which may, however, be kept by any transfer or other agent of the Corporation). The Secretary shall have custody of the seal of the Corporation, and the Secretary, or an Assistant Secretary shall have authority to affix it to any instrument requiring it, and, when so affixed, the seal may be attested by his or her signature or that of an Assistant Secretary. The Secretary shall have such other duties and powers as may be designated from time to time by the Board of Directors or the Chief Executive Officer. In the absence of the Secretary, any Assistant Secretary may perform his or her duties and responsibilities. Any Assistant Secretary shall have such powers and perform such duties as the Board of Directors or the Chief Executive Officer may from time to time designate.

SECTION 15. Other Powers and Duties. Subject to these By-laws and to such limitations as the Board of Directors may from time to time prescribe, the officers of the Corporation shall each have such powers and duties as generally pertain to their respective offices, as well as such powers and duties as from time to time may be conferred by the Board of Directors or the Chief Executive Officer.

ARTICLE IV

Capital Stock

SECTION 1. Certificates of Stock. Each stockholder shall be entitled to a certificate of the capital stock of the Corporation in such form as may from time to time be prescribed by the Board of Directors. Such certificate shall be signed by any two authorized officers of the Corporation. The Corporation seal and the signatures by the Corporation's officers, the transfer agent or the registrar may be facsimiles. In case any officer, transfer agent or registrar who has signed or whose facsimile signature has been placed on such certificate shall have ceased to be such officer, transfer agent or registrar before such certificate is issued, it may be issued by the Corporation with the same effect as if he or she were such officer, transfer agent or registrar at the time of its issue. Every certificate for shares of stock which are subject to any restriction on transfer and every certificate issued when the Corporation is authorized to issue more than one class or series of stock shall contain such legend with respect thereto as is required by law. Notwithstanding anything to the contrary provided in these By-laws, the Board of Directors of the Corporation may provide by resolution or resolutions that some or all of any or all classes or

series of its stock shall be uncertificated shares (except that the foregoing shall not apply to shares represented by a certificate until such certificate is surrendered to the Corporation), and by the approval and adoption of these By-laws the Board of Directors has determined that all classes or series of the Corporation's stock may be uncertificated, whether upon original issuance, re-issuance, or subsequent transfer.

SECTION 2. Transfers. Subject to any restrictions on transfer and unless otherwise provided by the Board of Directors, shares of stock that are represented by a certificate may be transferred on the books of the Corporation by the surrender to the Corporation or its transfer agent of the certificate theretofore properly endorsed or accompanied by a written assignment or power of attorney properly executed, with transfer stamps (if necessary) affixed, and with such proof of the authenticity of signature as the Corporation or its transfer agent may reasonably require. Shares of stock that are not represented by a certificate may be transferred on the books of the Corporation by submitting to the Corporation or its transfer agent such evidence of transfer and following such other procedures as the Corporation or its transfer agent may require.

SECTION 3. Record Holders. Except as may otherwise be required by law, by the Certificate or by these By-laws, the Corporation shall be entitled to treat the record holder of stock as shown on its books as the owner of such stock for all purposes, including the payment of dividends and the right to vote with respect thereto, regardless of any transfer, pledge or other disposition of such stock, until the shares have been transferred on the books of the Corporation in accordance with the requirements of these By-laws.

SECTION 4. Record Date. In order that the Corporation may determine the stockholders entitled to notice of or to vote at any meeting of stockholders or any adjournment thereof or entitled to receive payment of any dividend or other distribution or allotment of any rights, or entitled to exercise any rights in respect of any change, conversion or exchange of stock or for the purpose of any other lawful action, the Board of Directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which record date: (a) in the case of determination of stockholders entitled to vote at any meeting of stockholders, shall, unless otherwise required by law, not be more than sixty (60) nor less than ten (10) days before the date of such meeting and (b) in the case of any other action, shall not be more than sixty (60) days prior to such other action. If no record date is fixed: (i) the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day next preceding the day on which notice is given, or, if notice is waived, at the close of business on the day next preceding the day on which the meeting is held; and (ii) the record date for determining stockholders for any other purpose shall be at the close of business on the day on which the Board of Directors adopts the resolution relating thereto.

SECTION 5. Replacement of Certificates. In case of the alleged loss, destruction or mutilation of a certificate of stock of the Corporation, a duplicate certificate may be issued in place thereof, upon such terms as the Board of Directors may prescribe.

ARTICLE V

Indemnification

SECTION 1. Definitions. For purposes of this Article:

(a) “Corporate Status” describes the status of a person who is serving or has served (i) as a Director of the Corporation, (ii) as an Officer of the Corporation, (iii) as a Non-Officer Employee of the Corporation, or (iv) as a director, partner, trustee, officer, employee or agent of any other corporation, partnership, limited liability company, joint venture, trust, employee benefit plan, foundation, association, organization or other legal entity which such person is or was serving at the request of the Corporation. For purposes of this Section 1(a), a Director, Officer or Non-Officer Employee of the Corporation who is serving or has served as a director, partner, trustee, officer, employee or agent of a Subsidiary shall be deemed to be serving at the request of the Corporation. Notwithstanding the foregoing, “Corporate Status” shall not include the status of a person who is serving or has served as a director, officer, employee or agent of a constituent corporation absorbed in a merger or consolidation transaction with the Corporation with respect to such person’s activities prior to said transaction, unless specifically authorized by the Board of Directors or the stockholders of the Corporation;

(b) “Director” means any person who serves or has served the Corporation as a director on the Board of Directors of the Corporation;

(c) “Disinterested Director” means, with respect to each Proceeding in respect of which indemnification is sought hereunder, a Director of the Corporation who is not and was not a party to such Proceeding;

(d) “Expenses” means all attorneys’ fees, retainers, court costs, transcript costs, fees of expert witnesses, private investigators and professional advisors (including, without limitation, accountants and investment bankers), travel expenses, duplicating costs, printing and binding costs, costs of preparation of demonstrative evidence and other courtroom presentation aids and devices, costs incurred in connection with document review, organization, imaging and computerization, telephone charges, postage, delivery service fees, and all other disbursements, costs or expenses of the type customarily incurred in connection with prosecuting, defending, preparing to prosecute or defend, investigating, being or preparing to be a witness in, settling or otherwise participating in, a Proceeding;

(e) “Liabilities” means judgments, damages, liabilities, losses, penalties, excise taxes, fines and amounts paid in settlement;

(f) “Non-Officer Employee” means any person who serves or has served as an employee or agent of the Corporation, but who is not or was not a Director or Officer;

(g) “Officer” means any person who serves or has served the Corporation as an officer of the Corporation appointed by the Board of Directors of the Corporation;

(h) “Proceeding” means any threatened, pending or completed action, suit, arbitration, alternate dispute resolution mechanism, inquiry, investigation, administrative hearing or other proceeding, whether civil, criminal, administrative, arbitral or investigative; and

(i) “Subsidiary” shall mean any corporation, partnership, limited liability company, joint venture, trust or other entity of which the Corporation owns (either directly or through or together with another Subsidiary of the Corporation) either (i) a general partner, managing member or other similar interest or (ii) (A) fifty percent (50%) or more of the voting power of the voting capital equity interests of such corporation, partnership, limited liability company, joint venture or other entity, or (B) fifty percent (50%) or more of the outstanding voting capital stock or other voting equity interests of such corporation, partnership, limited liability company, joint venture or other entity.

SECTION 2. Indemnification of Directors and Officers.

(a) Subject to the operation of Section 4 of this Article V of these By-laws, each Director and Officer shall be indemnified and held harmless by the Corporation to the fullest extent authorized by the DGCL, as the same exists or may hereafter be amended (but, in the case of any such amendment, only to the extent that such amendment permits the Corporation to provide broader indemnification rights than such law permitted the Corporation to provide prior to such amendment), and to the extent authorized in this Section 2.

(1) Actions, Suits and Proceedings Other than By or In the Right of the Corporation. Each Director and Officer shall be indemnified and held harmless by the Corporation against any and all Expenses and Liabilities that are incurred or paid by such Director or Officer or on such Director’s or Officer’s behalf in connection with any Proceeding or any claim, issue or matter therein (other than an action by or in the right of the Corporation), which such Director or Officer is, or is threatened to be made, a party to or participant in by reason of such Director’s or Officer’s Corporate Status, if such Director or Officer acted in good faith and in a manner such Director or Officer reasonably believed to be in or not opposed to the best interests of the Corporation and, with respect to any criminal proceeding, had no reasonable cause to believe his or her conduct was unlawful.

(2) Actions, Suits and Proceedings By or In the Right of the Corporation. Each Director and Officer shall be indemnified and held harmless by the Corporation against any and all Expenses that are incurred by such Director or Officer or on such Director’s or Officer’s behalf in connection with any Proceeding or any claim, issue or matter therein by or in the right of the Corporation, which such Director or Officer is, or is threatened to be made, a party to or participant in by reason of such Director’s or Officer’s Corporate Status, if such Director or Officer acted in good faith and in a manner such Director or Officer reasonably believed to be in or not opposed to the best interests of the Corporation; provided, however, that no indemnification shall be made under this Section 2(a)(2) in respect of any claim, issue or matter as to which such Director or Officer shall have been finally adjudged by a court of competent jurisdiction to be liable to the Corporation, unless, and only to the extent that, the Court of Chancery or another

court in which such Proceeding was brought shall determine upon application that, despite adjudication of liability, but in view of all the circumstances of the case, such Director or Officer is fairly and reasonably entitled to indemnification for such Expenses that such court deems proper.

(3) Survival of Rights. The rights of indemnification provided by this Section 2 shall continue as to a Director or Officer after he or she has ceased to be a Director or Officer and shall inure to the benefit of his or her heirs, executors, administrators and personal representatives.

(4) Actions by Directors or Officers. Notwithstanding the foregoing, the Corporation shall indemnify any Director or Officer seeking indemnification in connection with a Proceeding initiated by such Director or Officer only if such Proceeding (including any parts of such Proceeding not initiated by such Director or Officer) was authorized in advance by the Board of Directors of the Corporation, unless such Proceeding was brought to enforce such Officer's or Director's rights to indemnification or, in the case of Directors, advancement of Expenses under these By-laws in accordance with the provisions set forth herein.

SECTION 3. Indemnification of Non-Officer Employees. Subject to the operation of Section 4 of this Article V of these By-laws, each Non-Officer Employee may, in the discretion of the Board of Directors of the Corporation, be indemnified by the Corporation to the fullest extent authorized by the DGCL, as the same exists or may hereafter be amended, against any or all Expenses and Liabilities that are incurred by such Non-Officer Employee or on such Non-Officer Employee's behalf in connection with any threatened, pending or completed Proceeding, or any claim, issue or matter therein, which such Non-Officer Employee is, or is threatened to be made, a party to or participant in by reason of such Non-Officer Employee's Corporate Status, if such Non-Officer Employee acted in good faith and in a manner such Non-Officer Employee reasonably believed to be in or not opposed to the best interests of the Corporation and, with respect to any criminal proceeding, had no reasonable cause to believe his or her conduct was unlawful. The rights of indemnification provided by this Section 3 shall exist as to a Non-Officer Employee after he or she has ceased to be a Non-Officer Employee and shall inure to the benefit of his or her heirs, personal representatives, executors and administrators. Notwithstanding the foregoing, the Corporation may indemnify any Non-Officer Employee seeking indemnification in connection with a Proceeding initiated by such Non-Officer Employee only if such Proceeding was authorized in advance by the Board of Directors of the Corporation.

SECTION 4. Determination. Unless ordered by a court, no indemnification shall be provided pursuant to this Article V to a Director, to an Officer or to a Non-Officer Employee unless a determination shall have been made that such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the Corporation and, with respect to any criminal Proceeding, such person had no reasonable cause to believe his or her conduct was unlawful. Such determination shall be made by (a) a majority vote of the Disinterested Directors, even though less than a quorum of the Board of Directors, (b) a

committee comprised of Disinterested Directors, such committee having been designated by a majority vote of the Disinterested Directors (even though less than a quorum), (c) if there are no such Disinterested Directors, or if a majority of Disinterested Directors so directs, by independent legal counsel in a written opinion, or (d) by the stockholders of the Corporation.

SECTION 5. Advancement of Expenses to Directors Prior to Final Disposition.

(a) The Corporation shall advance all Expenses incurred by or on behalf of any Director in connection with any Proceeding in which such Director is involved by reason of such Director's Corporate Status within thirty (30) days after the receipt by the Corporation of a written statement from such Director requesting such advance or advances from time to time, whether prior to or after final disposition of such Proceeding. Such statement or statements shall reasonably evidence the Expenses incurred by such Director and shall be preceded or accompanied by an undertaking by or on behalf of such Director to repay any Expenses so advanced if it shall ultimately be determined that such Director is not entitled to be indemnified against such Expenses. Notwithstanding the foregoing, the Corporation shall advance all Expenses incurred by or on behalf of any Director seeking advancement of expenses hereunder in connection with a Proceeding initiated by such Director only if such Proceeding (including any parts of such Proceeding not initiated by such Director) was (i) authorized by the Board of Directors of the Corporation, or (ii) brought to enforce such Director's rights to indemnification or advancement of Expenses under these By-laws.

(b) If a claim for advancement of Expenses hereunder by a Director is not paid in full by the Corporation within thirty (30) days after receipt by the Corporation of documentation of Expenses and the required undertaking, such Director may at any time thereafter bring suit against the Corporation to recover the unpaid amount of the claim and if successful in whole or in part, such Director shall also be entitled to be paid the expenses of prosecuting such claim. The failure of the Corporation (including its Board of Directors or any committee thereof, independent legal counsel, or stockholders) to make a determination concerning the permissibility of such advancement of Expenses under this Article V shall not be a defense to an action brought by a Director for recovery of the unpaid amount of an advancement claim and shall not create a presumption that such advancement is not permissible. The burden of proving that a Director is not entitled to an advancement of expenses shall be on the Corporation.

(c) In any suit brought by the Corporation to recover an advancement of expenses pursuant to the terms of an undertaking, the Corporation shall be entitled to recover such expenses upon a final adjudication that the Director has not met any applicable standard for indemnification set forth in the DGCL.

SECTION 6. Advancement of Expenses to Officers and Non-Officer Employees Prior to Final Disposition.

(a) The Corporation may, at the discretion of the Board of Directors of the Corporation, advance any or all Expenses incurred by or on behalf of any Officer or any Non-Officer Employee in connection with any Proceeding in which such person is involved by reason of his or her Corporate Status as an Officer or Non-Officer Employee upon the receipt by the

Corporation of a statement or statements from such Officer or Non-Officer Employee requesting such advance or advances from time to time, whether prior to or after final disposition of such Proceeding. Such statement or statements shall reasonably evidence the Expenses incurred by such Officer or Non-Officer Employee and shall be preceded or accompanied by an undertaking by or on behalf of such person to repay any Expenses so advanced if it shall ultimately be determined that such Officer or Non-Officer Employee is not entitled to be indemnified against such Expenses.

(b) In any suit brought by the Corporation to recover an advancement of expenses pursuant to the terms of an undertaking, the Corporation shall be entitled to recover such expenses upon a final adjudication that the Officer or Non-Officer Employee has not met any applicable standard for indemnification set forth in the DGCL.

SECTION 7. Contractual Nature of Rights.

(a) The provisions of this Article V shall be deemed to be a contract between the Corporation and each Director and Officer entitled to the benefits hereof at any time while this Article V is in effect, in consideration of such person's past or current and any future performance of services for the Corporation. Neither amendment, repeal or modification of any provision of this Article V nor the adoption of any provision of the Certificate inconsistent with this Article V shall eliminate or reduce any right conferred by this Article V in respect of any act or omission occurring, or any cause of action or claim that accrues or arises or any state of facts existing, at the time of or before such amendment, repeal, modification or adoption of an inconsistent provision (even in the case of a proceeding based on such a state of facts that is commenced after such time), and all rights to indemnification and advancement of Expenses granted herein or arising out of any act or omission shall vest at the time of the act or omission in question, regardless of when or if any proceeding with respect to such act or omission is commenced. The rights to indemnification and to advancement of expenses provided by, or granted pursuant to, this Article V shall continue notwithstanding that the person has ceased to be a director or officer of the Corporation and shall inure to the benefit of the estate, heirs, executors, administrators, legatees and distributees of such person.

(b) If a claim for indemnification hereunder by a Director or Officer is not paid in full by the Corporation within sixty (60) days after receipt by the Corporation of a written claim for indemnification, such Director or Officer may at any time thereafter bring suit against the Corporation to recover the unpaid amount of the claim, and if successful in whole or in part, such Director or Officer shall also be entitled to be paid the expenses of prosecuting such claim. The failure of the Corporation (including its Board of Directors or any committee thereof, independent legal counsel, or stockholders) to make a determination concerning the permissibility of such indemnification under this Article V shall not be a defense to an action brought by a Director or Officer for recovery of the unpaid amount of an indemnification claim and shall not create a presumption that such indemnification is not permissible. The burden of proving that a Director or Officer is not entitled to indemnification shall be on the Corporation.

(c) In any suit brought by a Director or Officer to enforce a right to indemnification hereunder, it shall be a defense that such Director or Officer has not met any applicable standard for indemnification set forth in the DGCL.

SECTION 8. Non-Exclusivity of Rights. The rights to indemnification and to advancement of Expenses set forth in this Article V shall not be exclusive of any other right which any Director, Officer, or Non-Officer Employee may have or hereafter acquire under any statute, provision of the Certificate or these By-laws, agreement, vote of stockholders or Disinterested Directors or otherwise.

SECTION 9. Insurance. The Corporation may maintain insurance, at its expense, to protect itself and any Director, Officer or Non-Officer Employee against any liability of any character asserted against or incurred by the Corporation or any such Director, Officer or Non-Officer Employee, or arising out of any such person's Corporate Status, whether or not the Corporation would have the power to indemnify such person against such liability under the DGCL or the provisions of this Article V.

SECTION 10. Other Indemnification. The Corporation's obligation, if any, to indemnify or provide advancement of Expenses to any person under this Article V as a result of such person serving, at the request of the Corporation, as a director, partner, trustee, officer, employee or agent of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise shall be reduced by any amount such person may collect as indemnification or advancement of Expenses from such other corporation, partnership, joint venture, trust, employee benefit plan or enterprise (the "Primary Indemnitor"). Any indemnification or advancement of Expenses under this Article V owed by the Corporation as a result of a person serving, at the request of the Corporation, as a director, partner, trustee, officer, employee or agent of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise shall only be in excess of, and shall be secondary to, the indemnification or advancement of Expenses available from the applicable Primary Indemnitor(s) and any applicable insurance policies.

ARTICLE VI

Miscellaneous Provisions

SECTION 1. Fiscal Year. The fiscal year of the Corporation shall be determined by the Board of Directors.

SECTION 2. Seal. The Board of Directors shall have power to adopt and alter the seal of the Corporation.

SECTION 3. Execution of Instruments. All deeds, leases, transfers, contracts, bonds, notes and other obligations to be entered into by the Corporation in the ordinary course of its business without director action may be executed on behalf of the Corporation by the Chairman of the Board, if one is elected, the President or the Treasurer or any other officer, employee or

agent of the Corporation as the Board of Directors or the executive committee of the Board may authorize.

SECTION 4. Voting of Securities. Unless the Board of Directors otherwise provides, the Chairman of the Board, if one is elected, the President or the Treasurer may waive notice of and act on behalf of the Corporation (including with regard to voting and actions by written consent), or appoint another person or persons to act as proxy or attorney in fact for the Corporation with or without discretionary power and/or power of substitution, at any meeting of stockholders or shareholders of any other corporation or organization, any of whose securities are held by the Corporation.

SECTION 5. Resident Agent. The Board of Directors may appoint a resident agent upon whom legal process may be served in any action or proceeding against the Corporation.

SECTION 6. Corporate Records. The original or attested copies of the Certificate, By-laws and records of all meetings of the incorporators, stockholders and the Board of Directors and the stock transfer books, which shall contain the names of all stockholders, their record addresses and the amount of stock held by each, may be kept outside the State of Delaware and shall be kept at the principal office of the Corporation, at an office of its counsel, at an office of its transfer agent or at such other place or places as may be designated from time to time by the Board of Directors.

SECTION 7. Certificate. All references in these By-laws to the Certificate shall be deemed to refer to the Third Amended and Restated Certificate of Incorporation of the Corporation, as amended and/or restated and in effect from time to time.

SECTION 8. Exclusive Jurisdiction of Delaware Courts or the United States Federal District Courts. Unless the Corporation consents in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on behalf of the Corporation, (ii) any action asserting a claim of, or a claim based on, a breach of a fiduciary duty owed by any current or former director, officer or other employee of the Corporation to the Corporation or the Corporation's stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law or the Certificate or By-laws (including the interpretation, validity or enforceability thereof), or (iv) any action asserting a claim governed by the internal affairs doctrine. Unless the Corporation consents in writing to the selection of an alternative forum, the federal district courts of the United States of America shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act of 1933, as amended. Any person or entity purchasing or otherwise acquiring any interest in shares of capital stock of the Corporation shall be deemed to have notice of and consented to the provisions of this Section 8.

SECTION 9. Amendment of By-laws.

(a) Amendment by Directors. Except as provided otherwise by law, these By-laws may be amended or repealed by the Board of Directors by the affirmative vote of a majority of the directors then in office.

(b) Amendment by Stockholders. Except as otherwise required by these By-laws or by law, these By-laws may be amended or repealed at any Annual Meeting, or special meeting of stockholders called for such purpose in accordance with these By-laws, by the affirmative vote of a majority of the outstanding shares entitled to vote on such amendment or repeal, voting together as a single class. Notwithstanding the foregoing, stockholder approval shall not be required unless mandated by the Certificate, these By-laws, or other applicable law.

SECTION 10. Notices. If mailed, notice to stockholders shall be deemed given when deposited in the mail, postage prepaid, directed to the stockholder at such stockholder's address as it appears on the records of the Corporation. Without limiting the manner by which notice otherwise may be given to stockholders, any notice to stockholders may be given by electronic transmission in the manner provided in Section 232 of the DGCL.

SECTION 11. Waivers. A written waiver of any notice, signed by a stockholder or director, or waiver by electronic transmission by such person, whether given before or after the time of the event for which notice is to be given, shall be deemed equivalent to the notice required to be given to such person. Neither the business to be transacted at, nor the purpose of, any meeting need be specified in such a waiver.

Adopted February 9th, 2022 and effective as of _____ , _____ .