UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

Form 10-K

(Mark One)

☑ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2023
OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission File Number:
001-41536
PRIME MEDICINE, INC.
(Exact name of registrant as specified in its charter)

Delaware	**84-3097762**
(State or other jurisdiction of incorporation or organization)	*(IRS Employer Identification No.)*
21 Erie Street, Cambridge, MA	**02139**
(Address of principal executive offices)	*(Zip Code)*

Registrant's telephone number, including area code:
(617) 564-0013
Securities registered pursuant to Section 12(b) of the Act:

Title of Class	Trading symbol(s)	Name of Exchange on Which Registered
Common stock, par value $0.00001 per share	PRME	Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☑

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☑

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☑ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☑ No ☐

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 Exchange Act.

Large accelerated filer ☐ Accelerated filer ☐ Non-accelerated filer ☑ Smaller reporting company ☑ Emerging growth company ☑

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. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☑

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The Nasdaq Global Market on June 30, 2023, was $603,127,652

As of February 23, 2024, there were 119,939,247 shares of Common Stock, $0.00001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2024 Annual Meeting of Stockholders to be filed pursuant to Regulation 14A within 120 days of the end of the registrant's fiscal year ended December 31, 2023 are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

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References to Prime Medicine

Throughout this Annual Report on Form 10-K, "Prime Medicine," "the Company," "we," "us," and "our," and similar expressions, except where the context requires otherwise, refer to Prime Medicine, Inc. and its consolidated subsidiaries, and "our board of directors" refers to the board of directors of Prime Medicine, Inc.

From time to time we may use our website, our Twitter account (@PrimeMedicine) or our LinkedIn profile at https://www.linkedin.com/company/prime-medicine to distribute material information. Our financial and other material information is routinely posted to and accessible on the Investors section of our website, available at www.primemedicine.com. Investors are encouraged to review the Investors section of our website because we may post material information on that site that is not otherwise disseminated by us. Information that is contained in and can be accessed through our website or our social media is not incorporated into, and does not form a part of, this Annual Report on Form 10-K.We intend to apply for various trademarks that we use in connection with the operation of our business. This Annual Report on Form 10-K 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 Annual Report on Form 10-K 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 Annual Report on Form 10-K may appear without the ®, ^{SM} and ™ 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.

Cautionary Note Regarding Forward-looking Information

This Annual Report on Form 10-K contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, and objectives of management, are forward-looking statements. The words "anticipate," "believe," "envision," "estimate," "expect," "goal," "intend," "may," "plan," "predict," "project," "strategy," "target," "potential," "will," "would," "could," "should," "continue," "contemplate," "vision" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Our business and our forward-looking statements in this Annual Report on Form 10-K involve substantial known and unknown risks and uncertainties, including, among other things, the risks and uncertainties inherent in our statements regarding:

- the initiation, timing, progress and results of our research and development programs, product candidates, 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 current and future 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 areas of focus and any other additional programs we may advance;
- 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 application submissions;
- the ability of our Prime Editing technology to address unmet medical needs in patients;
- the implementation of our strategic plans for our business, programs and technology;
- the scope and duration 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;
- our estimates of our expenses, capital requirements, needs for additional financing;
- the effect of unfavorable macroeconomic conditions or market volatility resulting from global economic conditions, and;
- other risks and uncertainties, including those listed under the caption "Risk Factors."

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in this Annual Report on Form 10-K, particularly in the "Summary Risk Factors" and "Risk Factors" sections, that could cause actual results or events to differ materially from the forward-looking

statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

This Annual Report on Form 10-K includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. All of the market data used in this Annual Report on Form 10-K involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. We believe that the information from these industry publications, surveys and studies is reliable. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of important factors, including those described in the sections titled “Summary Risk Factors” and “Risk Factors.”

Summary of the Material Risks Associated with Our Business

Our business is subject to a number of risks that if realized could materially affect our business, financial condition, results of operations, cash flows and access to liquidity. These risks are discussed more fully in the "Risk Factors" section of this Annual Report on Form 10-K. Our principal risks include the following:

- 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 relatively new technology that has not been extensively 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 current and future 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 current and future 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.
- Our in-licensed issued patents and 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.
- 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.
- 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.
- The FDA, the EMA and the National Institutes of Health, or NIH, have demonstrated caution as well as concern regarding potential long term impacts 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.

PART I

ITEM 1. 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. We are deploying Prime Editing technology, which we believe is a versatile, precise, and efficient gene editing technology.

In the past forty years, the genetic disorders causing many diseases have become more clear. Genetic mutations implicated in disease are diverse and can range from a single base error, which are known as point mutations, to errors that extend from two bases to several to thousands of bases, including multi-base insertions, deletions, duplications, or combinations thereof. Some mutations affect the coding regions of genes while others affect regulatory sequences that control the function of genes and can affect the function of larger biochemical and genetic pathways. Furthermore, as revealed by population-level genomic studies, natural genetic variations are known to protect against or to increase risk of disease. Given these insights, we believe that gene editing has the potential to treat and even cure many human diseases.

The field of genetic medicine has evolved tremendously over the last decade, with groundbreaking advances in gene therapy, cell therapy, ribonucleic acid, or RNA, therapy, and, more recently, gene editing. This past year saw the first CRISPR/Cas9-based gene editing therapy (CASGEVY™) approval by the U.S. Food and Drug Administration, or the FDA, for the treatment of sickle cell disease. These technologies represent significant advancements for genetic therapies but we believe Prime Editing is the only gene editing technology that, by itself, can edit, correct, insert and delete deoxyribonucleic acid, or DNA, sequences in any target tissue. We believe Prime Editing technology has transformative potential that could change the course of how many diseases is treated and overcome the challenges associated with current genetic therapies.

Prime Editing, originally developed by Dr. Liu and Dr. Anzalone and first described in a Nature publication in 2019, has potentially broad therapeutic applications. Prime Editing is the only gene editing technology that can edit, correct, insert and delete DNA sequences in any target tissue. It can correct mutations across many tissues, organs, and cell types, in dividing and non-dividing human cells. 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 tissues, organs and cell types.

In addition, we believe our Prime Assisted Site-Specific Integrase Gene Editing, or PASSIGE™ technology, may enable Prime Editing to insert gene-sized sequences precisely, potentially addressing large patient markets. PASSIGE uses Prime Editing to insert one or more recombinase recognition sequences at precisely chosen locations in the genome. In our preclinical studies, we have shown that a site-specific recombinase can locate the recombinase recognition sequence and carries out DNA recombination, resulting in the desired large DNA sequence insertion 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. Taken together, Prime Editing’s versatile gene editing capabilities have the potential to unlock opportunities across thousands of potential indications.

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 designed to produce 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.

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 built a diversified portfolio of investigational therapeutic programs organized around core areas of focus: hematology and immunology, liver, lung, ocular, and neuromuscular. We are advancing additional programs as potential partnership opportunities.

Recent highlights of the programs in our portfolio include the following:

- PM359, our first product candidate within our hematology area of focus, targets the p47phox variant of chronic granulomatous disease, or CGD, a serious life-threatening disease that presents in childhood. PM359 is comprised of autologous hematopoietic stem cells, or HSC, modified *ex vivo* using Prime Editors that have been designed to correct a high percentage of cells containing the disease-causing mutation. We plan to submit an investigational new drug, or IND, application with the FDA and/or clinical trial application, or CTA, in the first half of 2024. We believe Prime Editing is uniquely well-suited to address this form of CGD. We have completed our preliminary clinical trial design and selected global trial sites to maximize access to patients and expedite enrollment for PM359 clinical trials. In August 2023, we received rare pediatric drug designation, or RPDD, from the FDA for PM359. In addition, in January 2024, we received orphan drug designation, or ODD, from the FDA for PM359.
- Also in our hematology and immunology area of focus, in June 2023, we entered into a research collaboration with Cimeio Therapeutics, Inc., or Cimeio, to combine our Prime Editing platform and Cimeio's Shielded Cell and Immunotherapy Pairs, or SCIP, platform to develop Prime Edited SCIP for genetic diseases, acute myeloid leukemia, and myelodysplastic syndrome. The overall goal of the research is to reduce the toxicity of conditioning regimens and introduce new therapeutic options to meaningfully expand the utility of HSC transplant and enable the *in vivo* selection of edited HSCs to potentially remove the need for transplantation entirely.
- We have demonstrated Prime Editing of cells preclinically at predicted therapeutically relevant levels for all of our leading programs, including Wilson's Disease and Glycogen Storage Disease 1b, or GSD1b, in our liver area of focus, Retinitis Pigmentosa/Rhodopsin, or RHO, in our ocular area of focus, and Friedreich's Ataxia in our neuromuscular area of focus. In 2023, we presented preclinical research across multiple programs, including proof-of-concept data from *in vivo* rodent and large animal studies. Specifically:
    - In October 2023, we reported preclinical data demonstrating the ability of liver-targeted Prime Editors to precisely correct with high efficiency one of the most prevalent disease-causing mutations of GSD1b in non-human primates, or NHPs, and mouse models. These data are the first Prime Editing data in NHPs, which we believe provide further proof-of-concept for our Prime Editing approach to potentially address a wide range of diseases.
    - We presented additional *in vivo* data in October 2023, demonstrating that Prime Editors can efficiently and precisely correct the predominant mutations that cause RHO associated autosomal dominant retinitis pigmentosa. These data suggest that our proprietary dual adeno-associated virus, or AAV, platform can effectively deliver Prime Editors to the eye, with the potential to treat a range of retinal diseases.
- In our lung area of focus, we have expanded our efforts to develop Prime Editors for the treatment of Cystic Fibrosis, or CF, and in January 2024, we entered into a therapeutic development agreement with the Cystic Fibrosis Foundation, or CFF, in which CFF agreed to provide Prime Medicine with up to $15 million to support development of hotspot editing and PASSIGE in CF, as well as our ongoing efforts to develop lipid nanoparticles, or LNPs, for delivery to the lung. Through hotspot editing, we aim to address multiple mutations at mutational hotspots using a small number of Prime Editors, potentially addressing a large percentage of individuals with CF with only a few Prime Editors. In parallel, using PASSIGE, we aim to address nearly all people with CF using a single superexon insertion strategy.
- In our chimeric antigen receptor T cell, or CAR-T, program, we presented preclinical data in December 2023, demonstrating that PASSIGE was greater than 80 percent efficient for non-viral, site-specific delivery of chimeric antigen receptor to primary human T-cells to generate CAR-T cells, and can be

multiplexed with Prime Editing at other target sites by non-viral one-step delivery with no loss of efficiency.

- Lastly, our comprehensive suite of assays used to identify potential off-target events has been expanded to include new, unbiased genome-wide tools. These analyses have continued to demonstrate minimal to no detectable off-target edits, chromosomal rearrangements or translocations. No off-target activity has been detected in any of our leading programs, including CGD, Wilson's Disease, GSD1b, and RHO. We believe these preliminary analyses, across multiple editing programs, suggest a potentially best-in-class safety profile.
- 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 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 programs rely on three distinct delivery methodologies: (a) electroporation for efficient delivery to blood cells and immune cells *ex vivo*; (b) lipid nanoparticle, or LNP, 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, ear, and the central nervous system, or CNS, and muscle.
- We believe the modularity of our platform means that we will be able to accelerate our ongoing efforts and enable rapid generation of new product candidates. We believe the core components, such as Prime Editors, delivery, manufacturing, off-target assays, clinical, and regulatory can be leveraged to drive acceleration, efficiency and execution of our pipeline.

Team

We began operations in the summer of 2020, after being co-founded by David Liu, Ph.D., a world-renowned leader in the field of gene editing, along with co-founder Andrew Anzalone, M.D., Ph.D., who conceived of and developed Prime Editing along with Dr. Liu and others. Dr. Anzalone joined as our Head of Platform Development with years of experience in Prime Editing. Keith Gottesdiener, M.D., joined in 2020 as our President and Chief Executive Officer. Drawn by the promise of Prime Editing's ability to transform the field of gene editing, we have since assembled a diverse and growing team that has grown to approximately 230 as of December 31, 2023, with all key functional leadership and employees in place. Our research, technical, and clinical development teams consist 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, the manufacturing and delivery of genetic medicines, and clinical medicine and regulatory affairs.

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 gene editing and related technology for human therapeutic or prophylactic uses.

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.

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. 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.** 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. We have built a cross-disciplinary team consisting 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 programs into the clinic, initially focused on genetic diseases that we believe have a fast, direct path to treating patients, and those with high unmet need not currently addressable using other gene-editing approaches. Within our neuromuscular programs, for example, 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 we believe 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. Over time, we intend to push new and innovative technological developments to maximize Prime Editing's versatile therapeutic potential, and unlock broad opportunities beyond the genetic diseases in our initial pipeline, potentially including immunological diseases, cancers, infectious diseases, and targeting genetic risk factors in common diseases.
- **Advance our pipeline while simultaneously enhancing, validating and enabling our modular platform.** We have established a diverse pipeline of investigational therapeutic programs organized around core areas of focus: hematology and immunology, liver, lung, ocular, and neuromuscular. In addition, we are advancing additional programs, such as CAR-T, as potential partnership opportunities. We have designed a modular platform within each core area, which we believe will accelerate our ongoing efforts and enable rapid generation of new product candidates. We believe the core components, such as Prime Editors, off-target assays, delivery, manufacturing, clinical, and regulatory can be leveraged to accelerate our pipeline to clinical trials and potential approval.

  To unlock the full potential of our Prime Editing technology across our areas of focus, we are pursuing numerous clinically validated delivery modalities in parallel. For a given tissue type, we intend to use the delivery modality with the most compelling biodistribution and Prime Editing efficiency. We are currently focusing on three delivery modalities: (a) electroporation for delivery to blood cells and immune cells *ex vivo*; (b) LNP for non-viral *in vivo* delivery to the liver, lung and potentially other organs in the future; and (c) AAV for viral *in vivo* delivery to the eye, ear, and potentially the central nervous system, lung and muscle. Our goal is to develop highly modular delivery systems that allow us to rapidly develop new products targeting the same cells/tissues/organs by leveraging the approaches and data that precedes them.
- **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.
- **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 of our programs. Given the broad potential of our technology, we intend business development to play an important role in building Prime Medicine, with the goal of accelerating our pipeline, bolstering our financial resources, and maximizing the potential of Prime Editing. Our overall partnership strategy includes: 1) partnering within our core areas to accelerate and globalize our current pipeline programs at the "right" stage of development; 2) outside our core areas,

entering into collaboration or license agreements for programs now that we would not otherwise pursue in the near term; and 3) accessing enabling innovations, such as delivery and manufacturing capabilities.

- **Lead with our culture of integrity, ethics, innovation and respect 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. To push the boundaries of where gene editing can go, we are committed to jointly defining and maintaining a culture that is transparent, develops trust, values integrity and ethics, puts patients first, is science and data driven, and encourages innovation.

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 the mRNA vaccine for COVID-19. More recently, the first generation of CRISPR-Cas based gene editing approaches for gene disruption have demonstrated evidence of the ability to address diseases caused by genetic mutations, via either *in vivo* or *ex vivo* delivery to humans. In 2023, the first CRISPR/Cas9-based therapy (CASGEVY™) was approved by the FDA for the treatment of sickle cell disease, followed soon after by its approval for use in beta-thalassemia. In addition to first generation CRISPR approaches, several base editing investigational medicines, which enable targeted introduction of certain point mutations, have received IND clearance by the FDA, and clinical trials have begun.

Current Challenges for the Field of Genetic Medicines

Despite significant progress within gene therapy, cell therapy, and RNA therapeutics, 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.

Non-Targeted Gene Therapy

Non-targeted gene therapy includes using viral vectors, such as 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 copies of genes or parts of genes into cells in a non-targeted manner. While having some important benefits, non-targeted gene therapy approaches have many key limitations. Certain non-integrating viral vectors, such as AAV, may have limited durability, and pre-existing immunity to the vectors could limit their use and ability to be re-dosed. For approaches that integrate genes, including transposons, retrotransposons, and retroviral vectors, gene integration may occur randomly at hundreds or thousands of sites in the human genome because it is not currently possible to direct their integration to a specific, desired genetic location. Randomly integrating approaches also carry the risk of insertional mutagenesis. In addition, non-targeted gene therapy approaches do not take advantage of normal endogenous regulation of gene expression, and instead lead to variable gene expression due to an inability to fine tune the vector copy number per cell.

Nuclease Gene Editing and Base Editing

First generation gene editing methods rely on a class of enzymes called nucleases, such as CRISPR, ZFNs, engineered meganucleases 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 and randomly creates indels, or 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 have several key limitations. First, there is a lack of predictability in genetic outcomes at the target site in NHEJ, such as randomly creating indels (efficient if the goal is to disrupt or knock out a gene). Using HDR to make corrections, replacements, or insertions has low percentage editing efficiency, does not have the ability to correct genes in non-dividing cells because HDR DNA repair machinery is only expressed in dividing cells, and requires a DNA template with the desired, corrected gene sequence to be delivered simultaneously, which increases complexity.

Nuclease editing also leads to unwanted DNA modifications associated with double-stranded breaks, including cell death response, genomic instability, off-target editing and the potential for oncogenesis. Finally, making multiple edits with nucleases that generate double-stranded breaks at multiple genomic locations has the potential to lead to unwanted large scale translocations and rearrangements, potentially limiting applicability to multiplex 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, while enabling C-to-T or A-to-G base substitutions edits using either a Cytosine Base Editor, or CBE, or Adenine Base Editor, or ABE, respectively.

Base editing has several key limitations. Currently, base editing can reliably correct only four out of 12 possible single base mutations, and base editing cannot make or correct insertion or deletions, which limits the number of diseases base editing can address. Further, each base editor (CBE or ABE) has the ability to correct or introduce only a single point mutation at a specific location. Base editing also has been shown 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 but fall within the editing window. Finally, base editing may have limited optionality for targeting mutations 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 150 papers published in the primary scientific literature to date.

Advantages of our Prime Editing 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.
- Modular for targeting a broad set of mutations, meaning that by redesigning the pegRNA a new mutation can be targeted for correction.
- 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 in an approach we call PASSIGE.

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 extending beyond rare genetic diseases to also potentially include severe, chronic, and acute diseases. In addition to 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

Prime Editors have at least two major components, a Prime Editor protein and a pegRNA. 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. In Prime Editors, programmable DNA binding domains, such as Cas domains, for example Cas9 proteins, are modified such that they do not cause a double-stranded break in the DNA. 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

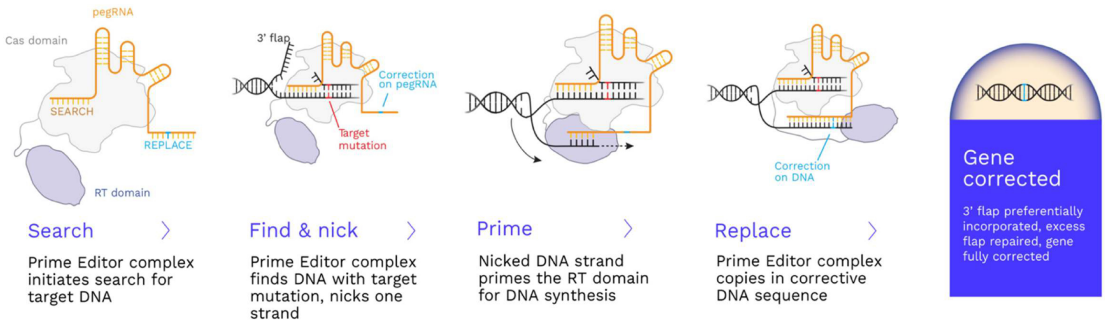
copying from an RNA template. In Prime Editing, the RT domain copies the edited DNA sequence directly into the target genomic site where the edit is made.

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 protein, exemplified using a Cas protein, 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 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



Further Enhancing the Prime Editing Platform

Over the last four 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.

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, long-flap Prime Editing, and PASSIGE.

Dual-flap Prime Editing and long-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 on a target gene, each of the Prime Editors creates a nick in the DNA and creates a flap; the two flaps are often designed to bind tightly to each other. This results in the looping out of the DNA between the Prime Editors, with replacement by 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. 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, as can be applied to our PASSIGE approach.

Additionally, we have developed a long-flap Prime Editing approach that, compared to standard Prime Editing, is designed to more efficiently insert or replace larger stretches of DNA that are a hundred bases or more in length, while also enabling precise deletions of up to thousands of base pairs. Long-flap Prime Editing can be applied for similar applications as dual-flap Prime Editing, including editing of hotspot regions in DNA, insertions of recombinase sites for PASSIGE, and the excision of expanded repeats. Together, dual-flap Prime Editing and long-flap Prime Editing broaden the capabilities of our Prime Editing platform.

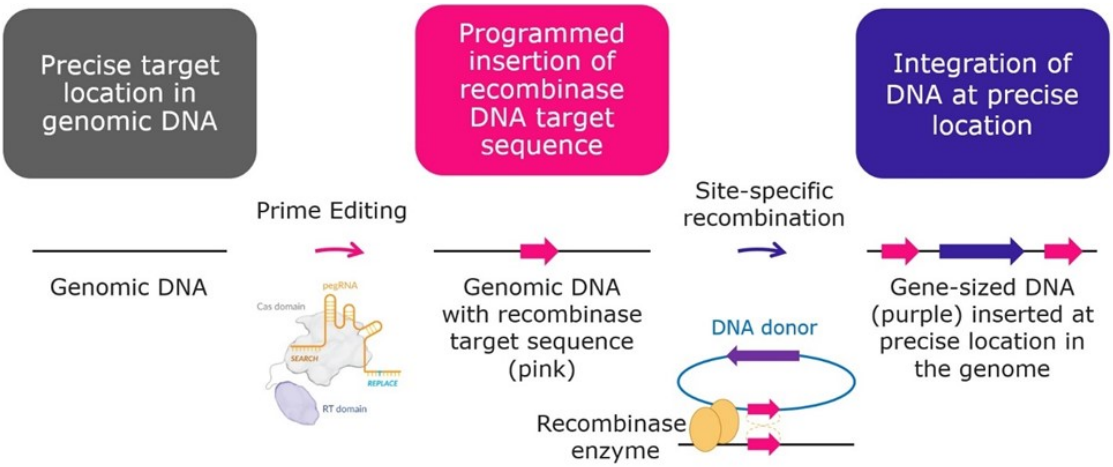
PASSIGE – Precise introduction of gene-sized pieces of DNA into the genome

We have in-licensed from the Broad Institute and are developing a technology that allows us to expand our gene editing toolbox to include programmable insertion, deletion, or inversion of thousands of bases of DNA. By combining Prime Editing with an integrase or site-specific recombinase enzyme, we can harness the precision of Prime Editing with the ability to introduce large gene-sized cargo into the genome as a potential one-time therapy for patients. This proprietary approach expands the versatility of Prime Editing and we believe broadens the range of permanent genomic edits that Prime Editing can make to encompass the ability to insert entire genes precisely into a patient's genome to treat disease. Although site-specific recombinases have been used as biology research tools to perform insertions, deletions or inversions of large pieces of DNA in the genome, their use in therapeutic applications has been limited by the extremely challenging task of engineering site-specific recombinases to be programmable or to target specific sequences in a gene or the genome. PASSIGE technology complements dual-flap Prime Editing, which is able to delete large pieces of DNA up to many kilobases in size, but which currently can only precisely insert a smaller piece of DNA. Therefore, in circumstances where a larger modification is required, this programmable technique can be used to insert or invert multi-kilobase-sized pieces of DNA.

PASSIGE leverages the programmability of Prime Editing to insert recombinase recognition sequences at precisely chosen targeted locations in the genome, as shown in the figure below. A site-specific recombinase, 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.

As shown in the figure below, PASSIGE may be used to insert DNA that contains a therapeutic gene, potentially such as a chimeric antigen receptor, or CAR, or the open reading frame of any other gene. Alternatively, using multiplex Prime Editing, two recombinase DNA target sequences can be inserted so that site-specific recombinases can replace, delete, or invert the intervening DNA sequences. These editing capabilities enable therapeutic opportunities to potentially treat genetic mutations occurring across a large region of DNA sequences within a single gene, and enable therapeutic opportunities to engineer cell therapies to treat disease.

PASSIGE™ – Extending Prime Editing to insert gene sized sequences precisely in the genome



Translating Prime Editors into Product Candidates - Multiple Modalities for Prime Editors

The optimal design and efficient generation of our Prime Editors are fundamental for the development of our pipeline. We have established capabilities to design and optimize our Prime Editors, and to design and develop the components needed for LNPs, vector genomes, Prime Editing of *ex vivo* cells, as well as to develop the manufacturing processes and analytical assays to ensure robust, scalable production of quality intermediates and products to support our programs. Many of these workflows are automated to allow rapid machine learning and/or artificial intelligence-based data analysis, correlation, visualization, and iterative optimization and innovation.

For each program in our pipeline, we determine the best option for delivering the Prime Editor and select the delivery technology with the most compelling biodistribution for a given tissue type. Our initial programs rely on three distinct delivery modalities: (a) electroporation for delivery to blood cells and immune cells *ex vivo*; (b) LNPs, for non-viral *in vivo* delivery to the liver, lung and potentially other organs in the future; and (c) AAVs for viral *in vivo* delivery to the eye and ear, and potentially the central nervous system, lung and muscle. A key feature of Prime Editing and associated delivery methods is the modularity of the technology platforms. Once the first program for each delivery platform is established, the design algorithms, workflows, non-clinical and CMC data, as well as the manufacturing process and majority of assays can be leveraged and applied to the next program which differs only in the pegRNA.

We believe these delivery technologies are foundational to successfully advancing our pipeline programs to the clinic and we are strategically developing our delivery platforms and generating data to accelerate our pipeline progress. Moreover, we continue to assess the many advancements in novel and experimental delivery approaches that are being made in the cell and gene therapy field and intend to license innovative delivery technologies that prove to provide a breakthrough.

We are designing Prime Editing product candidates to provide a “once and done” treatment. Our multi-pronged approach to enable our portfolio includes the following:

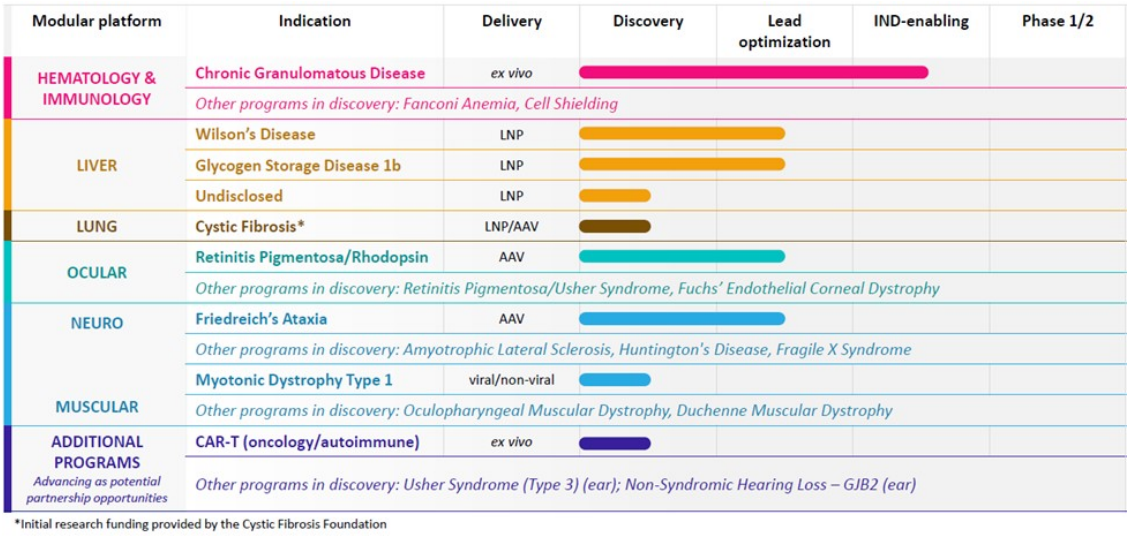
- pegRNA Design, High Throughput Screening and Synthesis: An important element of our capability is leveraging high throughput automated screening and design algorithms to identify optimal pegRNA sequences. The data is also used to develop proprietary machine learning algorithms for pegRNA activity prediction. Internal chemistry capabilities facilitate high-throughput optimization and manufacture of oligonucleotides for *in vivo* studies. We have established internal high-throughput pegRNA synthesis, pegRNA modifications with structure-activity-relationship to improve drug candidate properties, and pegRNA process chemistry.

- Optimization of Prime Editing proteins and recombinase proteins: We have developed internal protein engineering capabilities to optimize the Prime Editor proteins and recombinase proteins (for PASSIGE) for human therapeutic use, and have developed internal mRNA design and optimization, enzymatic chemistry, and process development capabilities to enhance drug candidate properties and characterize the mRNA for efficient, tolerable, and consistent delivery and translation of the Prime Editor protein.
- Prime Editing Specificity and Assays: 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 have developed multiple, complementary, but distinct, methods to measure such possible events. Our approach includes evaluation 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.
- Electroporation: Electroporation is a clinically and commercially validated technology for *ex vivo* delivery to CD34+ cells which utilizes electrical pulses to increase the cell membrane permeability to deliver the Prime Editing components. Electroporation is being used in our CGD program with *ex vivo* CD34+ cells. We have established a modular cell processing manufacturing platform process that can be used for autologous CD34+ cells, and it can be leveraged for the next *ex vivo* HSC programs, as well as for allogeneic T-cells with multiplexing. In the future, we plan to transition to *in vivo* editing of stem cells and other lymphocytes.
- LNP: LNP delivery has initially focused on *in vivo* delivery of Prime Editing to the liver. We have established end-to-end capabilities across our R&D organization consisting of lipid design, lipid synthesis, high throughput LNP discovery from our proprietary lipid library using screening with bar coding technology, LNP formulation process development for tissue targeted delivery, and manufacturing to support our preclinical and IND enabling studies. We are developing a universal liver targeting LNP comprised of 5 components and plan to leverage its modularity for our various programs aimed at Prime Editing in the liver, as well as to address additional mutations within the same indication. Similar approaches are being taken for developing modular LNPs to lung, and HSCs and T cells.
- Viral Delivery: We are using viral delivery to tissues and locations that can currently only be reached with AAV. To enable this delivery approach, we have developed capabilities to design and optimize the vector genome to efficiently deliver Prime Editors to the target tissue. We use our internal AAV Reagent Production Core, analytical development team, as well as outsourced resources and partners to generate AAV Prime Editors, quality control test as well as characterize them.
- Strategic Manufacturing Partnerships: Our overall strategy is to design manufacturing platforms to make the Prime Editing components and associated delivery systems with high throughput, high quality, high purity, modularity, and scalability. We are developing manufacturing processes and analytical methods both internally and partnering with suppliers to ensure the quality and consistency of the Prime Editor components and Prime Edited drug products needed for preclinical studies, IND application submission, and future clinical studies.

Our Pipeline

To maximize the potential of our Prime Editing technology, we have built a diversified portfolio of investigational therapeutic programs organized around core areas of focus: hematology and immunology, liver, lung, ocular, and

neuromuscular. We are advancing additional programs as potential partnership opportunities. The following table summarizes the status of certain of our programs:



*Initial research funding provided by the Cystic Fibrosis Foundation

Our Blood Programs

Chronic Granulomatous Disease

The Disease

Chronic granulomatous disease, or CGD, is a rare inherited hematologic disorder characterized by susceptibility to severe, difficult-to-treat infections, and inflammatory/autoimmune complications. CGD is caused by mutations in any one of the subunits comprising the NADPH oxidase complex, which is required for phagocytic cells, in particular neutrophils, to destroy many invasive microorganisms. CGD causative mutations are estimated to occur between one in 100,000 and one in 200,000 births in the United States, and most children are diagnosed within the first three years of life. Beginning in childhood, patients with CGD develop infections from a range of both typical and unsual bacteria, fungi and mycobacteria. These infections may present in various organ systems, and protracted infections can lead to long-term organ damage and failure. In addition, patients have non-infectious inflammatory disease, most commonly presenting as inflammatory bowel disease, soft tissue granulomas, and strictures of the urinary or digestive tract. Undiagnosed or untreated, the infectious manifestations of CGD are rapidly fatal. Approximately 60 percent of patients with CGD reach age 30 and refractory or antimicrobial resistant infection is the leading cause of mortality.

The NADPH oxidase complex has five domains encoded by five separate genes. Loss-of-function mutations in any of these genes can present as CGD. 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 p47phox protein. More than 78 percent of p47phox CGD patients have a specific, 2-nucleotide deletion, or ΔGT, in the NCF1 gene. The NCF1 gene location is complex, and also contains pseudogenes, or copies of the NCF1 gene that in most healthy individuals, and in individuals with CGD, are inactivated by the ΔGT mutation. Preclinical studies have demonstrated that correcting just one copy of the ΔGT mutation in either the NCF1 gene or any pseudogene restores protein expression and full NADPH oxidase activity.

Our Approach and Results: Direct correction of prevalent CGD mutations or hotspots

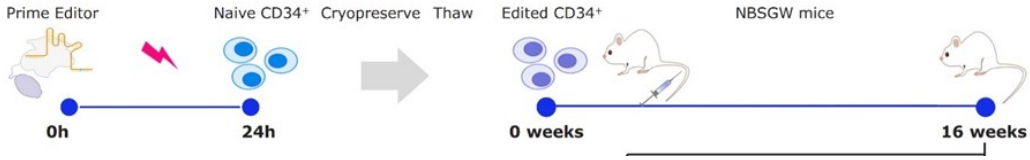
PM359, our first product candidate within our hematology and immunology area of focus, targets the p47phox variant of CGD. We have been able to demonstrate that Prime Editing precisely corrects the ΔGT mutation in the NCF1 gene to restore p47phox protein expression and NADPH oxidase activity. PM359 is comprised of autologous HSCs modified *ex vivo* using Prime Editors that have been designed to correct a high percentage of cells containing

the disease-causing mutation. PM359 is delivered as an autologous HSC transplant, and is designed to restore normal immunologic function in individuals with p47phox CGD, without the risks of graft-versus-host disease, or GVHD, graft rejection and post-transplant immunosuppression associated with allogeneic transplantation.

In order to develop PM359, a therapeutic product candidate to treat patients with p47phox CGD, we screened pegRNA and ngRNA to identify Prime Editing guides and guide pairs that have high activity and perform precise editing at the NCF1 locus. Because healthy donors have NCF1 pseudogenes bearing the same ΔGT mutation, we have been able to utilize healthy donor CD34+ HSCs to demonstrate precise editing of the ΔGT mutation. Using healthy donor CD34+ HSCs we also have been able to demonstrate a very low off-target potential, and robust engraftment and hematopoietic functionality of Prime Edited HSCs in mouse models. We have confirmed these findings using p47phox CGD patient-derived HSCs, and in addition have demonstrated that Prime Editing is able to restore NADPH oxidase activity in patient-derived cells.

The overall process for generating PM359 follows a similar paradigm to that employed by other investigational *ex vivo* HSC CRISPR-Cas9 therapeutics that have been validated in the clinic, with a few notable modifications. The Prime Editor complex is delivered to CD34+ HSCs using electroporation. 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. We believe 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.

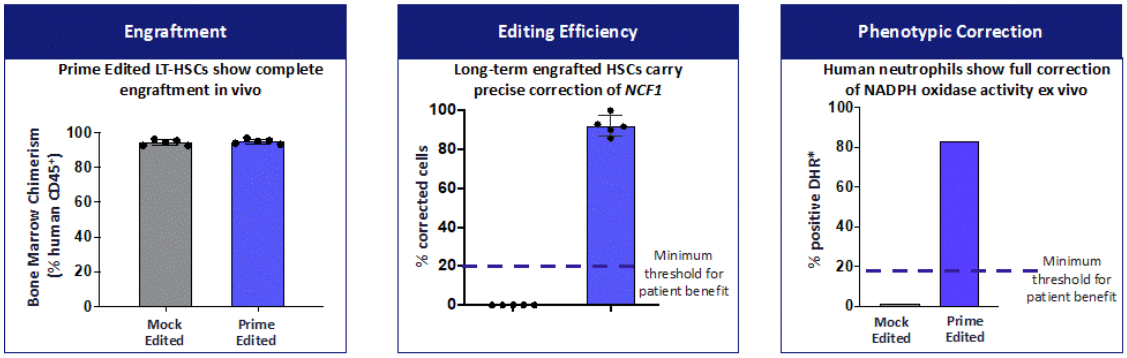
We have identified a Prime Editor complex that is able to correct over 80% of healthy donor CD34+ cells or CGD patient CD34+ cells at at least one ΔGT locus (pseudogene in healthy donor; pseudogene or NCF1 in patient). In order to be able to understand the effects of Prime Editing on the functionality of modified CD34+ cells and to determine the ability of Prime Edited cells to persist *in vivo*, we administered Prime Edited CD34+ cells to a specialized immunocompromised mouse model, the NBSGW mouse, which is capable of supporting engraftment of human HSCs as shown in the figure below. Mice are typically followed for 16 weeks in these experiments to allow for engraftment of the long-term HSCs, repopulation of the immune system by long-term HSCs, and evaluate durability of effect.



When Prime Edited healthy donor or CGD patient CD34+ cells are administered to NBSGW mice, they were able to engraft, and edited cells proliferated to repopulate the hematopoietic system. The left and middle panels in the figure below demonstrate results from a representative experiment in which healthy donor CD34+ cells, either Prime Edited or mock treated, were administered to NBSGW mice. In the left panel of the figure below, human hematopoietic cells, distinguished by the human CD45+ surface marker, were able to successfully engraft at high efficiency, with no differences between mock treated and Prime Edited cells. In the middle panel, after 16 weeks in the mice, long-term engrafted human CD34+ HSCs retained a very high degree of editing: over 80% of cells exhibited correction of the ΔGT mutation at at least one locus, compared to 0% of mock edited cells. Based on natural history studies of carriers of CGD-causative mutations, restoration of p47phox function in a minimum of 20% of neutrophils is believed to be sufficient to confer protection from serious infection with CGD-associated pathogens. Together these data suggest that Prime Editing is able to correct the ΔGT mutation at an efficiency many-fold above the lower bound of the projected threshold for therapeutic benefit, and that Prime Edited cells may effectively home to and stably engraft in the marrow after infusion.

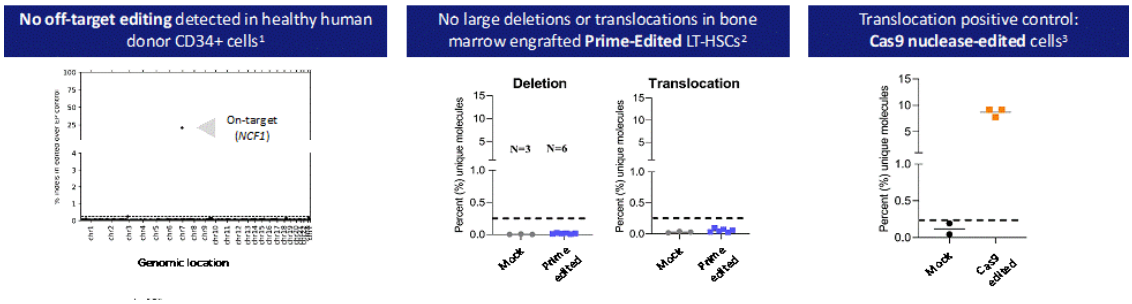
CD34+ HSCs from an individual with p47phox CGD were Prime Edited *ex vivo*, and these cells were differentiated *ex vivo* to allow assessment of NADPH oxidase activity in myeloid progeny. The panel on the right in the figure below demonstrates the results of one commonly used measure of NADPH oxidase activity, the dihyrorhodamine (DHR) assay. Mock edited CGD patient-derived and differentiated cells produced negligible amounts of NADPH oxidase, reflected in the absence of any DHR positive cells. In contrast, NADPH oxidase activity was restored in

approximately 80 percent of Prime Edited CGD patient cells, very closely corresponding to the editing rate observed in healthy donor CD34+ cells in the middle panel. This level significantly exceeds the projected therapeutic minimum threshold of DHR activity in 20 percent of neutrophils thought to be sufficient to prevent serious infection based on natural history studies. Additionally, these results confirm that editing rates in CGD patient derived CD34+ cells are similar to those in healthy donor cells, and that healthy donor cells are a useful proxy for understanding the Prime Editing reagents used to generate PM359.



HSC = hematopoietic stem cell; LT-HSC = long term HSC; DHR = dihydrorhodamine; normalized to healthy donor control. Data presented at ASGCT and ESGCT 2023.

Prime Editing has exhibited a very low level of undesirable genetic changes. Extensive in silico, *ex vivo* and *in vivo* analyses have been performed. The figure below demonstrates representative analyses. In the left panel, 550 of the most likely candidate off-target sites were nominated based on in silico assessment, and interrogated for off-targeting editing in Prime Edited healthy donor CD34+ cells; no significant off-target editing was detected. In the middle panel, the marrow of NBSGW mice receiving either mock or Prime Edited human CD34+ cells was assessed for large deletions or translocations 16 weeks after engraftment; there was no difference between mock treated and Prime Edited cells, and neither had any detectable evidence of deletions or translocation above the level of significance. In the right panel, a human cell line was transfected with spCas9 targeting NCF1 without the Prime Editing machinery. Unlike Prime Editing, spCas9 introduces double strand breaks in DNA as part of its expected mechanism of action. In contrast to the Prime Editor, spCas9 by itself introduced a high rate of translocations.



[1]Analysis of edited CD34+ cells from CGD program: Targeted in vitro Analysis of 550 potential off-target sites of off-target editing. [2]Data from in vivo analysis from mouse bone marrow harvested 16 weeks after engraftment was complete. [3]Positive control.

Overall, the data presented in the two figures above strongly support the clinical evaluation of PM359 in patients with p47phox CGD. We believe these data suggest that PM359 has the potential to meet and exceed the projected mutation correction rate sufficient to achieve disease amelioration, and that PM359 has a low probability of safety events potentially associated with *ex vivo* gene-edited HSC products.

Next Steps

Based on these results, we have selected a development candidate, designated PM359 and are in the process of completing IND-enabling studies with this candidate. We plan to submit an IND and/or CTA with the the FDA, in the first half of 2024. We have completed our preliminary clinical trial design and selected leading CGD transplant centers across the United States and other countries as clinical trial sites to maximize access to patients and expedite enrollment for PM359 clinical studies.

Study Prime-0101 is a planned, multinational, first-in-human trial designed to assess the safety, biological activity and preliminary efficacy of PM359 in adult and pediatric study participants who have p47phox CGD due to the ΔGT mutation in NCF1, and are medically suitable to undergo autologous HSCT. Autologous CD34+ cells will be collected by mobilization and apheresis and transferred to a centralized manufacturing facility, where they will be electroporated with Prime Editing reagents, cryopreserved and quality control tested, to generate PM359. PM359 will be infused after myeloablative conditioning, and study participants will be followed for three years in the primary study, and an additional 12 years as part of the long-term follow-up period. Initial study participants will be adults with stable disease. Once safety and biological activity has been demonstrated in initial participants, the study will enroll participants with active infection or inflammation, as well as adolescent and pediatric participants, under the supervision of a Data Monitoring Committee. Participants will be followed for safety, including engraftment and reconstitution of the hematopoietic system, as well as early biological markers of restored immune function including the DHR assay, and for the long-term resolution and prevention of infectious and inflammatory complications of CGD. We believe PM359 is uniquely well-suited to restore immune function and resolve infectious and inflammatory disease in patients with p47phox CGD.

In August 2023, we received RPDD from the FDA for PM359 for the treatment of CGD. Companies that receive approval for a New Drug Application, or NDA, or Biologics License Application, or BLA, for a rare pediatric disease may be eligible to receive a voucher for priority review of a subsequent marketing application for a different product. If we receive a priority review voucher, it may be used by us or sold to a third party. In addition, in January 2024, we received Orphan Drug designation from the FDA for PM359 for the treatment of CGD.

Other Programs in Discovery

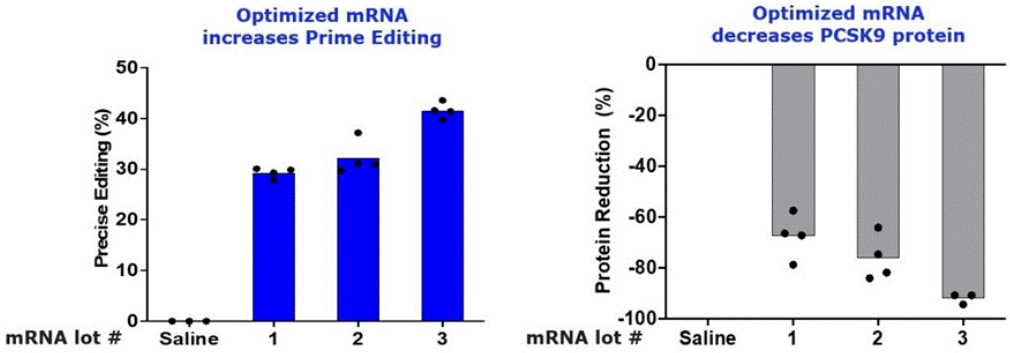
We continue to make progress in other programs in our hematology and immunology area of focus. We are exploring cell shielding to expand our HSC area of focus beyond rare diseases. In June 2023, we entered into a research collaboration with Cimeio to combine our Prime Editing platform and Cimeio's SCIP platform to develop Prime Edited SCIP for genetic diseases, acute myeloid leukemia, and myelodysplastic syndrome. The overall goal of the research is to reduce the toxicity of conditioning regimens and introduce new therapeutic options to meaningfully expand the utility of HSC transplant and enable the *in vivo* selection of edited HSCs to potentially remove the need for transplantation entirely. Additionally, we are also researching Fanconi anemia, a rare and life-threatening DNA repair disorder that arises from loss-of-function mutations in any of 23 genes.

Our Liver Programs

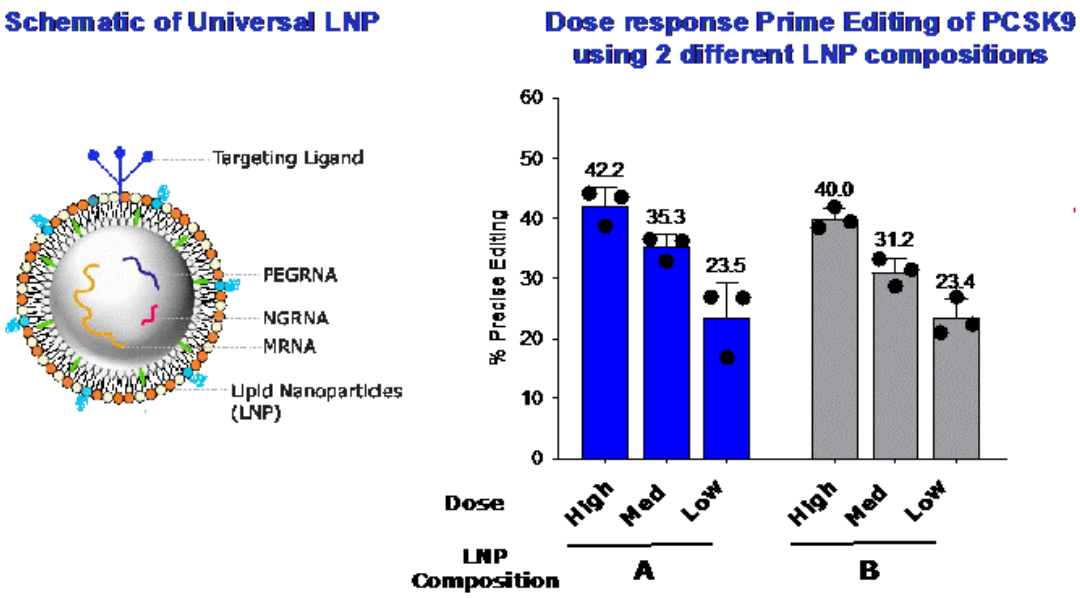
Non-Viral Delivery In Vivo with Lipid Nanoparticles

LNPs are multicomponent and encapsulate the Prime Editor cargo to prevent its degradation by the ubiquitous endonucleases present in biological fluids, thereby enabling the transient delivery and expression of the Prime Editor in cells. We are investing strategically to build our LNP formulations for delivery as a platform technology to enable target tissue delivery. Specifically, we are establishing end-to-end capabilities including design and synthesis of proprietary lipids, high-throughput LNP screening *in vivo* using complementary and orthogonal approaches such as DNA bar coding and next generation sequencing, LNP formulation process development, manufacturing of preclinical formulations, and *in vivo* evaluation of LNP delivered Prime Editors. We are integrating automation, analytical quality control, and characterization data, *in vitro* and *in vivo* preclinical data, along with data knowledge management tools such as machine learning to develop correlative analyses that we believe can expedite LNP discovery and inform drug product formulation development and drug product specification setting. We believe that building an iterative and integrated system will increase efficiencies in identifying potent and safe LNPs capable of delivering Prime Editors to extra-hepatic tissues.

For our first *in vivo* Prime Editor programs, we are building upon learnings from existing LNP technologies to develop a Universal Targeted LNP delivery system that is targeted to the liver, and specifically targets the LNP to the hepatocytes. This approach, we believe, will improve biodistribution to the target cell type. The LNP system will be modular in that simply swapping out the pegRNA (and ngRNA where required) will result in a new product. This approach will allow us to move the existing liver programs in to the clinic quickly and establish proof of concept, and potentially bring forward additional liver programs, quickly thereafter. To develop and optimize the LNP platform, Prime has developed a model system in mice to iteratively study and optimize the properties of our LNP formulations and the Prime Editor cargo. In this system, we inactivate the PCSK9 gene by precisely introducing a stop codon into the gene. PCSK9 protein is a factor controlling lipoprotein uptake into cells from the blood. This system enables us to look at levels of PCSK9 protein in the blood in response to editing. Following optimizations in this system, simply swapping the guide RNAs for PCSK9 Prime Editing for program specific guide RNAs will result in test articles that can be evaluated in humanized mice or in NHPs for the liver programs. Optimization of Prime Editors containing three different mRNA lots were formulated with one of our LNP formulations. One of our optimized mRNA lots showed more than 40 percent editing in whole liver, resulting in more than 90 percent reduction in circulating PCSK9 protein levels.



Panel shows an experiment delivering LNPs to the liver containing a Prime Editor precisely introducing a stop codon into the mouse PCSK9 gene. The experiment tested 3 different mRNA lots. Left graph shows precise editing of PCSK9 at seven days with optimized lots of mRNA. PCSK9 protein levels in the blood dropped by more than 90% of normal following editing, right graph. Note that LNPs deliver primarily to hepatocytes in liver. Therefore, maximum editing possible is predicted to be no more than 60%.



Panel shows a schematic of the Universal targeted LNP encapsulating the Prime Editor drug components (left) and dose responsive whole liver in vivo Prime Editing of the mouse PCSK9 gene using 2 different leading LNP formulations. on experiment delivering LNPs to the liver containing a Prime Editor precisely introducing a stop codon into the mouse PCSK9 gene. Note that the targeted LNPs deliver to hepatocytes in liver. Therefore, maximum editing possible is predicted to be no more than 60%.

Leading Prime Editor LNP formulations resulted in dose responsive Prime Editing of whole liver mouse PCSK9. Following optimizations of the components and their formulations in this system, by swapping only the guide RNAs (pegRNA and ngRNA) for PCSK9 Prime Editor for program specific guide RNAs test articles that can be evaluated in humanized mice or in NHPs for the liver programs, Wilson's Disease and Glycogen Storage Disease.

Wilson's Disease

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 in 10,000 and 1 in 30,000, 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.

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.

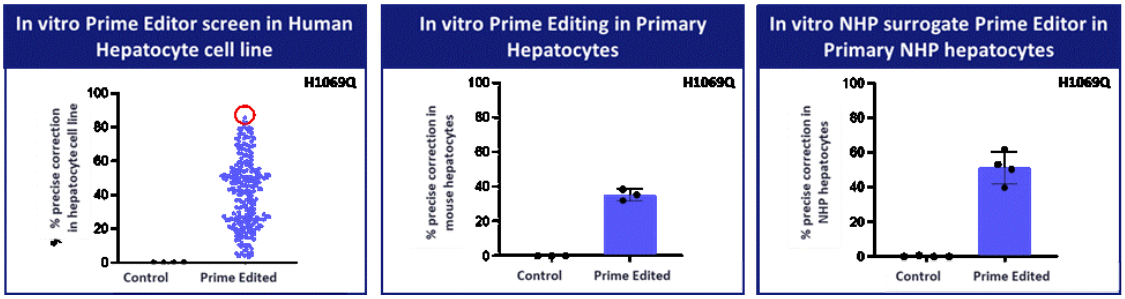
Both of these mutations lie adjacent to hotspots or areas with other pathogenic mutations, for which we are currently designing Prime Editors.

Genotyping of ATP7B is not routinely performed during diagnosis and is used to confirm the symptomatic diagnosis when necessary.

Our Approach and Results: Direct correction of prevalent ATP7B mutations

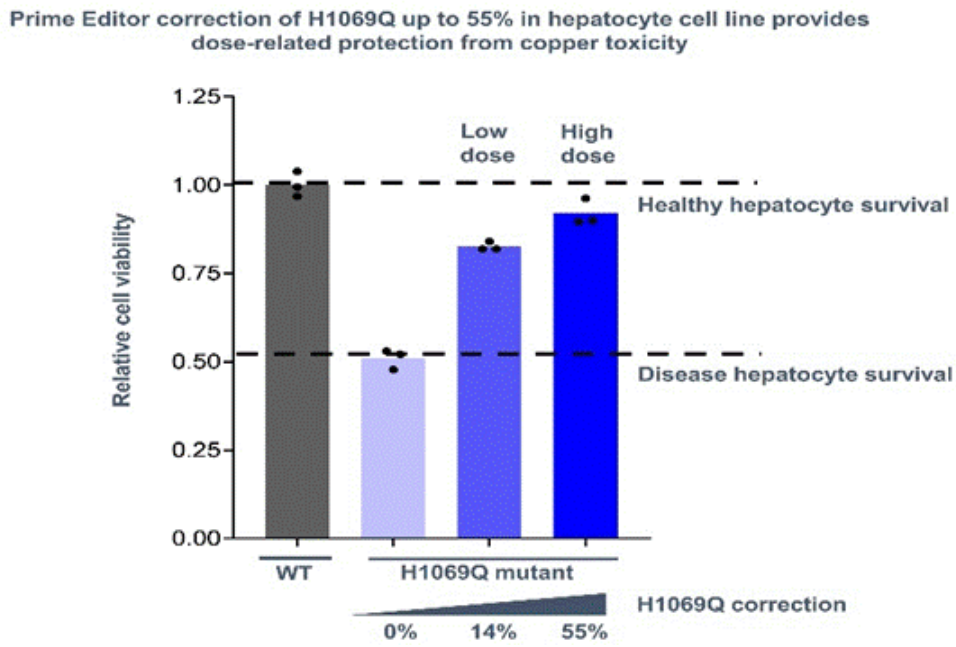
Our initial approach to WD is to correct the prevalent mutations ATP7B H1069Q and R778L in hepatocytes of the liver at their genomic location. A Prime Editor that corrects R778L will also correct R778W and R778G mutations, rarer mutations that are seen in the U.S. and Europe. We are also evaluating hotspot editors in the ATP7B gene region around R778L that could address additional patients. 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 WD mutation, we have identified Prime Editors that demonstrate precise correction of H1069Q ATP7B in approximately 80 percent of cells as shown in the figure below on the left. We have further demonstrated precise correction of approximately 40 percent in primary humanized mouse hepatocytes bearing the human ATP7B gene with the H1069Q mutation, which is shown in the figure below in the middle, and we have also observed approximately 50 percent precise correction using a surrogate Prime Editor in primary NHP hepatocytes, which is shown in the figure below on the right.



Note that each data point in the figure on the left represents the result from a different, individual Prime Editor, and the red circle highlights the best performing Prime Editor, with the average percent precise correction of cells shown in the bar graphs.

This high level of precise editing in primary hepatocytes meets our threshold of 25 to 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.



Initial genome-wide studies using patient cells and human hepatocytes have not identified any detectable off-target editing.

Next Steps

Leveraging our modular universal targeted LNP delivery platform, we are currently conducting preclinical studies to optimize our H1069Q and R778L Prime Editors in humanized mouse models and NHP.

Glycogen Storage Disease 1b

In October 2023, we reported new preclinical data demonstrating the ability of liver-targeted Prime Editors to efficiently and precisely correct one of the most prevalent disease-causing mutations of GSD1b in NHPs and mouse models. These data are the first Prime Editing data in NHPs and we believe provide further proof-of-concept for our Prime Editing approach to potentially address a wide range of diseases.

The Disease

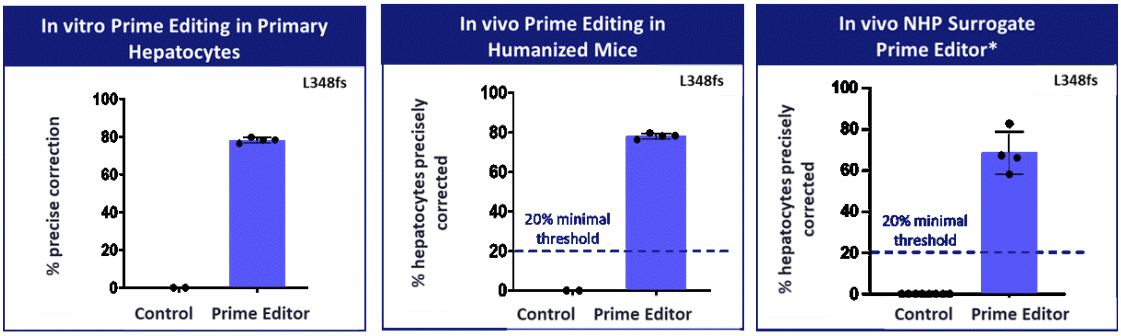
GSD1b is a rare, serious progressive and fatal disease affecting approximately 1,500 patients and caused by impaired glycogen metabolism. This autosomal recessive disease is caused by mutations in the glucose-6-phosphate transporter, G6PT also known as SLC37A4. Deficiencies in this transporter result 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.

Our Approach and Results: Direct correction of prevalent mutations in SLC37A4

Our initial approach to treating patients with GSD1b is to use our Universal Targeted LNP platform to deliver Prime Editor complex 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: L348fs, and G339C. 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. While heterozygote carriers have no disease and animal studies of GSD1b suggest that as little as 11 percent of normal activity has the potential to restore normoglycemia, we use an estimate that 20 percent of activity normalizes fasting glucose.

As shown in the left figure below, we have identified Prime Editors that demonstrate precise correction of the first mutation with approximately 80 percent efficiency in primary hepatocytes harboring the L348fs mutation. We formulated Prime Editors in our Universal Targeted LNP platform and, as shown in the right figure below, also demonstrated *in vivo* editing of the first mutation with approximately 80 percent efficiency in the livers of humanized SLC37A4 mice where the mouse gene has been replaced with the human gene harboring the L347fs mutation.



The NHP Prime Editor is directed to the same location in the SLC37A4 gene as the human Prime Editor, but the NHP genomic sequence is slightly different from the human sequence, hence the use of a surrogate.

To further evaluate our Universal Targeted LNP platform, we were also able demonstrate *in vivo* editing with approximately 70 percent efficiency in NHPs using surrogate SLC37A4 Prime Editor, as shown in the figure below. In our preliminary safety studies, the Universal Targeted LNPs were well tolerated in both rats and NHPs. Initial genomewide studies using patient cells and human hepatocytes have not identified any detectable off-target editing.

Next Steps

We are currently performing lead optimization of our GSD1b Prime Editors, establishing an efficacy and safety data package including genotype-phenotype biomarker response, and off-target, safety. In addition, we have developed a series of Prime Editors that precisely correct the G339C mutation with high levels of editing efficiency and are evaluating them in *in vivo* humanized mouse studies.

Expansion Opportunities in the Liver Pipeline

To accelerate our liver programs, we are continuing to develop our proprietary universal targeted LNP platform in liver. Now that we have established the ability to deliver Prime Editors via LNPs to hepatocytes *in vivo*, we could potentially advance other Prime Editing liver programs more quickly, reflecting the versatility and modularity of our platform, which potentially enables the rapid creation of new product candidates by merely swapping out pegRNAs.

Our Lung Programs

Cystic Fibrosis

The Disease

CF is a progressive lung disease characterized by production of thick mucus lung secretions which lead to blockage of airways, inflammation, and 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 two 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 thirties before lung failure necessitates lung transplantation, if available. Overall CF prevalence in the United States and Europe is

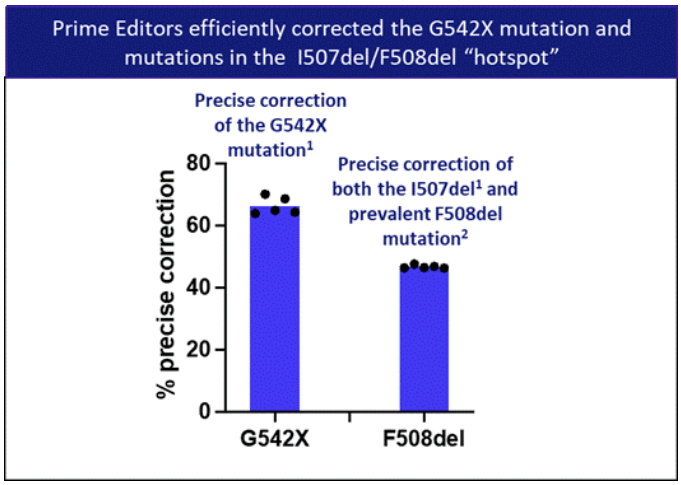
approximately 70,000 to 90,000 people (~40,000 in the United States), and while significant progress in the last decade has created therapeutic options for many patients (e.g. Trikaftor), there is no cure and existing treatments are ineffective or not tolerated for approximately 15 percent of patients.

The disease is inherited recessively and caused by loss-of-function mutations in a chloride protein transporter called CF 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 G553X / G551D and I507del. 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.

Our Approach: Correct prevalent mutations and mutational hotspots in the CFTR gene

We intend to progress two distinct strategies for applying Prime Editing to treat CF: hotspot editing and PASSIGE. Through hotspot editing, we aim to address multiple mutations at CFTR mutational hotspots with a small number of Prime Editors. This strategy has the potential to address a large percentage of individuals having CF with only a few Prime Editors, with a particular focus on the 15 percent of patients who cannot be treated with current therapy. Preclinical data generated by us suggest that using only eight hotspot Prime Editors could benefit more than 93 percent of all people with CF, including those living with nonsense and rare mutations whose disease is not amenable to treatment with currently approved therapies, as well as those who do not tolerate existing therapies.

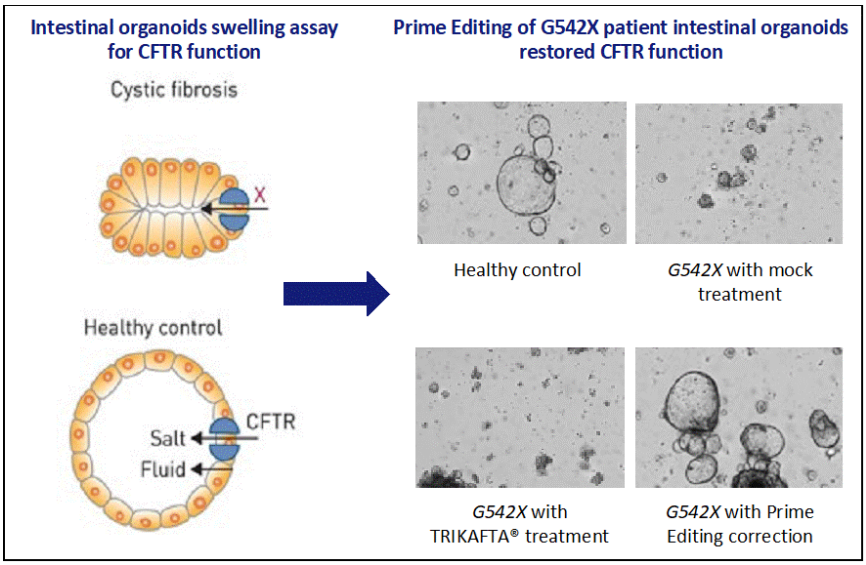
In parallel, with PASSIGE, we aim to address nearly all people with CF with a single CFTR superexon insertion strategy. Our preliminary screens have identified hotspot Prime Editors that achieve high levels of precise correction. As shown in the figure below, we observed approximately 70 percent precise editing of the G542X mutational hotspot (left bar), and approximately 50 percent precise editing of the hotspot encompassing I507del and prevalent F508del mutations (right bar) in patient cells.



[1]G542X and I507del are "high unmet need" mutations; F508del is one of the most prevalent CF mutations; [2]data show correction in patient induced pluripotent stem cells. Each dot shows a different Prime Editor.

In initial proof of concept studies, we developed an intestinal organoid swelling assay that enabled us to test the impact of our Prime Editors on CFTR protein function. As shown in the figure below, healthy donor intestinal organoids swell when stimulated as a result of the CFTR channel pumping salt and water into the organoid (top left image). Organoids from CF patients do not swell (top right image). We then edited the organoids from patients with

the G542X mutation and demonstrated that our Prime Editors restore swelling to levels seen in healthy donor organoids (bottom right image).



Next Steps

With CFF's support, pursuant to the therapeutic development agreement with the Cystic Fibrosis Foundation, or CFF, we are aiming to deliver one-time, non-viral therapy that offers first cure to all patients living with CF. We will perform optimizations of the hotspot Prime Editors from the early screens to increase efficiency and optimize Prime Editors for additional mutations. In addition, and in parallel we are developing a superexon insertion approach using Prime's PASSIGE technology. Screening for Prime Editors and superexon templates for PASSIGE is underway and we are building a series of assays to evaluate our Prime Editors on restoration of CFTR protein function. We are testing Prime Editors in patient-derived cells, including iPSCs, intestinal organoids, and human bronchial epithelium. Humanized mice with part of the mouse CFTR gene replaced with human CFTR gene containing the human mutation, have been developed for us to deliver Prime Editors initially to the lung epithelial basal cells which contain a population of lung stem cells. We are developing and optimizing LNP formulations to efficiently deliver our Prime Editors to human bronchial epithelial cells *in vitro* and to lung basal cells *in vivo*.

Our Ocular Programs

Retinitis Pigmentosa Caused by Rhodopsin Mutations: Our first eye indication using AAV delivery technology

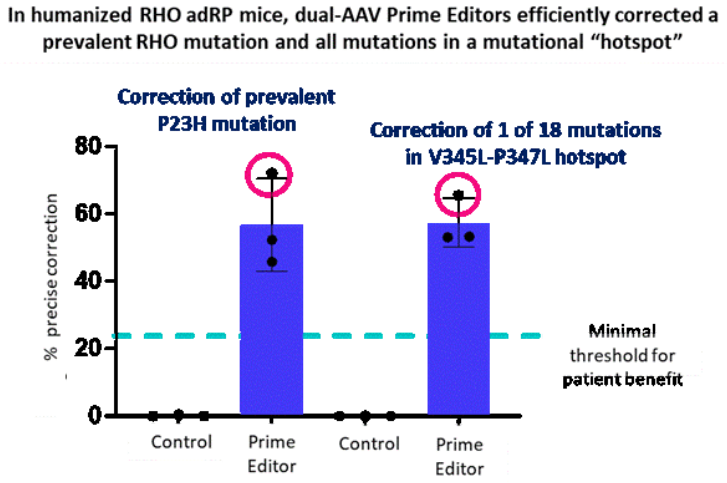
The Disease

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 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 the RHO gene 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 6,000-7,000 patients have adRP in the United States caused by RHO mutations. We are initially focused on the predominant mutations of P23H and two mutations V345L and P347L which occur in a mutational hotspot. These three mutations are highly prevalent in the United States and have been identified as causing disease in approximately 60 percent of all patients (approximately 3,000-4,000 patients). As we advance our portfolio, we believe that other frequent mutations may also be suitable targets for Prime Editing.

Our Approach and Results: Directly correct prevalent mutations in the RHO gene in photoreceptors of the retina

Our initial approach to adRP is to develop two Prime Editors to correct the RHO P23H point mutation and a mutational hotspot in RHO in rod photoreceptors of the retina at their natural genomic location. We believe a Prime Editor that corrects the P23H mutation will also correct rarer, nearby P23L and P23A mutations, while a single hotspot editor could correct 18 different pathogenic mutations in that genomic location, including the most prevalent mutations V345L and P347L. 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. Similarly to the liver programs, we have developed a modular delivery platform for delivery of Prime Editors to the retina. In the case of retina, our modular delivery platform is a dual AAV system. We have optimized the AAV genomes to precisely and efficiently deliver the Prime Editor protein and the Prime Editor guide RNAs, and have optimized the AAV capsid for delivery to photoreceptors.

As shown in the figure below, we have identified Prime Editors that demonstrate up to 65 to 70 percent percent precise correction of photoreceptors *in vivo* and that were generally well-tolerated with no detectable immune response. In regions of the retina delivered to, Prime Editors prevented retinal degeneration *in vivo*. There were also no off-target edits detected in human photoreceptors and no detectable evidence of viral vector integration into retinal cells.



Next Steps

For our ocular programs, we are optimizing the modular dual-AAV system comprised of an optimized AAV capsid to improve transduction of photoreceptors, optimized AAV genome to increase expression of Prime Editor components, and novel AAV production processes that we believe will enable us to efficiently support multiple products. We are evaluating the modular dual-AAV in humanized RHO adRP mice including studies to evaluate preservation of the retina following Prime Editor delivery, and we plan to evaluate our approach in NHP studies where the Prime Editors will be delivered by subretinal injections or suprachoroidal injections to mimic the anticipated route of administration in the clinic.

While we are advancing the RHO program with two Prime Editors for P23H and V345L-P347L, we are also identifying additional Prime Editors that can correct other prevalent mutations in the RHO adRP gene.

Other Programs in Discovery

Additionally, in our ocular area of focus, building on the modularity of our ocular platform and learnings from Rhodopsin program, we are also researching RP caused by mutations in USH2A resulting in Usher syndrome. By

simply swapping out the pegRNA and ngRNA in our retinal AAV delivery system we have the potential to accelerate the Usher syndrome program as well as advance additional retinal degeneration programs in the future.

In addition, we are researching Fuch's endothelial corneal dystrophy, a common repeat expansion disease affecting the cornea leading to progressive corneal opacification and blindness. We continue to make progress in both of these programs.

Our Neuromuscular Programs

Friedreich's Ataxia

The Disease

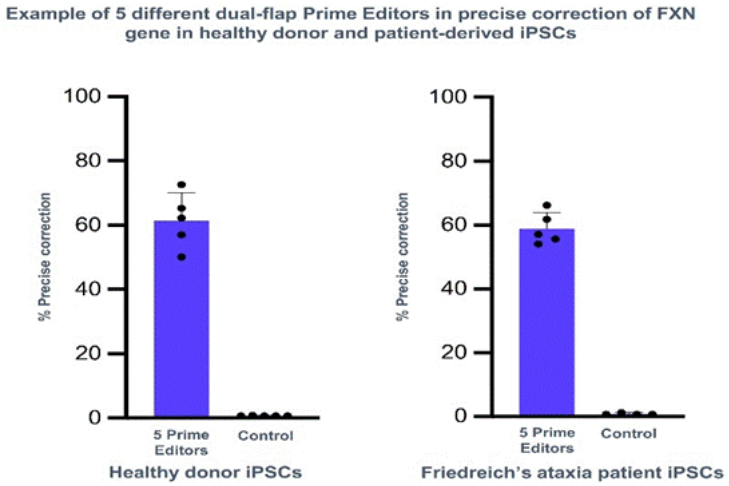
Friedreich's Ataxia, or FRDA, is a multisystem, autosomal recessive neurodegenerative disorder affecting the central and peripheral nervous system as well as the heart and other organs. FRDA significantly reduces survival for patients, with the mean age of death being 39 years. FRDA is characterized 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 19,000 patients globally.

FRDA is a repeat expansion disease 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*.

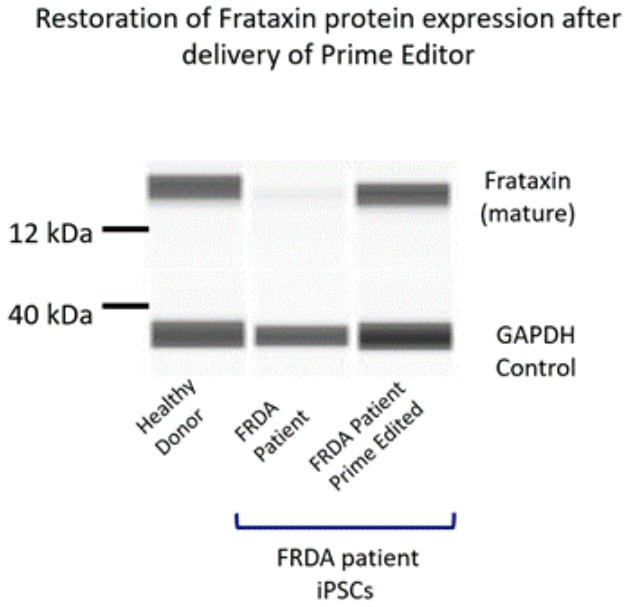
Our Approach and Results: Directly and precisely remove the pathogenic GAA repeats in the FXN gene

Our Prime Editing technology enables us to precisely remove the expanded repeat sequences that cause FRDA. Our goal is to precisely remove the pathological expanded GAA repeat sequence from intron 1 of the FXN gene to restore normal FXN regulation and normal expression of frataxin using dual-flap and long-flap Prime Editing technologies. The primary target tissues are for areas of the brain and spinal cord, but removal of repeats from FXN in the myocardium is also highly desirable to prevent cardiomyopathy and reduce mortality, and we plan to address cardiomyocytes as well.

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 up to 66 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. Remarkably, the total length of sequence precisely removed can be more than 7,000 nucleotides, or seven kilobase, using dual-flap Prime Editing.



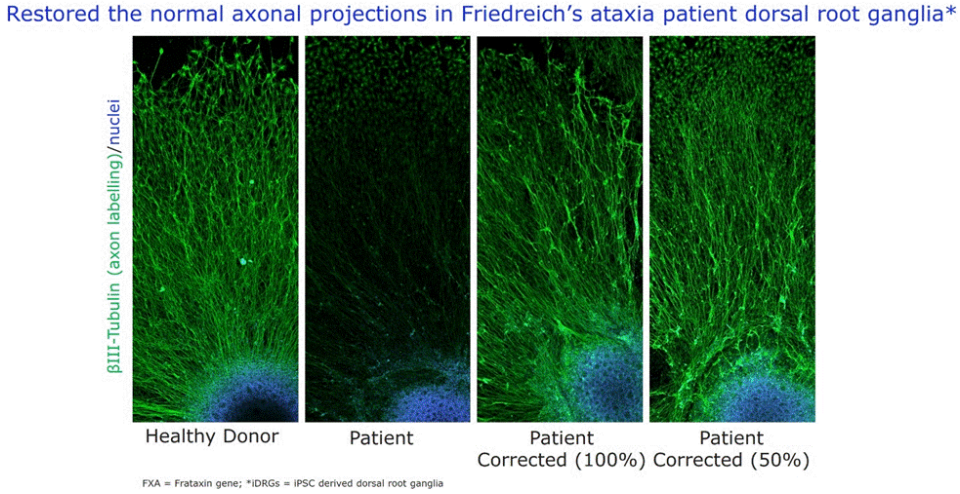
Consistent with the high levels of precise correction observed in patient iPSCs, we have also observed a restoration of frataxin expression to levels that approach those observed in healthy donor iPSCs. This is shown in the figure below which illustrates restoration of frataxin protein expression after delivery of the Prime Editor to patient iPSCs.



FRDA = Friedreich's Ataxia and GAPDH = a control housekeeping protein (glyceraldehyde-3-phosphate dehydrogenase).

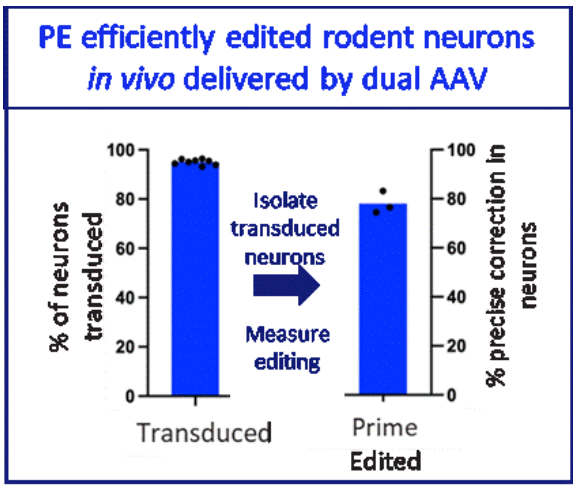
One of the hallmarks of Friedreich's Ataxia is the degeneration of the dorsal root ganglia, or DRGs. These structures of the central nervous system contain sensory neurons transmitting information to the brain cortex. To evaluate the effect of Prime Editing on the ability of DRG sensory neurons to grow and function, we have developed DRG organoids derived from patient stem cells, a model for growth of the sensory nervous system. These DRGs are multicellular 3D structures and model the growth of a patient DRG. In the figure below, unedited patient DRG organoids (Patient) produce many fewer axons, shown as green fibers, than healthy donor organoids (Healthy Donor).

We next edited patient DRG organoids with one of our FXN Prime Editors. When we correct 100 percent of the copies of FXN gene there is complete restoration of the sensory axon growth from the patient DRGs (Patient 100% Corrected). Even, when we correct 50 percent of the copies of the FXN gene there is also complete restoration of the sensory axon growth from the DRGs. We believe these *in vitro* results indicate that Prime Editors may have the potential to restore normal function of patient sensory neurons.



Fluorescence microscopy images at low magnification of dorsal root ganglia, or DRG, from healthy donor or patient, showing cell nuclei (blue) and axons (green). Patient DRG shows very few axons compared to healthy donors. Following Prime Editing to remove the expanded repeats and precisely correct the FXN gene, patient DRGs show normal axon growth.

We have established a preliminary dual-AAV delivery system for efficient delivery of Prime Editing to neurons and glial cells *in viv*o, as demonstrated in the figure below where we have observed robust transduction of over 95 percent of neurons within the injection site (left bar), and where we observed precise editing in approximately 80 percent of the transduced neurons (right bar); this high editing efficiency supports the robustness of the *dual*-AAV system. This system allows us to interrogate promising Prime Editors while we continue to develop an optimized dual-AAV delivery system as described in "Next Steps" below.



Tool Prime Editors were packaged into our preliminary dual-AAV system and together with a reporter AAV were injected into the brains of healthy adult mice. Four weeks later, brain tissues were collected and fluorescent regions indicating successful AAV transduction were isolated and evaluated for editing of target site.

Next Steps

For our neuromuscular programs, we are establishing a modular dual-AAV system comprised of an optimized AAV capsid to improve transduction across key brain regions using minimally-invasive route of administration, optimized AAV genome to increase safety, specificity and expression of Prime Editor components, and novel AAV production that we believe will enable us to efficiently support multiple products. In addition to the dual-flap technology used in our preliminary experiments, we are also evaluating a long flap approach to precisely correct the expanded GAA repeats in FXN, and the most promising Prime Editors of either approach will be incorporated into our modular dual-AAV system to be further evaluated in humanized FXN mice containing expanded GAA repeats to confirm editing efficiency *in vivo*. We will also evaluate the modular dual-AAV approach using tool or surrogate Prime Editors in NHPs.

Myotonic Dystrophy Type 1

The Disease

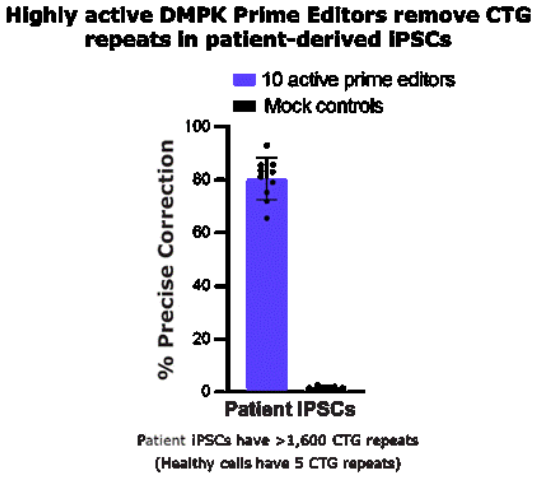
Myotonic Dystrophy type I, or DM1, is a common autosomal dominant muscular dystrophy among people of European ancestry and is principally a muscle disease affecting skeletal and cardiac muscle with multisystem manifestations. Recent newborn screening studies indicate that the true prevalence of DM1 is 1 in 2,300 (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, 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 gastrointestinal symptoms are most prominent.

DM1 is a repeat expansion disease caused by expanded CTG repeats in the 3' UTR of one copy of the DMPK gene. When transcribed into RNA, the expanded repeat nucleotides form toxic RNA foci in the nucleus that, sequester critical nuclear splicing factors, thereby preventing the correct function of many genes that regulate cell function.

Our Approach and Results: Directly and precisely remove the pathological repeats in the DMPK gene

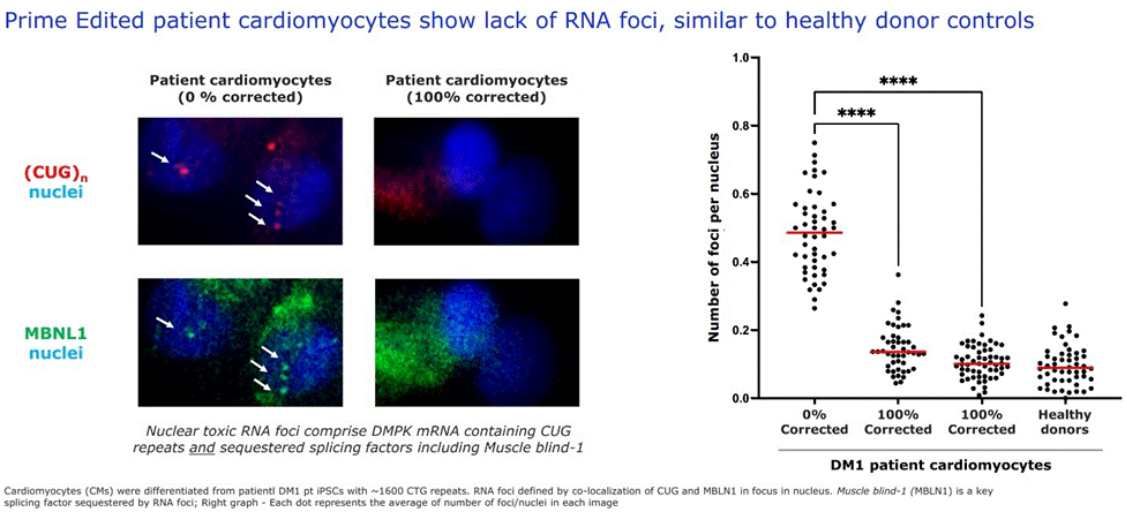
Our goal in DM1 is to leverage our Prime Editing technology to precisely remove the repeat sequence from the UTR region of the DMPK gene, to restore DMPK regulation and expression of DMPK protein back to normal levels. The primary target tissues are cardiac and skeletal muscle, which we believe could 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 patient-derived iPSCs, which contain approximately 1,600 pathological repeats, we have demonstrated precise removal of repeats, with our best Prime Editors achieving more than 90 percent precise editing and removal of the pathological repeats. These data are shown in the figure below, with each dot representing the data of a different individual Prime Editor.



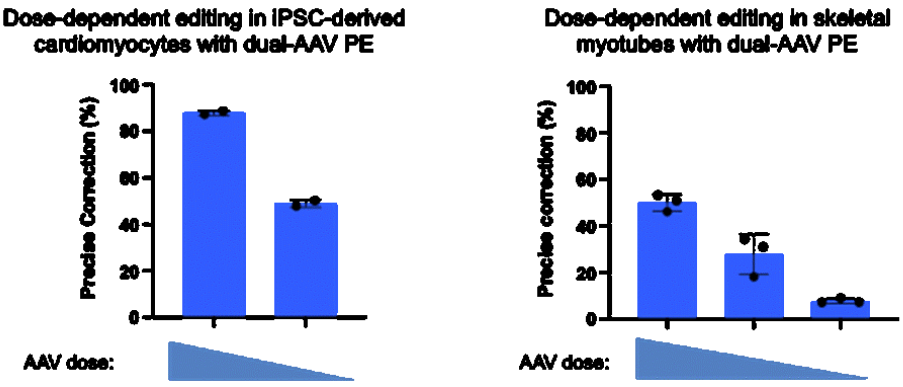
As mentioned above, a hallmark of the disease is toxic RNA *foci*, formed from the repeats, that sequester key splicing factors in the cells with this disease. For example, muscleblind-1, or MBLN1, is a known splicing factor that is deficient in these patient cells.

We have developed assays to identify these toxic RNA repeats. As shown in the left side of the figure below, toxic repeats of repetitive CUG sequence, or (CUG)n, can be identified in nuclei of patient cardiomyocytes (left column, top) but not seen in healthy donor cardiomyocytes (not shown). These toxic (CUG)n repeats sequester MBLN1, as expected (left column, bottom). We edited patient cardiomyocytes to remove the pathological repeats with one of our Prime Editors and evaluated the impact on the formation of toxic RNA repeats. As is also shown in the right side of the figure below, cardiomyocytes that have 100 percent of pathological DMPK gene corrected, RNA foci are no longer detectable (right column, top); nor is MBNL1 staining detectable (right column, bottom) with only background staining detectable. The right side shows a quantification and analysis of the results, with 100 percent correct patient cells showing levels of RNA *foci* similar to those in healthy donor cells.



Left hand panel shows fluorescence microscopy images at high magnification of patient cardiomyocyte nuclei. The cardiomyocytes are co-stained to show the RNA (CUG)n repeats (red) and MBLN1 splicing factor (green) in toxic RNA foci. Cardiomyocytes without Prime Editing shown in far left column images or after Prime Editing shown in right column images. The arrows indicate (CUG)n RNA repeats co-localized with sequestered MBLN1 in the nuclei (blue). After Prime Editing the toxic RNA foci are not visible. The graph, right panel shows results of RNA foci per nucleus from automated high content imaging analysis of the cardiomyocytes. Columns showing patient cardiomyocytes 100% corrected or 0% corrected (unedited) and healthy donors.

We have established a preliminary dual-AAV delivery system for efficient delivery of Prime Editing to muscle, as demonstrated in the figures below, left panel, where using tool Prime Editors we have observed precise editing of up to 90 percent in cardiomyocytes, and right panel, where we observed precise editing of up to 50 percent in skeletal myotubes. This system allows us to investigate promising DM1 Prime Editors while we continue to develop an optimized muscle delivery system as described in “Next Steps" below.



Human iPSC-derived cardiomyoctes (above left) and mouse skeletal myotubes differentiated from myoblasts (above right) were treated with tool Prime Editors packaged in dual-AAV system at various titers and evaluated for precise editing of target site.

Next Steps

We are evaluating the ability of Prime Editing to correct the mis-splicing of a panel of genes that are known to be mis-spliced as a result of the toxic RNA foci. In parallel, we plan to perform similar experiments in patient-derived skeletal muscle cells. To ultimately deliver Prime Editors to heart and skeletal muscle, we expect initially to rely on the tropism of AAV capsids, optimized to deliver our Prime Editors to the heart and skeletal muscle. We have established an AAV system for efficient delivery of Prime Editing in neurons and glial cells *in vivo*, as demonstrated

above in Friedreich's Ataxia. We are optimizing this system for the DM1 program and planning to evaluate our Prime Editors in a disease model in mice which contain the human DMPK gene with pathological repeats. While AAV delivery is our primary route of delivery for early programs such as this, we are actively determining whether a non-viral delivery system could be used to efficiently deliver the Prime Editor to muscle.

Other Programs in Discovery

Within our neuromuscular area of focus, we are also exploring other repeat expansion diseases, including amyotrophic lateral sclerosis, a rapidly progressive neurodegenerative disease characterized by progressive motor neuron loss; Huntington's disease, an autosomal dominant progressive neurodegenerative disease affecting teenagers through middle aged adults; Fragile X syndrome, an X chromosome-linked dominant rare disease that is the most common monogenic cause of childhood intellectual disability and autism; and oculopharyngeal muscular dystrophy, a rare autosomal dominant disease, characterized by progressive weakness in the muscles around the eyelids as well as in the tongue and pharynx.

In addition to the repeat expansion diseases, we are also exploring Duchenne muscular dystrophy, an X chromosome-linked recessive disease affecting boys that is characterized by early onset progressive muscle weakness affecting limbs.

Additional Programs

As one part of our overall partnering strategy, we are advancing the following programs as partnering opportunities:

Chimeric Antigen Receptor T-cell program (CAR-T)

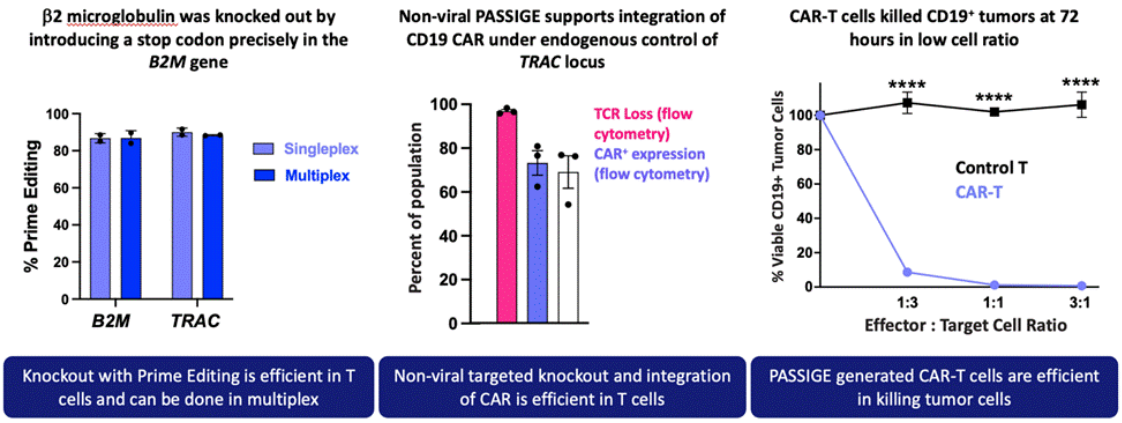
We are developing investigational CAR-T cell therapies for autoimmune and oncology indications. In combination with multiplex Prime Editing, we believe PASSIGE may be able to overcome existing challenges in developing CAR-T cells for human therapeutic use — such as manufacturing time, cost, yield for autologous cell therapy, cell quality issues, and safety risks associated with semi-random integration and double strand breaks at multiple genomic loci. Multiplex Prime Editing with PASSIGE has the potential to create a best-in-class allogeneic CAR-T cell product. In December 2023, we presented preclinical data suggesting PASSIGE is up to 80 percent efficient for non-viral, site-specific delivery of chimeric antigen receptor to primary human T-cells to generate CAR-T cells, and can be multiplexed with Prime Editing at other target sites by non-viral one-step delivery with no loss of efficiency. PASSIGE-generated CAR-T cells showed potent antigen-specific function and cytotoxicity *ex vivo* and *in vivo* against an established human B-cell tumor growing in immunodeficient mice. The potential advantages, we believe, of our CAR-T approach using Prime-Edited are shown in the table below.

	Existing Limitations	Prime Editing Solution
Multiplex Engineering	✗ Low payload integration efficiency ✗ Constrained to limited number of knock-outs and limited single base pair changes	✓ **>80% integration** efficiency to date, aimed at TRAC locus to maintain **endogenous control** ✓ Capable of **multiple edits done safely**, each with a **full suite of functional modifications**
Safety	✗ Random or semi-random integration ✗ High rate of translocations / chromosomal abnormalities	✓ **Precise on-target** transgene integration ✓ Based on our extensive off-target evaluations in other settings, **there is the potential for no detectable off-target edits, translocations, or unintended structural abnormalities** in Prime-Edited CAR-T's
Manufacturing / Cost of Goods	✗ Dependence on viral components ✗ Complicated by multi-step engineering	✓ **Entirely non-viral** manufacturing process ✓ **Single-step** editing and integration

As shown in the figure below, we have achieved multiplex Prime Editing in T cells to knock out the B2M gene and the endogenous T cell receptor, or TRAC, without loss in efficiency compared to single site editing (left panel). We have also delivered Prime Editing components and DNA recombinase components (PASSIGE components) in a single step to human primary T cells, without the use of viruses. The short recombinase DNA target sequence, used by the site-specific recombinase enzyme known as Bxb1, was inserted into human primary T cells at the TRAC

locus with greater than 95 percent efficiency, and a 3.5 kilobase anti-CD19 CAR gene cassette was precisely inserted into that recombinase site location in up to 80 percent of the T cells, resulting in positive expression of the CAR by those T cells (middle panel). As a result, the T cells acquired CD19+ tumor cell killing activity that was dependent on cell dose in a cell assay, indicating that the integrated CAR was functional (right panel).

PASSIGE and Multiplex Prime Editing Could Create Potentially Best-in-Class Allogenic CAR-T Cell Product



Next steps

This exploratory program is approaching lead optimization. Additional optimization of the Prime Editor and PASSIGE components is ongoing, and the scalable cell therapy process is being developed. A suite of assays to evaluate cell potency and cell fitness are currently being developed and we plan to evaluate CAR-T cell leads *in vivo* in established tumor killing studies.

Other Programs in Discovery

In addition to CAR-T, we are also exploring genetic hearing loss, including Usher's syndrome type III, which is characterized by progressive post-lingual hearing loss, variable vestibular dysfunction, as well as adolescent-onset progressive vision loss due to retinitis pigmentosa caused by mutations in the Clarin 1 protein encoded by the CLRN1 gene; and non-syndromic hearing loss due to mutations in GJB2, the most commonly mutated gene in non-syndromic hearing loss, which accounts for two thirds of genetic hearing loss.

Our License and Collaboration Agreements

License agreements with Broad Institute

In September 2019, we entered into a license agreement with Broad Institute, and in May 2020, February 2021 and December 2022, we entered into amendments to that license agreement. We refer to this 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 DNA sequences using a Prime Editor. Certain of the licensed patent rights are co-owned by Broad Institute with MIT and Harvard and certain are co-owned by Broad Institute with Harvard. In December 2022, following the timely exercise of an option under an existing option agreement with Broad Institute we entered into a second license agreement with Broad Institute, which we refer to as the 2022 Broad License Agreement. Under the 2022 Broad License Agreement, Broad Institute grants to us certain rights and licenses under certain patent rights it owns or controls related to MMR inhibition and prime editing improvements. The licensed patent rights are co-owned by Broad Institute with Harvard, The Trustees of Princeton University, or Princeton, and The Regents of the University of California, or University of California.

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.

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, which we refer to as enabled products, and (iv) a non-exclusive, worldwide license solely for internal research.

All of the above license grants specifically exclude human germline modification, the stimulation of biased inheritance of particular genes or traits within a plant or animal population, and certain modifications of the tobacco plant, and 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. Broad has not yet granted any march-in license to a third party.

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, which includes several developmental milestones for licensed products that we are required to meet 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. We may request an extension of the development milestone timelines by providing a reasonable explanation and plan 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. If we are successfully able to gain regulatory approval for any licensed product, 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.

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 623,529 shares of our common stock. Under the February 2021 and December 2022 amendments, as partial consideration for the addition of licensed patent rights relating to prime editing improvements, we paid Broad Institute amendment fees of approximately $0.1 million and $0.1 million, respectively.

We also are obligated to pay to Broad Institute an annual license maintenance fee in the low six-figures 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. 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.

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.

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.

2022 License Agreement with Broad Institute

Other than as summarized below, the general terms of the 2022 Broad License Agreement, including the scope and field of the license grants, are the same in all material respects as the terms of the Broad License Agreement, as summarized above.

The patent rights licensed under the 2022 Broad License Agreement are co-owned by Broad Institute, Harvard, Princeton, and University of California, collectively referred to as the 2022 Broad License Agreement Co-Owners. The license grants under the 2022 Broad License Agreement are subject to the same retained rights as set forth in the Broad License Agreement for the 2022 Broad License Agreement Co-Owners, as well as the U.S. federal government and HHMI.

As partial consideration for the rights granted to us under the 2022 Broad License Agreement, we paid Broad Institute an upfront fee of $0.2 million and are obligated to pay to Broad Institute an annual license maintenance fee in the mid-five figures for the term of the Agreement.

Broad Institute is entitled to receive clinical and regulatory milestone payments for a limited category of licensed products or enabled products, which category we refer to as royalty-bearing products, up to a total of $2.0 million per royalty-bearing product. Broad Institute is entitled to sales-based milestone payments up to a total of $3.0 million per royalty-bearing product, depending on the patient population to be treated by the royalty-bearing product achieving the applicable milestone. If we undergo a change of control at any time during the term of the 2022 Broad License Agreement, certain of the clinical and regulatory milestone payments will increase by a specified percentage. Broad Institute is entitled to lower payments to the extent the clinical and regulatory milestones or sales-based milestones are achieved by royalty-bearing products that are enabled products, rather than royalty-bearing products that are licensed products. Broad Institute is entitled to receive royalties of less than 0.2% on net sales of royalty-bearing products that are licensed products and lower royalties on net sales of for royalty-bearing products that are enabled products. Royalties payable to Broad Institute are subject to limited customary offsets and reductions. Broad Institute is entitled to a percentage of consideration that we receive from our sublicensees, with such percentage dependent on the development stage of products under the 2022 Broad License Agreement at the time of sublicense execution, all below 1%. The royalty term for a royalty-bearing product under the 2022 Broad License Agreement is determined in the same way as in the Broad License Agreement.

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. In August 2022, we amended and restated the Pledge to clarify that the funds may be used by the laboratory of David Liu, who is a member of Broad Institute and a faculty member at Harvard.

Collaboration and License Agreement with Beam Therapeutics

In September 2019, we entered into a collaboration and license agreement, which we refer to as the Beam Collaboration Agreement, with Beam Therapeutics Inc., or Beam. One of our founders, David Liu, is also a founder of Beam.

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 know-how that we control during the initial term, and improvements thereto that we control for a specified number of years following the initial term, and patent rights that cover such Prime Editing know-how during the term of the Agreement, 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. The Beam field 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.

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.

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.

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 1,608,337 shares of our common stock. Beam was also entitled to appoint a representative to our board of directors, which right has expired.

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 any such 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.

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.

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.

Our Business Development and Partnering Strategy

Our vision is to establish Prime Medicine as a leader in the field of gene editing by building a fully integrated biopharmaceutical company utilizing our Prime Editing platform to pioneer the discovery, development and commercialization of Prime Editing therapeutics that can have a transformative impact on the treatment of a wide spectrum of diseases with high unmet medical need. The potential therapeutic applications of our Prime Editing technology are broad, and we aspire to fully develop that potential.

To achieve our vision, and in addition to independently discovering, developing, and commercializing Prime Editing products, we will seek to selectively enter strategic collaborations to maximize the potential of the Prime Editing platform. Such collaborations may also facilitate our entry into additional therapeutic or geographic areas by leveraging the established capabilities of our partners as well as by funding the development of new Prime Editing platform or corporate capabilities which we can then utilize for additional Prime Medicine products outside such partnerships. In certain cases, we may use partnerships to create value in areas which we may not intend to enter ourselves in the near term. In our collaborations, we may cooperatively develop and commercialize products with our partners, have options to do so, or out-license products for development and commercialization by our partners. In each case, we expect to receive value in the form of upfront payments and milestones which will provide us with additional capital in the nearer term as well as royalties and where applicable, profit sharing, to participate in the value created through commercializing Prime Editing products.

We may also seek to access or develop enabling technologies or specific capabilities through licenses or partnerships. We will evaluate partnerships with both academic and corporate entities, and these potential collaborations may vary in both structure and scope. Technologies that may enable the application of Prime Editing may include viral and non-viral delivery modalities, manufacturing, and technologies that may be synergistic with Prime Editing or Prime Editing products.

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 Kamau Therapeutics, 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 ZFNs, engineered meganucleases and TALENs. Beam Therapeutics Inc. utilizes base editing technology. In addition, other private companies such as Tessera Therapeutics, Inc. 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, have reported the discovery of new DNA-cutting enzymes, and have announced gene editing programs. 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

Overview

We achieved many major milestones in 2023, including the issuance of two in-licensed U.S. patents and the allowance of another in-licensed U.S. patent application, which has since issued as a U.S. patent, in addition to the U.S. patent issued in 2022, all of which cover Prime Editing methods and its components and systems. Our success depends in large part on our ability to obtain and maintain additional 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 U.S. and certain foreign patent applications and issued patents and filing 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. While we in-license four issued patents, we do not currently own any issued patents in any jurisdiction covering our Prime Editing technology or product candidates. For information regarding the risks related to our intellectual property, please see "Risk Factors—Risks Related To Our Intellectual Property."

Our wholly owned patent applications and our in-licensed issued patents and 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 activities or properties
- 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.

Owned Patents

As of February 28, 2024, we owned approximately 20 pending U.S. provisional patent applications, 20 pending PCT applications, nine pending U.S. non-provisional patent applications and 13 pending ex-U.S. patent applications. The patent applications outside of the United States were filed in the European Patent Office, Japan, China and certain other foreign jurisdictions. Our owned patent applications are generally related to our Prime Editing technology, including claims to modified pegRNAs; Prime Editors with enhanced activities or properties (e.g., improved Prime Editing efficiency or smaller Prime Editors) and 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; PASSIGE systems including Prime Editors and integrases or recombinases, and methods of using PASSIGE; off-target testing methods; methods for synthesizing pegRNAs; and novel lipids and LNPs for delivery of Prime Editors. The 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 as early as 2044, excluding any additional term for patent term adjustments or patent term extensions or similar provisions in foreign jurisdictions. Our current owned U.S. non-provisional and PCT patent applications, if issued and if the appropriate maintenance or annuity fees are paid, are expected to expire as early as 2042, excluding any additional term for patent term adjustments or patent term extensions or similar provisions in foreign jurisdictions.

In-licensed Patents

As of February 28, 2024, we have in-licensed four issued U.S. patents, one granted ex-U.S. patent, approximately 12 pending U.S. non-provisional patent applications, three pending PCT applications, one pending U.S. provisional applications and 83 pending ex-U.S. patent applications, in each case, related to Prime Editing, from Broad Institute. The patent applications outside of the United States were filed in the European Patent Office, Japan, China and certain other foreign jurisdictions. The issued patents and 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; program-specific pegRNAs directed to targeting and correcting specific mutations; systems comprising Prime Editors and integrases or recombinases for use in PASSIGE; and delivery modalities for Prime Editing systems, including the use of AAV, in a split AAV system for viral delivery of a Prime Editor. The in-licensed issued patents and 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 patents and 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 patents and 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.

Additional 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.

Government Regulation

In the United States, biological products, including gene editing 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 trials, 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 and approved by the FDA before initiating clinical trials. In addition, FDA approval must be obtained before the marketing of biological products in the United States. 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.

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, including those requiring performance in accordance with 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 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, purity and potency of the proposed biological product for its intended use;
- submission to the FDA of a 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 practices, 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;
- 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, including a gene editing product, in humans, the product candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of a product candidate's 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 for certain nonclinical studies.

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 before interstate shipment and administration of any product candidate that is not the subject of an approved BLA or existing IND. 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 application. 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 application. 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, which may be full or partial. 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 full 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 investigation conducted under the IND. No more than 30 days after imposition of a full or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a full 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 advice to the sponsor as to whether or not a trial may move forward at designated check points based on pre-specified criteria and access to unblinded 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 National Institutes of Health, or 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 for recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

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. The biological product undergoes more extensive clinical trials to further evaluate dosage, 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 gather additional data 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 the 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, the FDA requires 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 seven 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.

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 in the United States. 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.

Within 60 days following submission of the application, the FDA reviews a BLA 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 10 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 12 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 its BLA review, 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. 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-approval clinical trials designed to further assess a biological product's safety, purity or potency, 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. 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 EU 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 of 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 with due diligence, and, under the Food and Drug Omnibus Reform Act of 2022, or FDORA, the FDA is permitted to require, as appropriate, that such trials be underway prior to approval or within a specific time period after the

date of approval for a product granted accelerated approval. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a product or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product. 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 be submitted to the agency for review, which could adversely affect the timing of the commercial launch of the product.

Under FDORA, a platform technology incorporated within or utilized by a drug or biological product is eligible for designation as a designated platform technology if certain conditions are met. A sponsor may request the FDA to designate a platform technology as a designated platform technology concurrently with, or at any time after, submission of an IND application for a drug that incorporates or utilizes the platform technology that is the subject of the request. If so designated, the FDA may expedite the development and review of any subsequent original NDA or BLA for a drug that uses or incorporates the platform technology. Designated platform technology status does not ensure that a drug will be developed more quickly or receive FDA approval. In addition, the FDA may revoke a designation if the FDA determines that a designated platform technology no longer meets the criteria for such designation.

RMAT Designation

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 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, and those supplying products, ingredients, and components of them, 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 any 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 for all formulations, dosage forms, and indications of the biologic. 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, provided that at the time pediatric exclusivity is granted there is not less than nine months of term remaining.

The ACA 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. The 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 the FDA will not approve an application for a biosimilar or interchangeable product based on the reference biological product until 12 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.

EU Clinical Trials Regulation

In April 2014, the EU overhauled the system of approvals for clinical trials in the EU. The transitory provisions of the new Clinical Trials Regulation provide that, by January 31, 2025, all ongoing clinical trials must have transitioned to the new Regulation. Specifically, the new Regulation, which is directly applicable in all Member States (meaning that no national implementing legislation in each EU Member State is required), aims at simplifying and streamlining the approval of clinical trials in the EU. 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, and in the additional Member States of the EEA (Norway, Iceland and Liechtenstein). 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 an 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 an 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 an 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.

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 product 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 product is removed from the market for three consecutive years, ceases to be valid (the so-called sunset clause).

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 an 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 EU's regulatory authorities to be an innovative medicinal product, and products may therefore not qualify for data exclusivity.

Orphan Drug Designation and Exclusivity

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers. The application for orphan designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the MAA if the orphan designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Products with an orphan designation in the EU can receive 10 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 medicinal product can also obtain an additional two years of market exclusivity in the EU where an agreed pediatric investigation plan for pediatric studies has been complied with. No extension to any supplementary protection certificate, or SPC, can be granted on the basis of pediatric studies for orphan indications.

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 medicinal product 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 of the authorized orphan medicinal product consents to a second orphan medicinal product application; or
- the marketing authorization holder of the authorized orphan medicinal product cannot supply enough orphan medicinal product.

Pediatric Development

In the EU, 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 product 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 an SPC, even where the trial results are negative, provided an application for such extension is made at the same time as filing the SPC application for the product, or at any point up to two years before the SPC expires. 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 product development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation, where the MAA 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. Applicants will typically be at the exploratory clinical trial phase of development and will have preliminary clinical evidence in patients to demonstrate the promising activity of the medicine and its potential to address, to a significant extent, an unmet medical need. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies if the applicant has compelling non-clinical data and tolerability data from initial clinical trials of the product. 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 MAA assessment once a dossier has been submitted. Importantly, a dedicated Agency contact and rapporteur from the CHMP or CAT are appointed early in the 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 EU. Although general requirements for advertising and

promotion of medicinal products are established under EU directives, the details are governed by regulations in each EU Member State and can differ from one country to another.

The aforementioned EU rules are generally applicable in the EEA.

Reform of the Regulatory Framework in the EU

The European Commission introduced legislative proposals in April 2023 that, if implemented, will replace the current regulatory framework in the EU for all medicines (including those for rare diseases and for children). The European Commission has provided the legislative proposals to the European Parliament and the European Council for their review and approval. In October 2023, the European Parliament published draft reports proposing amendments to the legislative proposals, which will be debated by the European Parliament. Once the European Commission's legislative proposals are approved (with or without amendment), they will be adopted into EU law.

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom, or UK, formally left the EU on January 31, 2020, and the EU and the UK have concluded a trade and cooperation agreement, or TCA, which has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products, and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations. At present, Great Britain has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the EU regulatory framework continues to apply in Northern Ireland). Except with respect to the new EU Clinical Trials Regulation, the regulatory regime in Great Britain therefore aligns in many ways with current EU medicines regulations, although it is possible that these regimes will diverge more significantly in the future now that Great Britain's regulatory system is independent from the EU, and the TCA does not provide for mutual recognition of UK and EU pharmaceutical legislation.

However, notwithstanding that there is no wholesale recognition of EU pharmaceutical legislation under the TCA, under a new framework by the Medicines and Healthcare Products Regulatory Agency, or MHRA, the MHRA has stated that it will take into account decisions on the approval of marketing authorizations from the EMA (and certain other regulators) when considering an application for a Great Britain marketing authorization.

The UK and the European Commission announced a political agreement in principle to replace the Northern Ireland Protocol with a new set of arrangements, known as the "Windsor Framework," to be effective as of January 1, 2025. This new framework fundamentally changes the existing system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK. In particular, the MHRA will be responsible for approving all medicinal products destined for the UK market (i.e., Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. A single UK-wide marketing authorization will be granted by the MHRA for all medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK.

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.

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. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. 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 monetary penalties. 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), certain other licensed healthcare practitioners and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- 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;
- 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 EU, 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 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:

- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program;
- extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care plans;
- established annual fees and taxes on manufacturers of certain branded prescription drugs;
- created a Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70 percent 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.; and
- expanded the entities eligible for discounts under the 340B Drug Pricing Program.

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, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress that include aggregate reductions of Medicare payments to providers of up to 2 percent per fiscal year, which will remain in effect through 2031. The American Taxpayer Relief Act of 2012 further reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Due to the Statutory Pay-As-You-Go Act of 2010, estimated budget deficit increases resulting from the American Rescue Plan Act of 2021, and subsequent legislation, Medicare payments to providers will be further reduced starting in 2025 absent further legislation. These laws and regulations may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Further, in 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions are subject to considerable legislative and executive actions and could impact the prices we obtain for our products, if and when licensed.

In August 2022, the Inflation Reduction Act, or the IRA, was signed into law. The IRA includes several provisions that will affect our business to varying degrees, including provisions that create a $2,000 out-of-pocket cap for Medicare Part D beneficiaries, impose new manufacturer financial liability on all drugs in Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D pricing for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for drug prices that increase faster than inflation, and delay the rebate rule that would require pass through of pharmacy benefit manager rebates to beneficiaries. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one orphan designation and for which the only approved indication is for that disease or condition. If a product receives multiple orphan designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The implementation of the IRA is currently subject to ongoing litigation challenging the constitutionality of the IRA's Medicare drug price negotiation program. The effects of the IRA on our business and the healthcare industry in general is not yet known.

In addition to pricing regulations, reforms of regulatory approval frameworks may adversely affect our pricing strategy. For example, the current administration has issued multiple executive orders that have sought to reduce prescription drug costs. In February 2023, HHS also issued a proposal in response to an October 2022 executive order from the current administration that includes a proposed prescription drug pricing model that will test whether targeted Medicare payment adjustments will sufficiently incentivize manufacturers to complete confirmatory trials for drugs approved through the FDA's accelerated approval pathway. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the current administration may reverse or otherwise change these measures, both the current administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

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. State 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.

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.

Employees and Human Capital Resources

As of December 31, 2023, we had 234 full-time employees, of which 112 have M.D. or Ph.D. degrees. Within our workforce, 202 employees are engaged in research and development and 32 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.

Our 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. Our telephone number is (617) 564-0013 and our website is located at www.primemedicine.com. References to our website are inactive textual references only and the content of our website should not be deemed incorporated by reference into this Annual Report on Form 10-K.

Available Information

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge on our website located at www.primemedicine.com as soon as reasonably practicable after they are filed with or furnished to the Securities and Exchange Commission, or SEC. These reports are also available at the SEC's website at www.sec.gov.

Our Code of Business Conduct and Ethics is posted on our website located at https://investors.primemedicine.com/corporate-governance/documents-charters. A copy of our Corporate Governance Guidelines, and the charters of the Audit Committee, Compensation Committee, and Nominating and Corporate Governance Committee are posted on our website, www.primemedicine.com, under the heading "Investors—Corporate Governance" and are available in print to any person who requests copies by contacting us by calling (617) 564-0013 or by writing to Prime Medicine, Inc., 21 Erie Street, Cambridge, Massachusetts 02139.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, together with all the other information in this Annual Report on Form 10-K, including the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and related notes, before you make an investment decision with respect to our securities. The risks and uncertainties described below and in our other filings with the SEC may not be the only ones we face. The occurrence of any of the events or developments described below, if they actually occur, could harm our business, financial condition, results of operations and growth prospects. As a result, the market price of our common stock could decline, and you may lose all or part of your investment in our common stock.

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 $198.1 million and $121.8 million for the years ended December 31, 2023, and 2022, respectively. As of December 31, 2023, we had an accumulated deficit of $491.3 million. To date, we have financed our operations primarily through proceeds from our IPO, follow-on public offering, and 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 year to year such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. 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 have identified or may identify in the future;
- seek to identify and progress additional research programs and product candidates;
- initiate preclinical studies and clinical trials for any product candidates we have identified or may identify in the future;
- experience any delays or interruptions due to global health crises, including delays in preclinical testing and clinical trials or interruptions in the supply chain for any current or 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;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any therapies for which we may obtain marketing approval;
- develop, maintain and enhance a sustainable, scalable, reproducible and transferable manufacturing process for the product candidates we may develop;
- hire additional research and development personnel beyond our current projections;
- hire clinical, operations, regulatory 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 and/or work with strategic partners to support and expand our scientific and clinical programs;
- establish and maintain collaborations;

- should we decide to do so, build and maintain a commercial-scale current good manufacturing practices, or cGMP, manufacturing facility;
- operate as a public company; and
- identify new opportunities to expand the use of Prime Editing beyond those currently available scientifically and clinically.

We have not yet initiated clinical development of any 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 preclinical development for our most advanced product candidates. 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 four areas of focus are blood, liver, eye, and neuromuscular indications. 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, we have incurred, and will continue to incur, 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, 2023, our cash, cash equivalents, and investments were $121.7 million, excluding restricted cash, or $135.2 million, including restricted cash. In connection with our IPO, completed in October 2022, we issued and sold 11,721,456 shares of our common stock, including 1,427,338 shares pursuant to the exercise of the underwriters' option to purchase additional shares, at a price to the public of $17.00 per share. As a result of the IPO, we received $180.2 million in net proceeds, after deducting underwriting discounts, commissions and offering costs of $19.1 million. Based on our current operating plan, we believe that our existing cash and cash equivalents and short-term investments, together with net proceeds from our follow-on public offering in February 2024, will be sufficient to fund our operating expenses and capital expenditure requirements into the third quarter of 2025. 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 current or future 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 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 advancing preclinical testing of current and future 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 stockholders or groups of stockholders 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 due to 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.

Unfavorable macroeconomic conditions or market volatility resulting from national or global economic conditions, including those affecting the financial services industry, could adversely affect our business, financial condition or results of operations.

Adverse macroeconomic conditions or market volatility resulting from national or global economic developments, political unrest, high inflation, rising interest rates, changes in international trade relationships and military conflicts, such as the ongoing conflict between Russia and Ukraine and the conflict in Israel, the post-COVID environment or other factors, could materially and adversely affect our business operations. For instance, actual events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. Investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. In addition, any further deterioration in the macroeconomic economy or financial services industry could lead to losses or defaults by our suppliers, which in turn, could have a material adverse effect on our current and/or planned business operations and our current or projected results of operations and financial condition. 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.

Further, U.S. government appropriations have been affected by larger U.S. government budgetary issues and related legislation. Government spending levels are difficult to predict beyond the near term due to numerous factors, including the external threat environment, future government priorities and the state of government finances. Significant changes in government spending or changes in U.S. government priorities, policies and requirements could have a material adverse effect on our results of operations, financial condition or liquidity.

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.

Risks Related To Discovery, Development and Commercialization

Gene editing, including platforms such as Prime Editing, is a relatively new technology that has not been extensively 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 relatively new and has not been extensively clinically validated. 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 or gene therapy 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 the Broad Institute, Inc., or 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., or Beam Therapeutics. 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.

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 relatively new and the regulatory landscape that will govern any product candidates we may develop is

uncertain and may change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for any product candidates.

The time required to obtain approval for any of our current or future 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. 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 relatively new, 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 the development of 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. The FDA's Office of Therapeutic Products, or OTP, reviews gene and cell therapies and related products and has been elevated to a "Super Office" to meet its growing cell and gene therapy workload. Gene therapy clinical trials may also be subject to review and oversight by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees certain 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. For example, more recently, some gene editing companies have seen significant delays in receiving FDA authorization to allow the initiation of their clinical trials, and has suspended ongoing trials, due to the FDA's placement of clinical holds on their IND applications.

The same applies in the EU. 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 the CHMP adopts its opinion which is submitted to the European Commission for the final decision on whether to grant a marketing authorization or not. In the EU, 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 current or future 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.

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 regulatory delays, negative or inconclusive results from our clinical trials, difficulty in designing well-controlled clinical trials, lack of regulatory authorization for our clinical trials, and patients or clinical trial sites dropping out of a trial.

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 applications to regulatory authorities, such as IND applications and clinical trial applications, or CTAs, 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), or may ask for additional endpoints to assess patient safety. 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 relatively new technology that makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval. Further, we expect our clinical trials to include surrogate endpoints, which may be novel or for which the FDA or regulatory authorities lack familiarity or experience, and which may increase the risk that the FDA or other regulatory authorities may disagree that such endpoints are sufficient, and could require that additional trials are conducted. Very few gene therapy products have received marketing authorization or marketing approval from the European Commission or the FDA, and only one gene editing therapeutic product has been approved in the United States and in Europe. Some of these gene therapy 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 we have not yet initiated clinical development of a 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.

The success of our business depends primarily upon our ability to identify, develop and commercialize product candidates. We are 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 and advancing our initial targeted disease indications to IND-enabling studies and towards initiating clinical trials. 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. We have announced our first product candidate, PM359 for the treatment of CGD, and are currently conducting IND-enabling studies. Our research methodology may be unsuccessful in identifying other product candidates, our 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 may experience delays in conducting or completing preclinical studies due to supply chain interruptions that could lead to shortages in materials or animals required for such studies. For example, it has been reported that there is a shortage of non-human primates for biomedical research, which are used in preclinical studies. We have not achieved preclinical proof of concept for many of our programs and there is no guarantee that we will achieve it for any specific program. Our proposed delivery methods with current or future 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. For example, gene therapy companies have been subject to a clinical hold before IND acceptance, in which the FDA has requested further information such as additional control data for preclinical studies and further analyses of certain off-target editing experiments. Accordingly, we may not obtain an immediate IND acceptance on submission and the FDA may request additional information or studies. 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 umbrella or basket clinical studies, studies where more than one mutation in a disease or more than one 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.

Even if we complete the necessary clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize our current or future product candidates in the United States or any other jurisdiction, if at all, and any such approval may be for a narrower 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 preclinical and clinical development; regulatory and marketing approval in multiple jurisdictions, including by the FDA and the EMA; manufacturing supply, capacity and expertise; building of 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 IND applications 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 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 current or future 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 investigation 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 current or future 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, making us subject to additional development challenges and risks. 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, or ZFNs, 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. Multiple companies are also developing alternative gene editing technologies, including Tessera Therapeutics, which states it is pioneering Gene Writing™, a new genome engineering technology that writes therapeutic messages into the genome to treat diseases at their source; Metagenomi, which states it is using metagenomics – the study of genetic material recovered from organisms found in the world's natural microbial environments) – and machine learning to discover novel genome editing systems for therapeutics development; Arbor Biotechnologies, which states it is developing genetic medicines through the discovery of programmable DNA editors to enable curative outcomes for patients; and Chroma Medicine and Moonwalk Therapeutics, both of which are focused on epigenetic editing to treat disease. In addition, 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. 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 licensed issued patents, 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.

Moreover, 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, including evolving regulatory guidance governing gene and gene editing therapy products, the potential risk of improper modulation of a gene sequence and extended follow-up observation periods that may be required by regulatory agencies.

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 current or 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 gene 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 current or future 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, or unintended consequences of on- and off-target 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 in 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, and 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. It is possible that we will detect such off-target edits or other unintended consequences of on- or off-target edits in our current or future product candidates. Our preclinical information for our current or future product candidates 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 or other unintended consequences of on- or 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.

Within our blood programs, we are developing next generation CAR-T cell product(s) for autoimmune or oncology indication(s). While we believe our potential CAR-T product is differentiated from current products, our approach uses PASSIGE technology, which requires the use of a recombinase enzyme and Prime Editing. The use of recombinase enzymes in a human therapeutic is new, and has the potential to result in off-target insertions in the genome. The FDA has recently placed black box warnings on all CAR-T products based on their oncological risks, including secondary T-cell malignancies, caused by integrating vectors such as lentiviral or retroviral vectors. We cannot be sure that our approach will not result in adverse events or be subject to future black box warnings. 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 reported to result in liver toxicity in clinical trials, and in preclinical studies LNPs have been shown to induce oxidative stress in the liver at certain doses. 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, opsonization 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.

We plan to use adeno-associated viruses, or AAVs, which is a relatively new approach for disease treatment. AAV vectors have known side effects and additional risks could develop in the future. In past clinical trials that were conducted by others with AAV vectors, several significant side effects were caused by gene therapy treatments, including, among others, reported cases of neurotoxicity, hepatotoxicity and death. Other potential side effects could include immunologic reactions 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 AAV vectors we use demonstrate similar side effects or other adverse events, we may be required to halt or delay further clinical development of any of our current or future product candidates. Furthermore, the FDA has stated that non-AAV 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. While we are developing a cell shielding approach which, combined with antibody depletion of bone marrow stem cells, has the potential to be a benign method to condition patients for hematopoietic stem cell transplant, antibody-mediated conditioning with cell shielding is at the preclinical stage, and may not be successful or may have unexpected safety concerns.

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 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, there is limited clinical evidence of their ability 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 current or future 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 Kamau Therapeutics, 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 ZFNs, engineered meganucleases and TALENs. Beam Therapeutics and Verve Therapeutics, Inc. are among a number of companies that utilize base editing technology. In addition, other private companies such as Tessera Therapeutics, Inc. 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 Moonwalk Biosciences, Inc., 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, have reported the discovery of new DNA-cutting enzymes, and have announced gene editing programs. 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, 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 current or future 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. For example, the death of a patient with an ultra-rare form of Duchenne Muscular Dystrophy enrolled in a clinical trial assessing a personalized, CRISPR-based gene therapy product candidate initiated by Cure Rare Disease, a non-profit organization, was reported to be caused by an immune response to the vector used in the gene therapy. In addition, a serious adverse event was reported in the first patient dosed in a clinical trial of an investigational gene therapy conducted by Graphite Bio, Inc., and Graphite Bio, Inc. later announced the discontinuation of further development of its gene therapy product candidate after the company concluded that the event was likely related to study treatment. These reports have raised concerns about gene editing approaches that may persist until, or after, details are available. 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.

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 on this issue, 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 current or future product candidates 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 are aiming to expand beyond our immediate target indications, including into broader populations, these approaches will require regulatory approval as discussed in the risk factor entitled "*We are very early in our development efforts and we have not yet 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*." In rare genetically defined diseases, 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 plan to obtain insurance coverage as we expand our clinical trials and/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, potentially 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. We may also have similar issues to other companies that have had difficulties in receiving FDA, or other regulatory agency approval for key potency assays needed for regulatory approval and/or drug release from the manufacturer.

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. In addition, we are broadening the types of edits that we can make by incorporating innovations in Prime Editing, including dual-flap Prime Editing and PASSIGE. The scientific evidence to support the feasibility of developing product candidates based on these technologies 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;
- delays if a clinical trial is suspended or terminated by us, by the IRBs or their ethics committees, the data review committee or data safety monitoring board for such trial or by the FDA, EMA or other foreign regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the regulatory authorities;
- 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; or
- 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 current and future 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 current and future 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 current and future 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 current and future product candidates, which could materially harm our business. If we were to provide patients with our current and future 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 current and future 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 have entered into collaborations, and may enter into additional collaborations, with 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.

As part of our strategy, we have entered into collaborations and intend to seek to enter into additional collaborations with third parties for one or more of our programs or product candidates we may develop. Our likely collaborators for any other collaboration arrangements include pharmaceutical and biotechnology companies, academic institutions, and foundations. We may seek such 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 current and future 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, and may have a reduced ability to prioritize programs and allocate resources.
- 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 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 the risk factor entitled "*The gene editing field is relatively new and is evolving rapidly, making us subject to additional development challenges and risks. 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 current and future 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 current and future 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 current and future 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 anticipated clinical trials, and expect to continue to do so for future 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 expect to continue to do so for preclinical studies and 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 and quality assurance.

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 current and future 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. 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 in-licensed issued patents, 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 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 two license agreements with Broad Institute. In September 2019, we entered into a license agreement with Broad Institute, or the Broad License Agreement, and in May 2020, February 2021, and December 2022, we entered into amendments to such license agreement. In December 2022, we entered into a new license agreement with Broad Institute, or the 2022 Broad License Agreement. Under the amended Broad License Agreement and the 2022 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. Each 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, if we initiate a program for a gene target, in accordance with the terms of each license agreement, we may block a march-in request by making certain showing and by continuing to use commercially reasonable efforts to continue to progress such development. 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. 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 under the Broad License Agreement are co-owned by Broad Institute with Harvard and certain of the licensed patent rights under the Broad License Agreement are co-owned by Broad Institute, Harvard, and Massachusetts Institute of Technology, or MIT. The patent rights that we license from Broad Institute under the 2022 Broad License Agreement are co-owned by Broad Institute with Harvard, the Trustees of Princeton University, or Princeton, and the Regents of the University of California, or University of California. In addition, some of the inventors of the licensed patent and 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 patents and patent applications from Broad Institute are dependent, in part, on inter-institutional or other operating agreements between Broad Institute, Harvard, MIT, University of California, Princeton and HHMI. If Broad Institute, Harvard, MIT, University of California, Princeton or HHMI breaches or terminates such inter-institutional or operating agreements, our rights to such in-licensed patents and 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 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, 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 Therapeutics, 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 Therapeutics under the Beam Collaboration Agreement may lead to co-owned patents and patent applications.

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 each license agreement are subject to certain retained rights of Broad Institute, MIT,

Harvard, Princeton, University of California, 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, each license agreement with Broad Institute 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 each license agreement with Broad Institute 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 patents and 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 patents and patent applications. We rely on such licensors to determine inventorship and perfect priority of their patent applications. We cannot be certain that these patents and 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 patents and patent applications or loses rights to such patents and 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 patents and 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 may have relied on third-party consultants or 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. If other third parties have ownership rights to our in-licensed issued patents and patent applications, 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 issued patents and 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 patents and 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 issued patent and 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 each license agreement with Broad Institute 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. 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 licenses agreements 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 Therapeutics 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 Therapeutics 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 in-licensed issued patents and 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 have in-licensed four issued U.S. patents, one granted ex-U.S. patent, and own and have in-licensed a number of patent applications that cover Prime Editing methods and its components and systems. 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. While we in-license four issued U.S. patents, we do not currently own any, or in-license any other, issued U.S. patents.

We have four in-licensed issued U.S. patents and one granted ex-U.S. patent, all of which cover Prime Editing methods and its components and systems. 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 or our licensors' current and 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 U.S. 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 one or more third parties with respect to certain of our Patent Cooperation Treaty, or PCT, patent applications as well as in patent applications filed in the European Patent Office in-licensed from Broad Institute directed to Prime Editing. Third parties may challenge the inventorship, priority of invention, validity, enforceability or scope of our in-licensed patents and our or our licensors' patent applications that successfully issue, 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 our in-licensed patents or 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 in-licensed patents and 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 in-licensed patents and 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 in-licensed patents and 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 our in-licensed patents or 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 in-licensed patents or our patents that may issue from our owned or in-licensed patent applications that cover our product candidates.

Likewise, our in-licensed issued patents and 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 2045, without taking into account any possible patent term adjustments or extensions. Our in-licensed issued patents, or 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 in-licensed issued patents and 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 in-licensed issued patents or 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 currently have in-licensed one ex-U.S. granted patent that covers Prime Editing components and methods of use. Although we own and have in-licensed numerous ex-U.S. patent applications, 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 future patents or our licensors' patent or 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 future patents or our licensors' patent or 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 patent or 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 exclude 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 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 may be construed to cover or be relevant to our Prime Editing and PASSIGE technologies 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 such as Moloney murine leukemia virus reverse transcriptase, as well as delivery technologies for product candidates we may develop. For our PASSIGE technology, we may require additional licenses from third parties for recombinase technologies.

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 relatively new, and only one therapeutic gene editing product has 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 administrative 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 and PASSIGE technologies and product candidates we may develop, including interference proceedings, post-grant review, inter partes review, derivation proceedings and reexamination 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 March 2022, it was reported that over 11,000 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 proteins, 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, including ones that may be relevant to our Prime Editing and PASSIGE technologies, owned or co-owned by Broad Institute, MIT, Rockefeller University, Harvard, Toolgen Inc. and Sigma-Aldrich. Additional patents and patent applications that we are aware of and directed to gene-editing, including ones that may be relevant to our Prime Editing and PASSIGE technologies, 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, University of California, Intellia, Editas Medicine, Tome Biosciences, Flagship Pioneering Innovations, Caribou Biosciences, University of Washington, University of California, Stanford University, Cellectis, and Inscripta.

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 CRISPR-Cas9 gene editing are currently involved in interference proceedings at the USPTO. The Patent Trial and Appeal Board, or PTAB, of the USPTO declared a second interference between 14 pending applications co-owned by the CVC and 13 patents and one pending application co-owned by Broad Institute, MIT, Rockefeller University and Harvard, which we refer to as the Boston Licensing Parties, in 2019 after the first interference between the two parties was terminated in 2018. In February 2022, the PTAB issued a decision in the second interference, granting priority to the patents and pending application co-owned by the Boston Licensing Parties over the pending applications co-owned by the CVC. In September 2022, the CVC appealed the PTAB's decision, at the U.S. Court of Appeals for the Federal Circuit and the appeal is ongoing. While the second interference was in progress, Toolgen 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. 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. The PTAB subsequently suspended the interferences involving Toolgen and Sigma-Aldrich until the Federal Circuit issues a decision in the appeal between the CVC and the Boston Licensing Parties over the PTAB's decision in the second interference. 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 and other third parties 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 issued patents or 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 issued or 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 issued or 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 patents and in-licensed patents and future patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our future owned patents or in-licensed patents or future 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 in-licensed patents or 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.

Even if we established infringement of any of our future patents or issued or future in-licensed patents by a competitive product, a court may decide not to grant an injunction against further infringing activity, thus allowing the infringing product to continue to be marketed by the competitor. It is difficult to obtain an injunction in U.S. patent litigation and a court could decide that the competitor should instead pay us a "reasonable royalty" as determined by the court, and/or other monetary damages. A reasonable royalty or other monetary damages may or may not be an adequate remedy. Loss of exclusivity and/or competition from a competitive product would have a material adverse impact on our business.

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 in-licensed patents, owned or licensed patent 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 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 issued in-licensed patents and future issued patents.

The U.S. Congress is responsible for passing laws establishing patentability standards. Interpretation of patent standards can change significantly over time. 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 or our licensors have obtained or 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. The application of Myriad to biotechnology inventions has continued to develop and may continue to change over time.

In addition, the U.S. Supreme Court recently decided the case *Amgen Inc. v. Sanofi*, which pertained to patent claims that defined a class of antibodies solely by their binding to a particular antigen. The U.S. Supreme Court determined that Amgen's claims broadly covered an entire class of antibodies while the patent specification described only a few antibodies and a trial and error approach to make and use all of the claimed antibodies. The U.S. Supreme Court held that the patent claims were invalid because Amgen's patent specification did not enable the claims over their broad scope. Certain claims in our patent portfolio relate to broad classes of gene editors. To the extent that a court finds that our patent specifications do not enable such broad classes of gene editors, a court could find such claims invalid.

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 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.

For example, a new court system relating solely to patent cases recently became operational in the EU. The Unified Patent Court, or the UPC, began accepting patent cases on June 1, 2023. The UPC is a common patent court with jurisdiction over patent infringement and revocation proceedings effective for multiple member states of the EU. The broad geographic reach of the UPC could enable third parties to seek revocation of any of our European patents that are subject to the jurisdiction of the UPC in a single proceeding at the UPC. Under the UPC, a successful revocation proceeding for a European Patent under the UPC could result in the partial or complete loss of patent protection in numerous EU countries. Such a loss of patent protection could have a material adverse impact on our business, including our ability to commercialize our technology and product candidates. Moreover, the controlling laws and regulations of the UPC will develop over time and we cannot predict what the outcomes of cases tried

before the UPC will be. The case law of the UPC may adversely affect our ability to enforce or defend the validity of our European patents. Patent owners have the option to opt-out their European Patents from the jurisdiction of the UPC, defaulting to pre-UPC enforcement mechanisms. We have decided to opt out all of our European patents and patent applications from the UPC at this time. However, if certain formalities and requirements are not met, our European patents and patent applications could be subject to the jurisdiction of the UPC. Further, our future European patents and patent applications may not be subject to the opt-out provisions.

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. 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 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 or inability 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 pharmaceutical industries, we employ individuals who were previously employed at universities, research institutions, or other biotechnology and pharmaceutical 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, if approved, 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 issued patents or 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 issued patents or 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 patents or 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 patents or 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 the patent or patents issuing from these patent applications to be held invalid or unenforceable;
- patents, if and when issued, 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 or patent applications may become involved with competitors, develop products or processes that design around our patent or patent applications, or become hostile to us or the patent, 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 or 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 the development of gene therapy products have changed frequently and may continue to change in the future. Recently, the FDA issued several new guidance documents on gene therapy products, and in January 2024, the FDA finalized its guidance document providing recommendations for human genome editing gene therapy products. In addition to the government regulators, the IBC and IRB of each institution at which we will conduct clinical trials of our current or future

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 current and future 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 current and future 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 also delay necessary manufacturing facility inspections by regulators and adversely affect the supply of any product candidates we may develop.

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.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or

otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, 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. For more information, see *"Business – Other Healthcare Laws and Compliance Requirements – Healthcare Reform."*

The continuing efforts of the government, insurance companies, managed care organizations and other payers of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any of our product candidates, if approved;
- the ability to set a price that we believe is fair for any of our product candidates, if approved;
- our ability to generate revenues and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical and biologic products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased

scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

We expect that the healthcare reform measures that have been adopted and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our product candidates could limit our product revenues.

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. In the United States, no uniform policy of coverage and reimbursement for drug or biological products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor-by-payor basis. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained. For more information, see "Business – Other Healthcare Laws and Compliance Requirements – Insurance and Coverage."

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 current and future 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 current or future 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 current or future 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 current and future 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 current or future 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 current or future 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 current or future 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 current or future 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 current or future 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 current or future 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 or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other 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 IMM. 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. Under FDORA, the FDA is permitted to require, as appropriate, that a post-approval confirmatory study or studies be underway prior to approval or within a specified time period after the date of approval for a product granted accelerated approval. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post-approval studies fail to verify the drug's predicted clinical benefit. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress. 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 be submitted to the Agency for review. 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. Receiving accelerated approval does not assure that the product's accelerated approval will eventually be converted to a traditional approval.

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 current or future 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.

We received orphan drug designation from the FDA for PM359 for the treatment of CGD. We may also seek rare orphan disease designation for some of our other current or future product candidates. 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 (as applicable) 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 (which can be extended to 12 years if the sponsor complies with an agreed upon pediatric investigation plan). The exclusivity period in the European Union can be reduced to six years if at the end of the fifth year it is determined that a product no longer meets the criteria for orphan drug designation, including if the product is sufficiently profitable so that market exclusivity is no longer justified. Legislation has been proposed by the European Commission that, if implemented, has the potential in some cases to shorten the 10-year period of orphan marketing exclusivity.

In order for the FDA to grant orphan drug exclusivity to one of our current or future 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.

The FDA may reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. In addition, the European Commission introduced a legislative proposal in April 2023 that, if implemented, could reduce the current 10-year marketing exclusivity period in the EU for certain orphan medicines. Depending on what changes the FDA and the European Commission may make to its orphan drug regulations and policies, our business could be adversely impacted.

We may seek rare pediatric disease designation for certain of our current or future product candidates, but we might not receive such designation, and even if we do, we may not be able to realize the intended benefits of such designation.

We received rare pediatric disease designation from the FDA for PM359 for the treatment of CGD. We may also seek rare pediatric disease designation for some of our other current or future product candidates. Designation of a product candidate as a product for a rare pediatric disease does not guarantee that a marketing application for such product candidate will meet the eligibility criteria for a rare pediatric disease priority review voucher, or PRV, at the time the application is approved. Under the Federal Food, Drug, and Cosmetic Act we will need to request a rare pediatric disease PRV in our original marketing application for any potential product candidates for which we have

received rare pediatric disease designation. The FDA may determine that a marketing application for any such product candidates, if approved, does not meet the eligibility criteria for a PRV. Under the current statutory sunset provisions, after September 30, 2024, the FDA may only award a PRV for an approved rare pediatric disease product application if the sponsor has rare pediatric disease designation for the drug or biologic that is the subject of such application, and that designation was granted by September 30, 2024. After September 30, 2026, the FDA may not award any rare pediatric disease PRVs. However, it is possible the authority for FDA to award rare pediatric disease PRV will be further extended by Congress. As such, if we do not obtain approval of a marketing application for any of our current or future product candidates on or before September 30, 2026, and if the PRV program is not extended by Congressional action, we may not receive a PRV.

We may seek designation for our Prime Editing platform technology as a designated platform technology, but we might not receive such designation, and even if we do, such designation may not lead to a faster regulatory review or approval process.

We may seek designation for our Prime Editing platform technology as a designated platform technology. Under FDORA, a platform technology incorporated within or utilized by a drug or biological product is eligible for designation as a designated platform technology if: (1) the platform technology is incorporated in, or utilized by, a drug approved under an NDA or BLA; (2) preliminary evidence submitted by the sponsor of the approved or licensed drug, or a sponsor that has been granted a right of reference to data submitted in the application for such drug, demonstrates that the platform technology has the potential to be incorporated in, or utilized by, more than one drug without an adverse effect on quality, manufacturing, or safety; and (3) data or information submitted by the applicable person indicates that incorporation or utilization of the platform technology has a reasonable likelihood to bring significant efficiencies to the drug development or manufacturing process and to the review process. A sponsor may request the FDA to designate a platform technology as a designated platform technology concurrently with, or at any time after, submission of an IND application for a drug that incorporates or utilizes the platform technology that is the subject of the request. If so designated, the FDA may expedite the development and review of any subsequent original NDA or BLA for a drug that uses or incorporates the platform technology. Even if we believe our Prime Editing platform technology meets the criteria for such designation, the FDA may disagree and instead determine not to grant such designation. In addition, the receipt of such designation for a platform technology does not ensure that a drug will be developed more quickly or receive a faster FDA review or approval process. Moreover, the FDA may revoke a designation if the FDA determines that a designated platform technology no longer meets the criteria for such designation.

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. We are also exposed to risks in connection with any insider trading violations by employees or others affiliated with us. We adopted a code of conduct and an insider trading policy 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 UK. 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, or may become, subject to a number of data privacy and protection laws, rules, regulations, policies, standards and contractual obligations that apply to our collection, transmission, storage, use, disclosure, transfer, maintenance and other processing of personal information. The legislative and regulatory landscape for privacy and data protection is rapidly evolving in the U.S. and Europe, as well as other jurisdictions worldwide, which may lead to increased regulatory scrutiny on privacy and data protection requirements. As a result of the complexity of data privacy and protection laws and regulations applicable to our business, and the uncertainty in how such regulations will be applied and interpreted, we cannot guarantee that we are, or have been, in compliance with all such

regulations. Additionally, we rely on certain third-party vendors to process certain confidential, sensitive or personal information on our behalf. Failure or perceived 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.

In the U.S., federal and state laws, rules and regulations related to the privacy and security of personal information apply, or may apply, to our business. At the federal level, for example, regulations promulgated pursuant to the Health Insurance Portability and Accountability Act of 1996, or HIPAA, establish data 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 technical safeguards to protect the confidentiality, integrity and availability of electronic protected health information.

If we fail to comply with applicable HIPAA privacy and security standards, we could face significant civil and criminal penalties. The Department of Health and Human Services, or HHS, has the discretion to impose penalties without attempting to resolve violations through informal means. Such enforcement activity can result in financial liability and reputational harm, and our responses to such enforcement activity can consume significant internal resources.

U.S. state laws also govern the privacy and protection of personal information. For example, the California Consumer Privacy Act, or the CCPA, establishes data privacy rights for individuals located in California and imposes certain requirements on how businesses can collect and use personal information about such individuals. The California Privacy Rights Act, or the CPRA, significantly modifies the CCPA and imposes additional obligations on companies covered by the legislation, including by expanding consumers' rights with respect to personal information, and establishes a state agency vested with the authority to enforce the CCPA. Many other states have either passed or implemented similar, comprehensive privacy and data protection legislation. Moreover, states are passing laws geared to protect specific categories of personal information, most notably Washington's My Heath Data Act, which provides an additional layer of protection to consumer health data, which is broadly defined. Many state privacy and data protection laws differ from each other in significant ways, and it is not yet fully clear how such laws will be enforced and interpreted. Thus, we may be required to incur substantial costs and expenses in an effort to comply with them, and may be required to modify our data collection and use practices.

Additionally, all 50 states have laws in place which may require businesses to provide notice to customers whose personal information has been disclosed as a result of a data breach. Determining whether personal information has been handled in compliance with applicable state breach notification requirements, privacy standards and our contractual obligations can be complex and may be subject to statutory and contractual interpretation, thus potentially complicating our compliance efforts.

Further, the Federal Trade Commission, or FTC, as well as other state attorneys general, regulate the content of our privacy policies and other public statements that provide promises and assurances about our data privacy and protection practices. 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. If such statements are found to be deceptive, unfair or misrepresentative of our actual practices, we may subject us to government enforcement actions or other legal claims. Over the past year, the FTC has focused enforcement efforts on protecting privacy in the context of personal health information.

In Europe, the collection and use of personal information is governed by the EU's General Data Protection Regulation and the UK's implementation of the same (collectively, the GDPR). Failure to comply with the requirements of the GDPR may result in significant fines and other administrative penalties. In addition, we may be required to put in place additional mechanisms to comply with current and future privacy and data protection regulations in Europe and other worldwide jurisdictions which are or will become applicable to our business. This may interrupt or delay our development activities and/or require us to change our business practices, which could adversely affect our business, financial condition, results of operations and prospects.

Data privacy and protection legislation and enforcement will continue to be an evolving landscape at both the domestic and international level, with new laws, rules and regulations coming into effect and presenting continued legal challenges, and our efforts to comply with them 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, and may not be consistent with one another. If any such legislation is enacted, we may be required to devote significant resources to understanding and complying with such legislation, and the lack of a unified approach to data privacy and protection laws in the U.S. could lead to complicated and potentially conflicting compliance requirements. Any failure or perceived failure to comply with these laws, rules or regulations, or with any related government investigations, may 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 Financial Officer, 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, Allan Reine, our Chief Financial Officer, 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, Dr. Duffield, 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.

Dr. Liu serves on our Scientific Advisory Board and as our paid consultant and retains 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.

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.

In connection with the growth and advancement of our pipeline and being 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, our current

physical and laboratory space may be insufficient for our near-term research and development hiring plans, and 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 current or future 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.

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. The risk of cyber incidents could also be increased by cyberwarfare in connection with the current conflict between Russia and Ukraine, including potential proliferation of malware into systems unrelated to the conflict. In addition, part of our workforce is currently working remotely. This could increase our cybersecurity risk, create data accessibility concerns, and make us more susceptible to communication disruptions. While we seek to protect our information technology systems from system failure, accident and security compromise or 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 compromise or failure or cybersecurity attack attributed to our third-party vendors as they relate to infrastructure they support or the information we share with them.

If we were to experience a cybersecurity compromise or 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 systems and 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, while we currently maintain cybersecurity insurance, coverage 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, compromise 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 confidential, personal, or proprietary 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.

Artificial intelligence presents risks and challenges that can impact our business including by posing security risks to our confidential information, proprietary information, and personal data.

Issues in the development and use of artificial intelligence, combined with an uncertain regulatory environment, may result in reputational harm, liability, or other adverse consequences to our business operations. As with many technological innovations, artificial intelligence presents risks and challenges that could impact our business. We may adopt and integrate generative artificial intelligence tools into our systems for specific use cases reviewed by legal and information security. Our vendors may incorporate generative artificial intelligence tools into their offerings without disclosing this use to us, and the providers of these generative artificial intelligence tools may not meet existing or rapidly evolving regulatory or industry standards with respect to privacy and data protection and may inhibit our or our vendors' ability to maintain an adequate level of service and experience. If we, our vendors, or our third-party partners experience an actual or perceived breach or privacy or security incident because of the use of generative artificial intelligence, we may lose valuable intellectual property and confidential information and our reputation and the public perception of the effectiveness of our security measures could be harmed. Further, bad actors around the world use increasingly sophisticated methods, including the use of artificial intelligence, to engage in illegal activities involving the theft and misuse of personal information, confidential information, and intellectual property. Any of these outcomes could damage our reputation, result in the loss of valuable property and information, and adversely impact our business.

Risks Related To Ownership of Our Common Stock

We do not know whether a market will be sustained 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.

Although our common stock is listed on the Nasdaq Global Market, an active trading market for our common stock may not be sustained. If a market for our common stock 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.

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

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;
- public health crises, pandemics, 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. In particular, in relation to uncertainty around inflation and the U.S. Federal Reserve's measures to slow inflation, the stock market has been exceptionally volatile. Market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. 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.

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 relies in part on the research and reports that industry or financial analysts publish about us or our business. 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 or the perception that these sales could occur. These sales, or the perception 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.

As of December 31, 2023, we had 97,377,121 shares of common stock outstanding. Shares of unvested restricted stock that were issued and outstanding will become available for sale immediately upon the vesting of such shares, as applicable. 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.

Certain holders of our common stock 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 have registered the offer and sale of all shares of common stock that we may issue under our equity compensation plans, and those shares are available for sale in the open market, unless such shares are subject to vesting restrictions with us or the lock-up restrictions described above. Once we register the offer and sale of shares for the holders of registration rights, they can be freely sold in the public market upon issuance, subject to the lock-up agreements.

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 have substantial influence over us, which could limit your ability to affect the outcome of key transactions, including a change of control.

Our directors and executive officers and their affiliates beneficially own a significant percentage 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.

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 certain other public companies.

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 are also a "smaller reporting company," meaning that the market value of our stock held by non-affiliates 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 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 have incurred, and continue to incur, increased costs as a result of operating as a public company, and our management must devote substantial time to compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an "emerging growth company," we have incurred, and will continue to 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 continue to need to hire additional accounting, finance and other personnel in connection with 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, the rules and regulations applicable to us as a public company make it more difficult and more expensive for us to maintain 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 are required to furnish a report by our management on our internal control over financial reporting. 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 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, the U.S. Treasury Department and non-U.S. taxing authorities. 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. For example, under Section 174 of the Code, in taxable years beginning after December 31, 2021, expenses that are incurred for research and development in the United States will be capitalized and amortized, which may have an adverse effect on our cash flow. 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. We will continue the process of reviewing and making appropriate changes to our internal controls and procedures for compliance with SOX Section 404, which requires 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.

If we 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.

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. Pursuant to SOX Section 404, we are required to furnish a report by our management on 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 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 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, 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 as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware; 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 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, the Exchange Act, the respective rules and regulations promulgated thereunder 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. 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 federal district courts of the United States 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 face risks related to health epidemics, pandemics and other widespread outbreaks of contagious disease, including COVID-19, 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, COVID-19 and the post-COVID environment, including supply chain, labor market and other disruptions, as well as volatility in the global financial markets, in each case driven by the pandemic, have affected segments of the global economy and our operations. Worldwide pandemics or outbreaks of any highly infectious or contagious diseases may adversely impact our operations, research and development, and as we continue development, 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; 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.

In addition, health pandemics and epidemics, such as COVID-19, could continue to produce significant and prolonged disruption of or volatility in global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. The extent to which COVID-19 and the post-COVID environment impact our business, results of operations and financial condition will depend on future developments. 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, the post-COVID environment or any future pandemic or other outbreak of contagious disease could exacerbate the other risks described in this section.

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.

Item 1B. Unresolved Staff Comments

None.

Item 1C. Cybersecurity

We recognize the importance of assessing, identifying, and managing material risks associated with cybersecurity threats, as such term is defined in Item 106(a) of Regulation S-K. These risks include, among other things: operational risks, intellectual property theft, fraud, extortion, harm to employees and violation of data privacy or security laws.

Oversight and Governance

Our cybersecurity risk management program is a significant part of our overall risk management program, which has been delegated by our Board of Directors to the Audit Committee of the Board of Directors ("Audit Committee"). As provided in the Audit Committee Charter, the Audit Committee is responsible for reviewing, assessing, and considering, in consultation with management and the Board, as appropriate, the overall risk management policies and procedures of the Company, including our major risk exposures such as cybersecurity.

Members of our senior management, including our Chief Executive Officer, Chief Financial Officer, and leaders from our legal and information technology functions, maintain responsibility for assessing and managing cybersecurity threats. This team has deep expertise in building and leading information systems and cybersecurity teams across a variety of institutions.

Risk Management and Strategy

Teams of internal and third-party cybersecurity professionals oversee cybersecurity risk management, which is based on the National Institute for Standards and Technology Cybersecurity Framework:

- Identify – Develop an organizational understanding to manage cybersecurity risk to systems, people, assets, data, and capabilities.
- Protect – Develop and implement appropriate safeguards to ensure delivery of critical services.
- Detect – Develop and implement appropriate activities to identify the occurrence of a cybersecurity event.
- Respond – Develop and implement appropriate activities to take action regarding a detected cybersecurity incident.
- Recover – Develop and implement appropriate activities to maintain plans for resilience and to restore any capabilities or services that were impaired due to a cybersecurity incident.

We maintain a comprehensive process for identifying, assessing, and managing material risks from cybersecurity threats as part of our broader risk management system and processes that is centered on three key components:

- Identification of risks: We obtain input, as appropriate, for our cybersecurity risk management program on the security industry and threat trends from multiple external experts and internal threat intelligence teams.
- Assessment of threats: We assess organization vulnerabilities and the likelihood that the risk scenarios could occur, including risk assessments of our existing systems, penetration testing, and other vulnerability analyses. This assessment also extends to critical third parties, such as contract research organizations, prior to being approved to work with the company, and includes reviews of Service Organization Control Type 2 reports.
- Execute: Internal and third-party experts coordinate implementation of necessary security controls to prevent or reduce the risk of security vulnerabilities from being exposed.

We also maintain an ongoing end-user cybersecurity awareness program that is designed to raise awareness of cybersecurity threats to reduce our vulnerability as well as to encourage consideration of cybersecurity risks across functions, including quarterly training and simulated phishing campaigns.

The Audit Committee and Board of Directors receive routine updates from senior management, including leaders from our information technology and legal functions regarding matters of cybersecurity. These updates include existing and new cybersecurity risks, status on how management is addressing and mitigating those risks, cybersecurity and data privacy incidents, if any, and status on key information security initiatives.

Item 2. Properties

We currently lease and occupy the following spaces:

- approximately 10,000 square feet of laboratory and office space at 21 Erie Street, Cambridge, MA 02139 for which we provided notice to terminate and such termination will become effective in June 2024;

- approximately 13,000 square feet of office space at 38 Sidney Street, Cambridge, MA 02139 under a lease term that expires in December 2024;
- approximately 27,000 square feet of combined laboratory and office space at 64 Sidney Street, Cambridge, MA 02139 under a lease term that expires in April 2025; and
- approximately 16,000 square feet of combined laboratory and office space at 480 Arsenal Street, Watertown, MA 02472 under a lease term that expires in April 2027.

In addition to these spaces, we have secured approximately 148,941 square feet in new office and laboratory space at 60 First Street, Cambridge, MA 02141 that we expect to begin to occupy in mid-2024.

We believe that our facilities are adequate for our current needs and for the foreseeable future and that suitable additional or substitute space at commercially reasonable terms will be available as and when needed.

Item 3. Legal Proceedings

We are not currently a party to any material legal or arbitration proceedings. No governmental proceedings are pending or, to our knowledge, contemplated against us. We are not currently a party to any material proceedings in which any director, member of senior management or affiliate of ours is either a party adverse to us or our subsidiaries or has a material interest adverse to us or our subsidiaries. In the ordinary course of business, we are from time to time involved in lawsuits, claims, investigations, proceedings, and threats of litigation related to intellectual property, commercial arrangements, and other matters. The outcome of any such legal proceedings, regardless of the merits, is inherently uncertain. In addition, litigation and related matters are costly and may divert the attention of our management and other resources that would otherwise be engaged in other activities. If we were unable to prevail in any such legal proceedings, our business, results of operations, liquidity, and financial condition could be adversely affected.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities Market Information

Our common stock has been publicly traded on the Nasdaq Global Market under the symbol "PRME" since October 20, 2022. Prior to that time, there was no public market for our common stock.

Holders

As of February 26, 2024, there were approximately 76 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

Dividends

We have not declared or paid any cash dividends on our capital stock since our inception. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends to holders of common stock in the foreseeable future.

Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Item 12, *Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters*, of this Annual Report on Form 10-K.

Recent Sales of Unregistered Securities

None.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Use of proceeds from registered securities

In October 2022, our Registration Statement on Form S-1 (File No. 333-267579) was declared effective by the SEC pursuant to which we issued and sold 11,721,456 shares of our common stock, including 1,427,338 shares pursuant to the exercise of the underwriters' option to purchase additional shares, at a price to the public of $17.00 per share. From the sale, we received $180.2 million in net proceeds, after deducting underwriting discounts, commissions and offering costs of $19.1 million. J.P. Morgan Securities LLC, Goldman Sachs & Co. LLC, Morgan Stanley & Co. LLC, and Jefferies LLC acted as joint book-running managers of the offering.

There has been no material change in our planned use of the net proceeds described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act on October 21, 2022.

Item 6. [Reserved]

Not Applicable.

Item 7. 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 and other financial information included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. You should review "Item 1A, Risk Factors" of this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

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. We are deploying Prime Editing technology, which we believe is a versatile, precise, and efficient gene editing technology.

To maximize the potential of our Prime Editing technology, we have built a diversified portfolio of investigational therapeutic programs organized around core areas of focus: hematology and immunology, liver, lung, ocular, and neuromuscular. We are advancing additional programs as potential partnership opportunities.

Chronic granulomatous disease, is our most advanced blood program, and we have designated PM359 as our development candidate. We plan to submit an investigational new drug application with the U.S. Food and Drug Administration in the first half of 2024.

Programs within our other areas of focus are in earlier stages of preclinical development and include:

- Liver programs: Wilson's disease and glycogen storage disease 1b
- Lung program: Cystic fibrosis
- Ocular program: Retinitis pigmentosa caused by Rhodopsin mutations.
- Neuromuscular programs: Friedreich's ataxia and myotonic dystrophy type 1
- Additional program: CAR-T

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.

Components of Our Results of Operations

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts, and the development of our product candidates. These expenses include:

- the cost allocated to acquire in-process research and development, with no alternative future use associated with asset acquisitions or transactions to license intellectual property, such as our 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 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. 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.

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 expect our research and development expenses to continue to increase substantially for the foreseeable future with our planned 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.

General and Administrative Expenses

General and administrative expenses consist 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 research and development activities; increased accounting, legal, insurance, and investor and public relations costs as we continue to operate as a public company; and additional intellectual property-related expenses as we file patent applications to protect innovations arising from our research and development activities.

Other Income (Expense)

Other income (expense), net consists of:

- interest and other income earned on our short-term investments; and
- the change in the fair value of our short-term investment in Beam Therapeutics Inc. (“Beam”), a related party, in connection with the Beam Collaboration Agreement, which is discussed in greater detail in Item 1. *Business*, of this Annual Report on Form 10-K.

Results of Operations — Comparison of the Years Ended December 31, 2023 and 2022

Operating Expenses

Research and Development Expenses

(in thousands)	Year ended December 31, 2023	2022	Change
Research and development expenses:			
Lab supplies	$ 59,609	$ 30,658	$ 28,951
Personnel expenses	51,095	31,624	19,471
Facility related	24,221	16,100	8,121
Professional and consultant fees	6,845	2,186	4,659
License, intellectual property fees, and other	6,135	6,157	(22)
Total research and development expenses	$ 147,905	$ 86,725	$ 61,180

The $61.2 million increase in research and development expense for the year ended December 31, 2023 as compared to the year ended December 31, 2022 is primarily driven by:

- $29.0 million increase in lab supplies expense due to continued discovery efforts and expansion of our research and development activities, including ongoing IND-enabling activities, and increased personnel in our R&D function;
- $19.5 million increase in personnel expense, including an increase in stock-based compensation expense of $3.5 million, and $4.7 million increase in professional and consultant fees, both driven by our increased headcount as we continue to build out our research and development function; and
- $8.1 million increase in facility-related expense primarily due to the expansion and build out of our office and laboratory space.

Settlement Payment — Related Party

In January 2024, we entered into a settlement agreement with Myeloid to resolve two arbitration proceedings. Under the terms of the agreement, the parties agreed to resolve and settle all disputes between the parties and release all claims between them relating to the parties' license agreement and the arbitrations in exchange for our payment to Myeloid of $13.5 million, certain mutual covenants, and other consideration.

General and Administrative Expenses

(in thousands)	Year ended December 31, 2023	2022	Change
General and administrative expenses:			
Professional and consultant fees	$ 17,642	$ 13,013	$ 4,629
Personnel expenses	17,076	11,094	5,982
Facility related and other	8,669	5,712	2,957
Total general and administrative expenses	$ 43,387	$ 29,819	$ 13,568

The $13.6 million increase in general and administrative expense for the year ended December 31, 2023 as compared to the year ended December 31, 2022 is primarily driven by:

- $4.6 million increase in professional and consultant fees and $6.0 million increase in personnel expenses, which includes an increase in stock-based compensation expense of $3.9 million, both driven by growth in

personnel as we operate as a public company and to support our growing research and development function; and

- $3.0 million increase in facility related expenses primarily due to the expansion and build out of our office space.

Other Income (Expense)

(in thousands)	Year ended December 31, 2023	2022	Change
Other income (expense):			
Change in fair value of short-term investment — related party	$ (2,382)	$ (8,128)	$ 5,746
Other income, net	8,762	1,903	6,859
Total other income (expense), net	$ 6,380	$ (6,225)	$ 12,605

Change in Fair Value of Related Party Short-Term Investment

For all periods presented, the change in fair value of related party short-term investment for each of the periods presented is a result of Beam's stock price movement from the start of each respective year to the end of each respective year.

Other Income (Expense), Net

For all periods presented, the amount of other income, net, net primarily consists of interest income from short-term investments.

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 sales of preferred stock and public offerings of our common stock. As of December 31, 2023, we had cash and cash equivalents, short-term investments, and related party short-term investments of $121.7 million, excluding our restricted cash, or $135.2 million, including restricted cash.

In November 2023, we entered into an Open Market Sale Agreement℠ (the "Sales Agreement") with Jefferies LLC ("Jefferies") under which we may, from time to time, issue and sell shares of our common stock having aggregate sales proceeds of up to $300.0 million, in a series of one or more at-the-market equity offerings (the "2023 ATM Program"). Jefferies is not required to sell any specific share amounts but acts as our sales agent, using commercially reasonable efforts consistent with its normal trading and sales practices. We will pay Jefferies a commission equal to 3.0% of the aggregate gross proceeds we receive from each sale of our shares of common stock. Pursuant to the Sales Agreement, any shares will be sold pursuant to our shelf registration statement on Form S-3 (File No. 333-275321) filed with the SEC on November 3, 2023, including the base prospectus contained therein, as declared effective by the SEC on November 13, 2023. Our common stock will be sold at prevailing market prices at the time of the sale, and as a result, prices may vary. As of December 31, 2023, we have not sold any shares of common stock under the 2023 ATM program.

In February 2024, we issued and sold 22,560,001 shares of our common stock, including 3,360,000 shares pursuant to the exercise of the underwriters' option to purchase additional shares, at a price to the public of $6.25 per share. Further, in lieu of common stock to certain investors, we sold pre-funded warrants to purchase 3,200,005 shares of common stock at a public offering price of $6.24999 per pre-funded warrant, which represents the per share public offering price of each share of common stock less the $0.00001 per share exercise price for each pre-funded warrant. As a result of the offering, we received approximately $150.9 million in net proceeds, after deducting underwriting discounts, commissions and estimated offering costs of $10.1 million.

Cash Flows

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

(in thousands)	Year ended December 31, 2023	2022
Net change in cash, cash equivalents, and restricted cash		
Net cash used in operating activities	$ (165,412)	$ (131,827)
Net cash provided by (used in) investing activities	18,711	(47,096)
Net cash provided by (used in) investing activities	655	181,494
Net change in cash, cash equivalents, and restricted cash	$ (146,046)	$ 2,571

Operating Activities

Net cash used in operating activities for the year ended December 31, 2023 was driven primarily by the following uses of cash:

- $198.1 million net loss;
- $12.3 million change in lease liabilities; and
- $9.5 million change in prepaid and other current assets.

These were offset by:

- $30.1 million of non-cash amounts included in net loss, which consisted primarily of stock-based compensation expense, non-cash lease expense, depreciation and amortization expense, and change in fair value of short-term investment — related party;
- $13.5 million change in accrued settlement payment — related party;
- $9.1 million change in accounts payable; and
- $1.8 million change in accrued expenses and other assets.

Net cash used in operating activities for the year ended December 31, 2022 was driven primarily by the following uses of cash:

- $121.8 million net loss;
- $25.9 million change in accrued expenses and other current liabilities;
- $10.2 million change in lease liabilities; and
- $1.7 million change in prepaid and other current assets.

These were offset by:

- $25.4 million of non-cash amounts included in net loss, which primarily consisted of change in non-cash lease expense, fair value of short-term investment — related party, and stock-based compensation expense; and
- $2.5 million change in accounts payable.

Investing Activities

Net cash provided by investing activities for the year ended December 31, 2023 was driven primarily by the following:

- $27.6 million of maturities of short-term investments, net of purchases; offset by
- $8.7 million of purchases of property and equipment.

Net cash used in investing activities for the year ended December 31, 2022 was driven primarily by the following:

- $30.3 million of purchases of short-term investments, net of maturities; and
- $16.1 million of purchases of property and equipment.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2022 was driven primarily by the following:

- $185.3 million of net proceeds from the sale of our common stock in our IPO; offset by
- $4.0 million payment of deferred offering costs.

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, we have incurred, and expect to continue to incur, 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 our existing cash, cash equivalents, and investments will be sufficient to fund our operating expenses and capital expenditure requirements into the third quarter of 2025. 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, 2023, we have future remaining operating lease payments of $14.6 million relating to leases we have recognized on our consolidated balance sheet. In addition, we have one lease that has been entered into but has not yet commenced, as of December 31, 2023, for which we expect to pay approximately $208.7 million over the 10 year lease term. Refer to Note 10, *Leases,* to our consolidated financial statements appearing within this Annual Report on Form 10-K for more information on our lease obligations.

Under our license and collaboration agreements, we are potentially obligated to pay certain milestones, royalty fees, licensing maintenance fees, and reimbursement of patent maintenance costs. These amounts are contingent upon the occurrence of future events and the timing and likelihood of such potential obligations are not known with certainty.

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, *Summary of Significant Accounting Policies,* to our consolidated financial statements appearing within this Annual Report on Form 10-K, 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.

Stock-Based Compensation Expense

Subsequent to our IPO, 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. Compensation expense for those awards is recognized over the requisite service period, which is generally the vesting period of the respective award, using the straight-line method. We account for forfeitures of stock-based awards as they occur.

The Black-Scholes option pricing model used to determine the fair value of our stock options includes various assumptions, including the expected term of the award, the expected volatility, and the expected risk-free interest rate, expected dividend payments, and the fair value of the common stock underlying the stock-based award.

We consider the expected volatility to be a critical accounting estimate. As we do not have sufficient trading history, we use the average historical volatility of a representative group of publicly traded biopharmaceutical companies to calculate the expected volatility for use in the Black-Scholes option pricing model. This assumption reflects our best estimate; but determining a representative peer group involves subjective considerations. As a result, if a different peer group is used to estimate volatility, the resulting volatility could have a material impact on our stock-based compensation expense.

Determination of the Fair Value of Our Common Stock Issued Prior to Our IPO

Prior to our IPO in October 2022, there was no public market for our common stock. As a result, prior to our IPO, the estimated fair value of our common stock was determined by our board of directors as of the date of each option

grant, 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 grant.

Prepaid and Accrued Research and Development Expenses

As part of preparing our consolidated financial statements, we are required to estimate research and development expenses. This process involves reviewing quotations and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. These estimates of the expenses incurred are based on facts and circumstances known to us at that time. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could have a significant impact on reported amounts.

If the payments made exceed the expenses incurred, the excess amount is reflected as prepaid expenses and other current assets. If the expenses incurred exceed payments made, the difference is reflected as accrued expenses and other current liabilities.

Non-refundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized in prepaid expenses and other current assets. The capitalized amounts are expensed as the related goods are delivered or services are performed.

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, *Summary of Significant Accounting Policies*, to our consolidated financial statements appearing within this Annual Report on Form 10-K.

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.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

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, 2023, we held cash and cash equivalents, short-term investments, and related party short-term investments of $121.7 million, excluding restricted cash, which consisted of cash, money market funds, equity securities, and U.S. Treasuries, or $135.2 million, including restricted cash. 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.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor and research and development costs. Although we do not believe that inflation has had a material impact on our financial position or results of operations to date, we may

experience some effect in the future due to an impact on the costs to conduct research and development, labor costs we incur to attract and retain qualified personnel, and other operational costs.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those financial statements is found in Item 15, *Exhibits and Financial Statement Schedules*, of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Based on the evaluation of our disclosure controls and procedures as of December 31, 2023, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures as of such date are effective at the reasonable assurance level.

Management's Annual Report on Internal Controls Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our board of directors, management, and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with United States GAAP. Our internal control over financial reporting includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately, and fairly reflect our transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with United States GAAP, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become

inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2023. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in its 2013 Internal Control – Integrated Framework. Based on our assessment, our management has concluded that, as of December 31, 2023, our internal control over financial reporting is effective based on those criteria.

Attestation Report of the Registered Public Accounting Firm

This Annual Report does not include an attestation report of out registered public accounting firm due to an exemption provided by the JOBS Act for "emerging growth companies."

Changes in Internal Control over Financial Reporting

We continuously seek to improve the efficiency and effectiveness of our internal controls, which may result in changes to our systems and refinements to our processes. However, there were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the fiscal quarter ended December 31, 2023 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2023.

Item 11. Executive Compensation

The information required under this item (excluding the information under the subheading "Pay Versus Performance") is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2023.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2023.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2023.

Item 14. Principal Accountant Fees and Services

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2023.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(1) Financial Statements

For a list of the financial statements included herein, see Index to the Consolidated Financial Statements on page F-1 of this Annual Report on Form 10-K, incorporated into this Item by reference.

(2) Financial Statement Schedules

Schedules have been omitted since they are either not required or not applicable or the information is otherwise included herein.

(3) Exhibits

Exhibit number	Description of exhibit
3.1	Third Amended and Restated Certificate of Incorporation of Prime Medicine, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed with the SEC on October 24, 2022)
3.2	Amended and Restated Bylaws of Prime Medicine, Inc. (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K, filed with the SEC on October 24, 2022)
4.1	Amended and Restated Investors' Rights Agreement among the Registrant and certain of its stockholders, dated April 20, 2021 (incorporated by reference to Exhibit 4.1 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
4.2	Form of Common Stock Certificate (incorporated by reference to Exhibit 4.2 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
4.3*	Description of Securities (incorporated by reference to Exhibit 4.3 of the Registrant's 2022 Annual Report on Form 10-K, filed with the SEC on March 9, 2023)
4.4	Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.1 of the Registrant's Current Report on Form 8-K, filed with the SEC on February 16, 2024)
10.1#	2019 Stock Option and Grant Plan, as amended, and forms of award agreements thereunder (incorporated by reference to Exhibit 10.1 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.2#	2022 Stock Option and Incentive Plan and forms of award agreements thereunder (incorporated by reference to Exhibit 10.2 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.3#	2022 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.3 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.4#	Senior Executive Cash Incentive Bonus Plan (incorporated by reference to Exhibit 10.4 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.5#	Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.5 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.6#	Form of Officer Indemnification Agreement (incorporated by reference to Exhibit 10.6 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.7#	Form of Director Indemnification Agreement (incorporated by reference to Exhibit 10.7 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.8#	Amended and Restated Employment Agreement, dated July 7, 2022, between the Registrant and Keith Gottesdiener (incorporated by reference to Exhibit 10.8 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.9#	Amended and Restated Employment Agreement, dated July 20, 2022, between the Registrant and Jeremy Duffield (incorporated by reference to Exhibit 10.9 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.10#	Amended and Restated Employment Agreement, dated July 11, 2022, between the Registrant and Ann Lee (incorporated by reference to Exhibit 10.10 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)

Exhibit number	Description of exhibit
10.11#	Amended and Restated Employment Agreement, dated July 7, 2022, between the Registrant and Carman Alenson (incorporated by reference to Exhibit 10.11 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022
10.12#	Amended and Restated Employment Agreement, dated July 7, 2022, between the Registrant and Meredith Goldwasser (incorporated by reference to Exhibit 10.12 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.13#	Employment Agreement, effective as of January 17, 2024, between the Registrant and Allan Reine (incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed with the SEC on January 5, 2024)
10.14†	Collaboration and License Agreement, dated September 26, 2019, between Beam Therapeutics Inc. and the Registrant (incorporated by reference to Exhibit 10.13 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.15†	License Agreement, dated September 26, 2019, between The Broad Institute, Inc. and the Registrant, as amended (incorporated by reference to Exhibit 10.14 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.16†	Amendment No. 1 to License Agreement, dated May 5, 2020, between The Broad Institute, Inc. and the Registrant (incorporated by reference to Exhibit 10.15 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.17†	Amendment No. 2 to License Agreement, dated February 18, 2021, between The Broad Institute, Inc. and the Registrant (incorporated by reference to Exhibit 10.16 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.18†	Amendment No. 3 to License Agreement, dated December 22, 2022, between The Broad Institute, Inc. and the Registrant (incorporated by reference to Exhibit 10.17 of the Registrant's Annual Report on Form 10-K, filed with the SEC on March 9, 2023)
10.19†	License Agreement, dated December 22, 2022, between The Broad Institute, Inc. and the Registrant (incorporated by reference to Exhibit 10.17 of the Registrant's Annual Report on Form 10-K, filed with the SEC on March 9, 2023)
10.20	Pledge from Prime Medicine, amended and restated August 2022, between The Broad Institute, Inc. and the Registrant (incorporated by reference to Exhibit 10.17 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.21+	License Agreement, dated March 16, 2020, between MIL 21E, LLC and the Registrant, as amended (incorporated by reference to Exhibit 10.18 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.22*	Amendment No. 12 to License Agreement, dated October 2, 2023, between MIL 21E, LLC and the Registrant
10.23+	Consulting Agreement between the Registrant and David Liu, dated September 13, 2019 (incorporated by reference to Exhibit 10.19 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.24	Amendment No. 1 to the Consulting Agreement between the Registrant and David Liu, dated October 22, 2021 (incorporated by reference to Exhibit 10.20 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.25+	Andrew Anzalone Offer Letter, dated December 20, 2019 (incorporated by reference to Exhibit 10.21 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.26	Andrew Anzalone Confidentiality, Assignment and Nonsolicitation Agreement, dated October 16, 2020 (incorporated by reference to Exhibit 10.22 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
10.27#	Form of Executive Employment Agreement (incorporated by reference to Exhibit 10.23 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022
10.28#	Amendment No. 1 to Amended and Restated Employment Agreement, dated July 6, 2023, between Registrant and Keith Gottesdiener (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q filed with the SEC on November 3, 2023).
10.29	Lease Agreement, dated as of November 22, 2021, between NW Cambridge Property Owner, LLC and the Registrant (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q filed with the SEC on August 7, 2023)

Exhibit number	Description of exhibit
21.1	Subsidiaries of the Registrant (incorporated by reference to Exhibit 21.1 of the Registrant's Registration Statement on Form S-1/A (File No. 333-267579) filed on October 17, 2022)
23.1*	Consent of PricewaterhouseCoopers, LLP, Independent Registered Public Accounting Firm
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1**	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2**	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
97.1*	Prime Medicine, Inc. Compensation Recovery Policy, dated September 15, 2023
101.INS*	Inline XBRL Instance Document
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104*	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Filed herewith.

** The certifications furnished in Exhibit 32.1 and Exhibit 32.2 hereto are deemed to accompany this Annual Report on Form 10-K and will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended. Such certifications will not be deemed to be incorporated by reference into any filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

# 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.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Prime Medicine, Inc.

March 1, 2024

By: /s/ Keith Gottesdiener
Keith Gottesdiener
President and Chief Executive Officer

POWER OF ATTORNEY AND SIGNATURES

Each person whose individual signature appears below hereby authorizes and appoints Keith Gottesdiener, Allan Reine, and Carman Alenson, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this Annual Report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, 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, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his or her substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Keith Gottesdiener Keith Gottesdiener	President, Chief Executive Officer and Director (Principal Executive Officer)	March 1, 2024
/s/ Allan Reine Allan Reine	Chief Financial Officer (Principal Financial Officer)	March 1, 2024
/s/ Carman Alenson Carman Alenson	Chief Accounting Officer (Principal Accounting Officer)	March 1, 2024
/s/ Thomas Cahill Thomas Cahill	Director	March 1, 2024
/s/ Wendy Chung Wendy Chung	Director	March 1, 2024
/s/ Kaye Foster Kaye Foster	Director	March 1, 2024
/s/ Michael Kelly Michael Kelly	Director	March 1, 2024
/s/ Jeff Marrazzo Jeff Marrazzo	Director	March 1, 2024
/s/ Robert Nelsen Robert Nelsen	Director	March 1, 2024
/s/ David Schenkein David Schenkein	Director	March 1, 2024

PRIME MEDICINE, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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, 2023 and 2022, 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 then ended, 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, 2023 and 2022, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

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. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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.

Emphasis of Matter

As discussed in Note 1 to the consolidated financial statements, the Company will require additional financing to fund future operations. Management's evaluation of the events and conditions and management's plans to mitigate these matters are also described in Note 1.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 1, 2024

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, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 41,574	$ 187,620
Short-term investments	74,639	98,467
Short-term investment — related party	5,452	7,834
Prepaid expenses	19,057	2,451
Other current assets	2,254	246
Total current assets	142,976	296,618
Property and equipment, net	22,659	19,009
Operating lease right-of-use assets	13,941	29,545
Restricted cash	13,496	13,496
Other assets	779	1,646
Total assets	$ 193,851	$ 360,314
Liabilities and Stockholders' Deficit		
Current liabilities:		
Accounts payable	$ 19,537	$ 4,332
Accrued expenses and other current liabilities [(1)]	14,110	10,688
Accrued settlement payment — related party	13,500	—
Operating lease liability	9,276	11,694
Total current liabilities	56,423	26,714
Operating lease liability, net of current	4,357	17,051
Non current deferred tax liability	—	279
Total liabilities	60,780	44,044
Commitments and contingencies (Note 12)		
Stockholders' equity		
Common stock, par value of $0.00001 per share; 775,000,000 shares authorized; 97,377,121 and 97,209,213 shares issued and outstanding as of December 31, 2023 and 2022, respectively	2	2
Additional paid-in capital	624,414	609,849
Accumulated other comprehensive loss	(15)	(384)
Accumulated deficit	(491,330)	(293,197)
Total stockholders' equity	133,071	316,270
Total liabilities and stockholders' equity	$ 193,851	$ 360,314

(1) Includes related party amount of $0.3 million as of December 31, 2022.

The accompanying notes are an integral part of these consolidated financial statements.

PRIME MEDICINE, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(in thousands, except share and per share amounts)	Year Ended December 31, 2023	2022
Operating expenses:		
Research and development [1]	$ 147,905	$ 86,725
Settlement payment — related party	13,500	—
General and administrative	43,387	29,819
Total operating expenses	204,792	116,544
Loss from operations	(204,792)	(116,544)
Other income (expense):		
Change in fair value of short-term investment — related party	(2,382)	(8,128)
Other income, net	8,762	1,903
Total other income (expense), net	6,380	(6,225)
Net loss before income taxes	(198,412)	(122,769)
Benefit from income taxes	279	948
Net loss	$ (198,133)	$ (121,821)
Cumulative dividend on preferred stock	—	(20,193)
Net loss attributable to common stockholders	$ (198,133)	$ (142,014)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.18)	$ (4.19)
Weighted-average common shares outstanding, basic and diluted	90,969,327	33,891,264
Comprehensive loss:		
Net loss	$ (198,133)	$ (121,821)
Change in unrealized loss on investments, net of tax	369	(357)
Comprehensive loss	$ (197,764)	$ (122,178)

(1) Includes related party amounts of $0.6 million and $0.7 million for the years ended December 31, 2023 and 2022, respectively.

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 Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount				
Balances at December 31, 2021	115,761,842	$ 196,157	45,658,957	$ 199,643	32,413,860	$ —	$ 15,163	$ (27)	$ (171,376)	$ (156,240)
Issuance of common stock upon exercise of stock options	—	—	—	—	59,774	—	219	—	—	219
Reclassification of forward contract — related party	—	—	—	—	1,101,525	—	12,020	—	—	12,020
Conversion of convertible preferred stock to common stock upon closing of initial public offering	(115,761,842)	(196,157)	(45,658,957)	(199,643)	51,923,758	1	395,800	—	—	395,801
Issuance of common stock from initial public offering, net of issuance costs and underwriting fees of $5.1 million	—	—	—	—	11,721,456	1	180,188	—	—	180,189
Repurchase of unvested restricted common stock	—	—	—	—	(11,160)	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	6,459	—	—	6,459
Change in unrealized loss on investments, net of tax	—	—	—	—	—	—	—	(357)	—	(357)
Net loss	—	—	—	—	—	—	—	—	(121,821)	(121,821)
Balances at December 31, 2022	—	$ —	—	$ —	97,209,213	$ 2	$ 609,849	$ (384)	$ (293,197)	$ 316,270
Issuance of common stock upon exercise of stock options	—	—	—	—	167,908	—	655	—	—	655
Stock-based compensation expense	—	—	—	—	—	—	13,910	—	—	13,910
Change in unrealized loss on investments, net of tax	—	—	—	—	—	—	—	369	—	369
Net loss	—	—	—	—	—	—	—	—	(198,133)	(198,133)
Balances at December 31, 2023	—	$ —	—	$ —	97,377,121	$ 2	$ 624,414	$ (15)	$ (491,330)	$ 133,071

The accompanying notes are an integral part of these consolidated financial statements.

PRIME MEDICINE, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(in thousands)	Year Ended December 31, 2023	2022
Cash flows used in operating activities:		
Net loss	$ (198,133)	$ (121,821)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	13,910	6,459
Non cash lease expense	12,788	9,790
Depreciation expense	4,653	2,224
Change in fair value of short-term investment — related party	2,382	8,128
Loss on disposal of property and equipment	28	8
Amortization of premiums and discount on short-term investments	(3,408)	(250)
Deferred income taxes	(279)	(964)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(9,455)	(1,738)
Accounts payable	9,140	2,458
Accrued expenses and other current liabilities	1,758	(25,873)
Accrued settlement payment — related party	13,500	—
Lease liability	(12,296)	(10,248)
Net cash used in operating activities	(165,412)	(131,827)
Cash flows provided by (used in) investing activities:		
Maturities of investments	132,556	93,000
Purchases of investments	(104,951)	(123,336)
Purchases of property and equipment	(8,724)	(16,095)
Payments of security deposits	(170)	(665)
Net cash provided by (used in) investing activities	18,711	(47,096)
Cash flows provided by financing activities:		
Net proceeds from stock option exercises	655	219
Proceeds from initial public offering, net of underwrites discounts and commissions and deferred offering costs	—	185,317
Payments of deferred offering costs	—	(4,042)
Net cash provided by financing activities	655	181,494
Net change in cash, cash equivalents, and restricted cash	(146,046)	2,571
Cash, cash equivalents, and restricted cash at beginning of period	201,116	198,545
Cash, cash equivalents, and restricted cash at end of period	$ 55,070	$ 201,116
Reconciliation of cash, cash equivalents and restricted cash:		
Cash, cash equivalents, and restricted cash at end of period	$ 55,070	$ 201,116
Restricted cash	13,496	13,496
Total cash, and cash equivalents	$ 41,574	$ 187,620

The accompanying notes are an integral part of these consolidated financial statements.

PRIME MEDICINE, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(in thousands)	Year Ended December 31, 2023	2022
Supplemental cash flow information:		
Decrease in right-of-use assets due to lease termination	$ 6,081	$ —
Right-of-use assets obtained in exchange for new operating lease liabilities	$ 3,265	$ 28,590
Supplemental disclosure of non-cash investing and financing activities:		
Purchases of property and equipment included in accounts payable and accrued expenses	$ 575	$ 969
Conversion of convertible preferred stock to common stock upon closing of initial public offering	$ —	$ 395,800
Settlement of related party forward contract	$ —	$ 12,020
Cash taxes paid	$ —	$ 141

The accompanying notes are an integral part of these consolidated financial statements.

PRIME MEDICINE, INC.

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 delivering a new class of differentiated one-time curative genetic therapies to address the widest spectrum of diseases. The Company is deploying Prime Editing technology, which it believe is a versatile, precise, and efficient gene editing technology. The Company was incorporated in the State of Delaware in September 2019. Its principal offices are in Cambridge, Massachusetts.

Liquidity and Capital Resources

Since its inception, the Company has devoted substantially all of its resources to building its Prime editing platform and advancing development of its portfolio of programs, establishing and protecting its intellectual property, conducting research and development activities, organizing and staffing the company, business planning, raising capital and providing general and administrative support for these operations. To date, the Company has funded its operations primarily with proceeds from sales of preferred stock and from public offerings of its common stock.

In February 2024, the Company issued and sold 22,560,001 shares of its common stock, including 3,360,000 shares pursuant to the exercise of the underwriters' option to purchase additional shares, at a price to the public of $6.25 per share. Further, in lieu of common stock to certain investors, the Company sold pre-funded warrants to purchase 3,200,005 shares of common stock at a public offering price of $6.24999 per pre-funded warrant, which represents the per share public offering price of each share of common stock less the $0.00001 per share exercise price for each pre-funded warrant. As a result of the offering, the Company received approximately $150.9 million in net proceeds, after deducting underwriting discounts, commissions and estimated offering costs of $10.1 million.

Since its inception, the Company has incurred substantial losses. As of December 31, 2023, the Company had an accumulated deficit of $491.3 million and expects to generate operating losses and negative operating cash flows for the foreseeable future. As of December 31, 2023, the Company maintains cash, cash equivalents, short-term investments, and related party short-term investments of $121.7 million and expects that this, together with the net proceeds from the February equity offering of approximately $150.9 million, will be sufficient to fund operations for at least the next twelve months from the date of issuance of this Annual Report on Form 10-K.

The Company will need additional financing to support its continuing operations and pursue its growth strategy. Until such time as the Company can generate significant revenue from product sales, if ever, it expects to finance its operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. The Company may be unable to raise additional funds or enter into such other agreements when needed on favorable terms or at all. The inability to raise capital as and when needed would have a negative impact on the Company's financial condition and its ability to pursue its business strategy. The Company will need to generate significant revenue to achieve profitability, and it may never do so.

Risks and Uncertainties

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, 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.

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").

Principles of Consolidation

The Company's consolidated financial statements include the accounts of Prime Medicine, Inc. and its wholly owned subsidiary Prime Medicine Massachusetts Securities Corp., a Massachusetts securities corporation. All significant intercompany balances and transactions have been eliminated in consolidation.

Reverse Stock Split

On October 12, 2022, in connection with the Company's initial public offering ("IPO"), the Company effected a 1-3.10880 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios of each series of the Company's preferred stock. Accordingly, all share and per share amounts for all periods presented in the accompanying condensed consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this stock split and adjustment of the preferred stock conversion ratios.

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 expenses during the reporting periods. 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. Significant estimates, as determined by the Company, are discussed in greater detail in Item 7, *Management's Discussion and Analysis of Financial Condition and Results of Operations*.

Concentrations of Credit Risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents, short-term investments, and restricted cash. The Company invests in U.S. Treasury securities 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.

Restricted Cash

Restricted cash consists of letters of credit that are required to be maintained in connection with the Company's lease arrangements. The Company classifies its restricted cash as current or non-current on the consolidated balance sheets based on the expected release dates of the restrictions.

Short-term Investments and Related Party Short-Term Investment

The Company's short-term investments consist of investments in 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. The Company classifies its investments as available-for-sale and carries them at fair market value. The unrealized losses on the Company's available-for-sale debt securities are recorded in other comprehensive loss 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 short-term investment — related party was obtained from the collaboration agreement with Beam, which is a public company trading on the Nasdaq Exchange. At each reporting date, the Company recognizes the fair value of the short-term investment — related party on the consolidated balance sheets. 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.

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 and short-term investments are carried at fair value, determined according to the fair value hierarchy described above. 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. Depreciation expense is recognized using the straight-line method over the estimated useful life of each asset as follows:

Asset Class	Estimated Useful Life
Laboratory equipment	5 years
Furniture and fixtures	5 years
Computer hardware and software	3 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.

Leases

The Company accounts for leases in accordance with ASC 842, *Leases*. In accordance with ASC 842, 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 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. 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. If initially determined that it is not reasonably certain but subsequently the Company

determines that it is reasonably certain to exercise its renewal options or early-termination provisions, the Company would reassess the lease classification, remeasure the lease liability, and adjust the right-of-use asset.

In addition to evaluating arrangement that are leases, 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.

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.

Patent Costs

The Company expenses all patent-related costs incurred in connection with filing and prosecuting patent applications in the period incurred 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.

Stock-Based Compensation

The Company measures 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 Black-Scholes option pricing model estimates the fair value of the equity award using the expected term, expected volatility, risk-free interest rate, dividend rate, and the fair value of the common stock underlying the stock-based award.

The Company estimates the expected life stock options using the "simplified" method, whereby, the expected life equals the arithmetic average of the vesting term and the original contractual term of the option. Due to the lack of sufficient company-specific historical and implied volatility data, the Company has based its computation of expected volatility on the historical volatility of a representative group of public companies with similar characteristics to the Company, including stage of product development and life science industry focus. The risk-free interest rates for periods within the expected life of the option were based on the U.S. Treasury yield curve in effect during the period the options were granted. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock. The Company recognizes forfeitures as they occur.

Prior to the IPO, the fair value of common stock underlying stock-based awards was based on an estimate at each grant date by the Company's board of directors. The Company determined the estimated per share fair value of its common stock at various dates considering contemporaneous and retrospective valuations in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, Valuation of Privately-Held Company Equity Securities Issued as Compensation. Each of these inputs is subjective and generally requires judgment and estimation by management.

Subsequent to the IPO, the fair value of the common stock underlying shared based awards is the quoted market price of the Company's common stock on the date of the grant.

The Company recognizes stock-based compensation expense on a straight-line basis over the requisite service period of the awards for service-based awards, which is generally the vesting period. Stock-based compensation expense is classified in the 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.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity that result from transactions and economic events other than those with stockholders. The Company's only element of other comprehensive loss is unrealized gains and losses on marketable securities.

Net Loss per Share Attributable to Common Stockholders

The Company applies the two-class method when computing net 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 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 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 loss for the period had been distributed. 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. The Company has no participating securities outstanding.

Basic net loss per share attributable to common stockholders is computed by dividing the net 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 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 loss per share attributable to common stockholders is computed by dividing the diluted net loss attributable to common stockholders by the weighted-average number of common shares outstanding for the period, including potential dilutive common shares.

In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is generally the same as basic net loss per share attributable to common stockholders since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

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.

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.

As of December 31, 2023, there are no new accounting pronouncements that are expected to have a material impact on the Company's financial statements.

3. Fair Value Measurements

The following tables present the Company's fair value hierarchy for its assets that are measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair value:

	December 31, 2023			
(in thousands)	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ —	$ 24,209	$ —	$ 24,209
Short-term investment:				
U.S. Treasury and government securities	—	74,639	—	74,639
Related party short-term investment:				
Beam equity securities	5,452	—	—	5,452
Total cash equivalents and investments	$ 5,452	$ 98,848	$ —	$ 104,300

	December 31, 2022			
(in thousands)	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ —	$ 120,511	$ —	$ 120,511
Short-term investment:				
U.S. Treasury and government securities	—	98,467	—	98,467
Related party short-term investment:				
Beam equity securities	7,834	—	—	7,834
Total cash equivalents and investments	$ 7,834	$ 218,978	$ —	$ 226,812

Money market funds were valued by the Company based on observable inputs, which represent a Level 2 measurement within the fair value hierarchy. The Company classifies its U.S. Treasury securities as short-term based on each instrument's underlying contractual maturity date. The fair value of the Company's U.S. Treasury and government securities 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.

Investments in Debt Securities

Unrealized gains and losses of investments in debt securities consisted of the following:

	December 31, 2023			
(in thousands)	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Short-term investments in debt securities:				
U.S. Treasury and government securities	$ 74,654	$ 7	$ (22)	$ 74,639
Total short-term investments in debt securities	$ 74,654	$ 7	$ (22)	$ 74,639

	December 31, 2022			
(in thousands)	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Short-term investments in debt securities:				
U.S. Treasury and government securities	$ 98,851	$ —	$ (384)	$ 98,467
Total short-term investments in debt securities:	$ 98,851	$ —	$ (384)	$ 98,467

The contractual maturities of the Company's investments in debt securities held were as follows:

	December 31, 2023	December 31, 2022
Due within one year	$ 74,639	$ 98,467

Marketable securities in unrealized loss positions consisted of the following:

	December 31, 2023		
(in thousands, except number of securities)	Number of Securities	Fair Value	Gross Unrealized Losses
Investments in continuous loss position for less than 12 months:			
U.S. Treasury and government securities	11	$ 28,348	$ (22)

4. Property and Equipment, Net

Property and equipment, net consisted of the following:

	December 31,	
(in thousands)	2023	2022
Property and equipment:		
Laboratory equipment	$ 23,873	$ 19,422
Leasehold improvement	579	564
Furniture and fixture	278	235
Computer hardware and software	11	11
Construction in progress	5,402	1,608
Total property and equipment	30,143	21,840
Less: Accumulated depreciation	(7,484)	(2,831)
Total property and equipment, net	$ 22,659	$ 19,009

Depreciation expense related to property and equipment is as follows:

	Year ended December 31,	
(in thousands)	2023	2022
Depreciation expense	$ 4,653	$ 2,224

5. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

	December 31,	
(in thousands)	2023	2022
Accrued expenses and other current liabilities		
Accrued employee compensation and benefits	$ 8,270	$ 6,529
Accrued professional fees	2,273	2,162
Lab-related supplies and services	1,962	1,219
Accrued research and development expense – related party	—	329
Other	1,605	449
Total accrued expenses and other current liabilities	$ 14,110	$ 10,688

6. Stockholder's Equity

Reverse Stock Split

As described in Note 1, *Nature of the Business and Basis of Presentation*, in connection with the Company's IPO in October 2022, the Company effected a 1-for-3.10880 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios of each series of the Company's preferred stock. Accordingly, all share and per share amounts for all periods presented in the accompanying condensed consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this stock split and adjustment of the preferred stock conversion ratios.

Common Stock

Under the Third Amended and Restated of Certificate of Incorporation, the Company's common stock had a par value of $0.0001 and each share of common stock entitles the holder to one vote 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.

At-The-Market Equity Program

In November 2023, the Company entered into Open Market Sale Agreement℠ (the "Sales Agreement") with Jefferies LLC, acting as the Company's agent and/or principal (the "Sales Agent"), with respect to an "at the market offering" program under which the Company may, from time to time, at its sole discretion, issue and sell shares of its common stock having an aggregate offering price of up to $300.0 million through the Sales Agent. As of December 31, 2023, there have been no sales of common stock pursuant to the Sales Agreement.

7. 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.

In October 2022, the Company completed its IPO, and in connection with the closing, the board of directors determined that no further awards would be granted under the 2019 Plan. Upon effectiveness of the 2022 Stock Option and Incentive Plan (the "2022 Plan"), shares remaining available for grant under the 2019 Plan were included in the 2022 Plan. Additionally, 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 2022 Plan.

2022 Stock Option and Incentive Plan

On February 9, 2022, the Company's board of directors adopted, and on October 10, 2022 its stockholders approved, the 2022 Plan, which became effective immediately preceding the date on which the registration statement for the Company's IPO was declared effective by the SEC. The 2022 Plan allows the Company to make equity-based and cash-based incentive awards to its officers, employees, directors, and consultants. The 2022 Plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted common stock awards, restricted stock units and other stock-based awards.

The 2022 Plan provides for an automatic increase in the number of shares reserved and available for issuance on January 1, 2023 and each January 1 thereafter, by five percent of the outstanding number of shares of common stock on the immediately preceding December 31 or such lesser number of shares as determined by the compensation committee. On January 1, 2024, the annual increase for the 2022 Plan resulted in an additional 4,868,856 shares authorized for issuance being added to the 2022 Plan.

As of December 31, 2023, the Company had 16,681,302 shares reserved under the 2022 Plan and the 2019 Plan, and 8,627,709 shares available for issuance under the 2022 Plan.

2022 Employee Stock Purchase Plan

On February 9, 2022, the Company's board of directors adopted, and on October 10, 2022 its stockholders approved, the 2022 Employee Stock Purchase Plan (the "2022 ESPP"), which became effective immediately preceding the date on which the registration statement for the Company's IPO was declared effective by the SEC.

The 2022 ESPP provides for an annual increase beginning on January 1, 2023 and each January 1 thereafter through January 1, 2032, by the least of (i) 971,350 shares of common stock, (ii) one percent of the outstanding number of shares of common stock on the immediately preceding December 31, or (iii) such number of shares of common stock as determined by the administrator of the 2022 ESPP. There was no annual increase for the 2022 ESPP on January 1, 2024. As of December 31, 2023, the Company had 1,942,700 shares available for issuance under the 2022 ESPP.

No shares of the Company's common stock were issued during the years ended December 31, 2023 and 2022 under the 2022 ESPP.

Stock Option Valuation

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:

	Year ended December 31,	
	2023	2022
Risk-free interest rate	3.7 %	3.0 %
Expected term (in years)	6.0	6.0
Expected volatility	80.00 %	74.77 %
Expected dividend yield	— %	— %

Time-Based Stock Options

The following table summarizes the Company's time-based stock option activity for the year ended December 31, 2023:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2022	3,954,265	$ 6.43	9.02	$ 48,030
Granted	4,167,494	12.67		
Exercised	(167,908)	3.91		
Forfeited	(311,988)	8.76		
Outstanding at December 31, 2023	7,641,863	$ 9.79	8.68	$ 12,014
Vested and exercisable at December 31, 2023	2,334,721	$ 7.18	8.19	$ 6,860
Vested and expected to vest at December 31, 2023	7,641,863	$ 9.79	8.68	$ 12,014

Other information related to the time-based stock option activity of the Company was as follows:

	Year ended December 31,	
	2023	2022
Weighted-average fair value of options granted	$ 8.96	$ 7.40
Intrinsic value of options exercised (in thousands)	$ 1,368	$ 681

As of December 31, 2023 there was $40.9 million of total unrecognized compensation cost related to time-based unvested stock options, and the Company expects to recognize such amount over a remaining weighted-average period of 2.7 years.

Performance-Based Stock Options

The Company has granted stock options to certain employees to purchase shares of common stock that contain certain performance-based vesting criteria related to corporate milestones. The performance-based stock options were granted "at-the-money" and have a term of 10 years.

The fair value of each option grant under the performance share option plan was estimated on the date of grant. Recognition of stock-based compensation expense associated with these performance-based stock options commences when the performance condition is considered probable of achievement, using management's best estimates, which consider the inherent risk and uncertainty regarding the future outcomes of the milestones.

The following table summarizes the Company's performance-based stock option activity for the year ended December 31, 2023:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2022	411,730	$ 6.65	9.17	$ 4,912
Granted	—	—		
Exercised	—	—		
Forfeited	—	—		
Outstanding at December 31, 2023	411,730	$ 6.65	8.15	$ 1,362
Vested and exercisable at December 31, 2023	121,160	$ 5.11	8.06	$ 454

Other information related to the performance-based stock option activity of the Company was as follows:

	Year ended December 31,	
	2023	2022
Weighted-average fair value of options granted	$ —	$ 9.55

As of December 31, 2023 there was $2.3 million of total unrecognized compensation cost related to performance-based stock options.

Restricted Common Stock Awards

The Company awarded restricted common stock to employees and non-employees under its 2019 Plan and may continue to award restricted common stock to employees and non-employees under the 2022 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. The vesting of these restricted stock awards are time-based or performance-based.

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 ($0.00004) or (ii) the fair market value per share as of the date of the Company elects to exercise its repurchase right.

Time-Based Restricted Common Stocks Awards

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.

The following table summarizes the Company's time-based restricted common stock award activity for the year ended December 31, 2023:

	Number of Shares	Weighted-Average Grant-Date Fair Value
Unvested restricted common stock at December 31, 2022	5,015,034	$ 0.10
Issued	—	—
Vested	(4,111,807)	0.08
Repurchased	—	—
Unvested restricted common stock at December 31, 2023	903,227	$ 0.17

As of December 31, 2023, there was $0.2 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 0.7 years.

Performance-Based Restricted Common Stock Awards

Performance-based restricted common stock awards vest upon the achievement of performance-based milestones related to corporate milestones.

Stock-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. 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.

The following table summarizes the Company's performance-based restricted common stock award activity for the year ended December 31, 2023:

	Number of Shares	Weighted-Average Grant-Date Fair Value
Unvested restricted common stock at December 31, 2022	3,832,769	$ 0.07
Issued	—	—
Vested	—	—
Repurchased	—	—
Unvested restricted common stock at December 31, 2023	3,832,769	$ 0.07

As of December 31, 2023, there was $0.3 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:

	Year ended December 31,	
(in thousands)	2023	2022
Stock-based compensation expense:		
Research and development	$ 7,950	$ 4,440
General and administrative	5,960	2,019
Total stock-based compensation expense	$ 13,910	$ 6,459

8. Income Taxes

Income tax (benefit) expense consists of the following:

(in thousands)	Year Ended December 31, 2023	2022
Current provision:		
Federal	$ —	$ —
State	—	16
Total current provision	—	16
Deferred income tax benefit:		
Federal	279	314
State	—	650
Total deferred income tax benefit	279	964
Total benefit from income taxes	$ 279	$ 948

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31, 2023	2022
Federal income tax expense at statutory rate	21.0 %	21.0 %
State income taxes, net of federal benefit	7.3 %	7.7 %
Tax credits	2.0 %	2.9 %
Permanent differences	(0.9)%	(0.9)%
Other	(0.4)%	— %
Change in valuation allowance	(28.9)%	(30.0)%
Effective income tax rate	0.1 %	0.7 %

Net deferred tax assets (liabilities) consisted of the following:

(in thousands)	December 31, 2023	2022
Deferred tax assets:		
Capitalized research and development costs	$ 49,990	$ 19,974
U.S. and state net operating loss carryforwards	35,977	20,427
Depreciation and amortization	13,204	13,307
Tax credits	12,863	7,268
Accrual	5,817	1,649
Lease Liability	3,711	7,853
Stock Compensation	1,473	122
Other	9	—
Total deferred tax assets	123,044	70,600
Deferred tax liabilities:		
Right of Use Asset	(3,794)	(8,072)
Other	—	(675)
Total deferred tax liabilities	(3,794)	(8,747)
Valuation allowance	(119,250)	(62,132)
Net deferred tax assets (liabilities)	$ —	$ (279)

The following is a summary of the Company's net operating loss and tax credit carryforwards, both of which may be available to reduce future tax liabilities:

(in thousands)	December 31, 2023	2022
U.S. federal net operating loss - do not expire	$ 131,608	$ 75,202
State net operating loss - expire at various dates beginning in 2039	132,009	73,339
Federal research and development tax credits - expire at various dates beginning in 2040	8,085	4,865
State research and development tax credits - expire at various dates beginning in 2036	6,047	3,042

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 Tax Cuts and Jobs Act requires taxpayers to capitalize and amortize research and development expenditures under section 174 for tax years beginning after December 31, 2021. This rule became effective for the Company for the year ended December 31, 2022. For the years ended December 31, 2023 and 2022, the Company capitalized R&D costs of $137.2 million and $80.7 million, respectively. The Company will amortize these costs for tax purposes over 5 years if the R&D was performed in the U.S. and over 15 years if the R&D was performed outside the U.S.

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 years ended December 31, 2023 and 2022, 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 short-term investment — related party can only support 80 percent of the federal deferred tax assets and none of the state deferred tax assets. The Company reevaluates the positive and negative evidence at each reporting period.

For the year ended December 31, 2023, the valuation allowance increased primarily due to the increases in net operating loss carryforwards, capitalized research and development costs, and research and development tax credit carryforwards. The changes in the valuation allowance were as follows:

(in thousands)	Year Ended December 31, 2023	2022
Valuation allowance at beginning of year	$ 62,132	$ 25,253
Increases (decreases) recorded to income tax provision	57,118	36,879
Valuation allowance at end of year	$ 119,250	$ 62,132

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 of 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, 2023, 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, 2023, there were no pending tax examinations. The Company is open to future tax examination under statute from 2019 to the present.

9. 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. This lease was subject to various amendments with the last material amendment entered into in April 2023 for additional office and laboratory space and to extended the term of the sublease through March 2025. The amended lease agreement provides for escalating monthly rental payments with fixed costs for expenses and property taxes included in each payment. Under the terms of the amended lease, the security deposit was increased to $0.7 million, which is classified as other assets on the consolidated balance sheet as of December 31, 2023. In November 2023, the Company exercised its option to terminate this lease with a seven-month notice. This termination was deemed reasonably certain during the year ended December 31,2023, and the Company reassessed the lease and recorded a $6.1 million reduction to the Company's operating lease liability and its operating lease right-of-use asset on the condensed consolidated balance sheet.

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 commenced in April 2022 and will 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, with rent commencing in March 2024, subject to any credits pursuant to the terms of the lease. Also subject to any credits pursuant to the terms of the lease, the Company expects to pay up to approximately $208.7 million over the initial non-cancelable term of the lease of 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 sheets as of December 31, 2023 and December 31, 2022.

Under ASC 842, the Company expects that the lease will commence in March 2024.

480 Arsenal Street, Watertown, Massachusetts Lease

In May 2022, the Company entered into a non-cancelable operating lease to sublease office space located at 480 Arsenal Street, Watertown, Massachusetts. The lease commenced in May 2022 and will expire in April 2027. 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. The Company secured the lease with a $0.4 million security deposit, which was recorded as restricted cash on the consolidated balance sheet as of December 31, 2023 and December 31, 2022.

In conjunction with the lease, the Company entered into a sublease agreement to sublet a portion of the office space at 480 Arsenal Street Watertown, Massachusetts (the "Arsenal Street Sublease"). The Arsenal Street Sublease commenced in May 2022 and will expire in April 2025. The Company was not relieved of its primary obligation under the operating lease as a result of the sublease.

Summary of lease costs recognized

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 years ended December 31, 2023 and December 31, 2022.

The components of lease cost were as follows:

	Year Ended December 31,	
(in thousands)	2023	2022
Lease cost:		
Operating lease cost	$ 13,664	$ 10,999
Variable lease cost	2,145	1,111
Short-term lease cost	2,816	1,401
Sublease income	(168)	(294)
Total lease cost	$ 18,457	$ 13,217

The weighted-average remaining lease term and discount rate were as follows:

	December 31,	
	2023	2022
Weighted average remaining lease term (in years)	1.9 years	2.7 years
Weighted average discount rate	6.92 %	4.92 %

Future annual lease payments under non-cancelable operating leases as of December 31, 2023 were as follows:

(in thousands)	Undiscounted Amounts
Undiscounted lease payments:	
2024	$ 9,669
2025	2,656
2026	1,683
2027	567
Total undiscounted lease payments	14,575
Less: imputed interest	(942)
Total operating lease liability	$ 13,633

As the lease for the office and laboratory space at 60 First Street, Cambridge, Massachusetts had not commenced as of December 31, 2023, the table above excludes any amounts related to this lease. Subject to any credits pursuant to the terms of the lease, the Company expects to pay up to approximately $208.7 million over the initial non-cancelable term of the lease of ten years.

10. License and Collaboration Agreements

For a more detailed discussion of our license and collaboration agreements, please refer to Item 1, *Business — Our License and Collaboration Agreements*, of this Annual Report on Form 10-K.

License Agreements with Broad Institute

2019 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, February 2021 and December 2022, the Company entered into amendments to this license agreement, for certain patents related to the field of prevention or treatment of human disease by editing or targeting 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 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. 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 which the Company issued 623,529 shares of common stock, with a fair value of $39,000. In April 2021, 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.

Under the Broad License Agreement, the Company is obligated to pay Broad Institute an annual license maintenance fee of low six-figures dollar amount beginning in 2022. Broad Institute is also entitled to receive clinical and regulatory milestone payments up to a total of $20.0 million and sales-based milestone payments up to a total of $54.0 million per licensed product. Further, the Broad Institute is entitled to receive mid-single digit percentage royalties, subject to customary offsets and reductions, on net sales of licensed products, and low single-digit percentage royalties of enabled products.

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.

2022 License Agreement with Broad Institute

In December 2022, the Company entered into a second license agreement with Broad Institute, (the "2022 Broad License Agreement"). Under the 2022 Broad License Agreement, Broad Institute grants to us certain rights and licenses under the patent rights it owns or controls related to MMR inhibition and prime editing improvements and specifically, (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, the Company also has the right to grant sublicenses to its affiliates and third parties, subject to certain requirements.

The Company is also obligated to pay Broad Institute an annual license maintenance fee of mid five-figures for the term of the Agreement. Broad Institute is also entitled to receive clinical and regulatory milestone payments for a limited category of royalty-bearing products, up to a total of $2.0 million and sales-based milestone payments up to a total of $3.0 million. Further, Broad Institute is entitled to receive royalties of less than 0.2% on net sales of royalty bearing products.

Unless earlier terminated, the 2022 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 royalty bearing product in a country. The Company can terminate the 2022 Broad License Agreement for convenience following prior written notice to Broad Institute. Each party may terminate the 2022 Broad License Agreement for the other party's uncured material breach. Broad Institute may also immediately terminate the 2022 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.

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 2022 (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. In August 2022, the Company amended and restated the Pledge to clarify that the funds may be used by the laboratory of David Liu, who is a member of Broad Institute and a faculty member at Harvard.

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 both the years ended December 31, 2023 and 2022, the Company recognized $5.0 million of research and development expense in connection with the Pledge.

Beam Collaboration Agreement — Related Party

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, 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 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.

Subject to certain provisions, 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.

Before and within 30 days 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 (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." 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.

Under the terms of the Beam Collaboration Agreement, the Company is entitled to following milestones:

Development milestones	
Protected product	Up to $35.5 million
Collaboration product	Up to $17.8 million
Sales milestones	
Protected product	Up to $84.5 million
Collaboration product	Up to $42.3 million

For eligible products, Beam is obligated to pay the Company tiered royalties, subject to customary offsets and reductions, ranging from a high-single digit percentage to a low double-digit percentage, but less than teens on net sales of protected products worldwide and net sales of collaboration products outside of the United States. In addition, Beam must 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.

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.

On the first anniversary of the Beam Collaboration Agreement, the Company received 200,307 shares of Beam common stock, with a fair value of $5.5 million and, in return, the Company issued to Beam 1,608,337 shares of the Company's common stock, with a fair value of $0.2 million.

Accounting Considerations

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, 2023 and 2022 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.

The Company recognizes revenue for the license performance obligations at a point in time, as control of these licenses are transferred upon issuance and Beam could begin to use and benefit from the licenses. There was no revenue recognized during the years ended December 31, 2023 or 2022.

The change fair value of the related party short-term investment consisting of Beam shares are recognized as unrealized gain (loss) in the consolidated statements of operations and comprehensive loss.

Research Collaboration, Option and License Agreement with Myeloid — Related Party

In December 2021, the Company and Myeloid, a related party, entered into the Myeloid Agreement. Upon entering into the Myeloid Agreement, Myeloid was entitled to receive an upfront payment of $30.0 million in cash and an aggregate of 1,101,525 shares of the Company's common stock, with a then fair value of $12.0 million, both of which Myeloid received in January 2022.

During the second quarter of 2023, the Company provided notice to Myeloid of its intent to terminate the Myeloid Agreement, which became effective during the third quarter of 2023.

In September 2023, Myeloid filed an arbitration claim with the American Arbitration Association alleging that the Company breached its obligations under the Myeloid Agreement by failing to pay a $17.5 million milestone payment and seeking, among other things, damages in the amount of $17.5 million. In October 2023, the Company filed an arbitration claim with the American Arbitration Association alleging that Myeloid breached numerous obligations under the Agreement and seeking, among other things, a declaration that Myeloid breached the Agreement, rescission of the Agreement and damages in the amount of $43.5 million. In January 2024, the Company and Myeloid entered into a settlement agreement resolving the two arbitration proceedings. Under the terms of the settlement agreement, the parties agreed to resolve and settle all disputes between the parties and release all claims between them relating to the License Agreement and the arbitrations in exchange for the Company's payment to Myeloid of $13.5 million, certain mutual covenants, and other consideration. Accordingly, for the year ended December 31, 2023, the Company recorded a charge of $13.5 million within its consolidated balance sheets and consolidated statement of operations.

11. Commitments and Contingencies

Leases

The Company’s commitments under its operating leases are described in Note 9, *Leases*.

License and Collaboration Agreements

The Company entered into various license and collaboration agreements under which it is obligated to make fixed and contingent payments as described in Note 10, *License and Collaboration Agreements*.

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 discussed in Note 10, *License and Collaboration Agreements*, for the year ended December 31, 2023 the Company recognized $13.5 million under its settlement agreement with Myeloid. As of December 31, 2022, the Company was not a party to any material legal proceedings or claims.

12. Net Loss per Share

As described in Note 2, *Summary of Significant Accounting Policies*, for periods in which the Company reports a net loss, potentially dilutive securities have been excluded from the computation of diluted net loss per share as their effects would be anti-dilutive. Therefore, the weighted average number of common shares outstanding used to calculate both basic and diluted net loss per share is the same. The Company excluded the following potential common shares presented based on amounts outstanding at period end, from the computation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	Year Ended December 31,	
	2023	2022
Anti-dilutive common stock equivalents:		
Stock options to purchase common stock	7,763,023	4,365,995
Unvested restricted common stock awards	4,735,996	8,847,803
Total anti-dilutive common stock equivalents	12,499,019	13,213,798

Basic and diluted loss per share is computed by dividing net loss by the weighted-average common shares outstanding:

(in thousands, except share and per share data)	Year Ended December 31, 2023	2022
Numerator:		
Net loss	$ (198,133)	$ (121,821)
Cumulative dividend on preferred stock	—	(20,193)
Net loss attributable to common stockholders	$ (198,133)	$ (142,014)
Denominator:		
Weighted-average common shares outstanding, basic and diluted	90,969,327	33,891,264
Net loss per share attributable to common stockholders, basic and diluted	$ (2.18)	$ (4.19)

13. Related Party Transactions

Founder Consulting Services

For the years ended December 31, 2023, and 2022 the Company made payments of $0.2 million in each period to one of the co-founder shareholders for scientific consulting and other expenses. As of December 31, 2023 and 2022, there were no amounts included within accounts payable.

Myeloid Therapeutics

In December 2021, the Company and Myeloid entered into the Myeloid Collaboration Agreement and Myeloid Subscription Agreement during which time the Company and Myeloid had one common board member, who is also an affiliate of Newpath, one of the Company's holders of common stock. In 2023, the Company terminated the Myeloid Collaboration Agreement.

In January 2024, the Company and Myeloid entered into a settlement agreement resolving two arbitration proceedings, which are described in Note 10, *Licenses and Collaboration Agreements*. Under the terms of the settlement agreement, the parties agreed to resolve and settle all disputes between the parties and release all claims between them relating to the License Agreement and the arbitrations in exchange for the Company's payment to Myeloid of $13.5 million, certain mutual covenants, and other consideration.

The Company recognized the following amounts related to Myeloid:

(in thousands)	2023	2022
Expense incurred		
Settlement	$ 13,500	$ —
Research and development	560	688
Amounts accrued		
Settlement	13,500	—
Research and development	—	329

14. Subsequent Events

Cystic Fibrosis Foundation

In January 2024, the Company entered into an agreement with the Cystic Fibrosis Foundation to develop therapies for the treatment of Cystic Fibrosis. Under the term of the agreement, the Company is entitled to received up to $15 million. Funding from the Cystic Fibrosis Foundation will allow Prime Medicine to progress two distinct strategies for applying Prime Editing to treat Cystic Fibrosis. If successful, Cystic Fibrosis Foundation is entitled to receive royalties on net sales.

Public Offering

In February 2024, the Company issued and sold 22,560,001 shares of its common stock, including 3,360,000 shares pursuant to the exercise of the underwriters' option to purchase additional shares, at a price to the public of $6.25 per share. Further, in lieu of common stock to certain investors, the Company sold pre-funded warrants to purchase 3,200,005 shares of common stock at a public offering price of $6.24999 per pre-funded warrant, which represents the per share public offering price of each share of common stock less the $0.00001 per share exercise price for each pre-funded warrant. As a result of the offering, the Company received approximately $150.9 million in net proceeds, after deducting underwriting discounts, commissions and estimated offering costs of $10.1 million.

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The summary of the general terms and provisions of the registered securities of Prime Medicine, Inc. (the "Company," "we," "us," and "our") set forth below does not purport to be complete. It is subject to and qualified in its entirety by reference to our Third Amended and Restated Certificate of Incorporation ("certificate of incorporation") and our Amended and Restated By-laws ("bylaws"), each of which are incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.3 is a part, and by applicable law. We encourage you to read our certificate of incorporation, our bylaws and the applicable provisions of the Delaware General Corporation Law for additional information.

General

Our authorized capital stock consists 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 are undesignated.

Common Stock

Only our common stock is registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act").

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. All outstanding shares are validly issued, fully paid and non-assessable.

Undesignated Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 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. The purpose of authorizing our board of directors to issue preferred stock in one or more series and determine the number of shares in the series and its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. 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.

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. No shares of preferred stock are outstanding as of the date of our Annual Report on Form 10-K with which this Exhibit 4.3 is filed as an exhibit.

Registration Rights

Certain of our stockholders are entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of the Amended and Restated Investors' Rights Agreement between us, certain holders of our common stock and holders of our preferred stock dated as of April 20, 2021 (the "amended and restated investors' rights agreement"). 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 our initial public offering, certain stockholders 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 our initial public offering or (c) at such time after our initial public 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 special meetings of stockholders may only be called by or at the direction of our board of directors 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 at an annual meeting of stockholders 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

We are 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 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 as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware, or (4) any action asserting a claim that is governed by the internal affairs doctrine; provided, however, that the this provision shall not apply to any causes of action arising under the Securities Act, Exchange Act or to any claim for which the federal courts have exclusive jurisdiction. In addition, our bylaws 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, the Exchange Act or the respective rules and regulations promulgated thereunder. To the fullest extent permitted by law, 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

Our common stock is listed on the Nasdaq Global Market under the trading symbol "PRME."

Transfer Agent and Registrar

The Transfer Agent and Registrar for our common stock is Computershare Inc. and Computershare Trust Company, N.A.

Twelfth Amendment to License Agreement

This Twelfth Amendment to License Agreement ("**Twelfth Amendment**") is dated October 2, 2023 ("**Effective Date**") and entered into by and between Prime Medicine, Inc. ("**Licensee**") and MIL 21E, LLC ("**Licensor**").

WHEREAS, Licensor and Licensee are parties to a certain License Agreement dated March 16, 2020, as amended by that certain First Amendment to License Agreement dated August17, 2020, as amended by that certain Second Amendment to License Agreement dated October 21, 2020, as amended by that certain Third Amendment to License Agreement dated May 24, 2021, as amended by that certain Fourth Amendment to License Agreement dated July 27, 2021, as amended by that certain Fifth Amendment to License Agreement dated December 20, 2021, as amended by that certain Sixth Amendment to License Agreement dated April 5, 2022, as amended by that certain Seventh Amendment to License Agreement dated May 27, 2022, as amended by that certain Eighth Amendment dated June 21, 2022, as amended by that certain Ninth Amendment dated March 17, 2023, as amended by that certain Tenth Amendment dated April 14, 2023, as amended by that certain Eleventh Amendment dated May 4, 2023 (collectively "**License Agreement**");

WHEREAS, Licensee warrants and represents that, to the best of its knowledge, Licensor has fulfilled its obligations under the License Agreement and is not in default of any covenants or obligations contained in the License Agreement;

WHEREAS, Licensor and Licensee desire to amend the License Agreement in certain respects as set forth herein; and,

WHEREAS, all capitalized terms contained herein shall, unless otherwise defined in this Twelfth Amendment, have the same meaning as set forth in the License Agreement.

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties agree that the License Agreement agree as follows:

1. Lab Bench Premises and Lab Bench Term. Section 2(a) of the Licensed Agreement is hereby modified be adding the following new sentence to the end of the Section:

   > The parties acknowledge and agree to extend the Lab Bench Expiration Date such that it shall now be defined as March 14, 2025. For the avoidance of doubt, it is acknowledged and agreed that in the event Licensee elects the Early Termination as defined in the Sixth Amendment to License Agreement that the Lab Bench Expiration Date shall be accelerated pursuant to the terms of such election.

2. License Fee. The following shall be added to the end of Section 3(a) of the License Agreement:

   > For the avoidance of doubt Licensee shall pay Licensor the Lab Bench Premises Fee, in addition to all other fees due pursuant to the License Agreement, through the Lab Bench Expiration Date as defined in this Twelfth Amendment, all as shown on Schedule A attached hereto.

3. Ratification. Except as amended herein, all terms and conditions of the License Agreement shall remain unchanged and in full force and effect.

4. Counterparts. This Twelfth Amendment to License Agreement may be executed in any number of counterparts, each of which shall be an original and all of which together shall constitute one and the same document.

IN WITNESS WHEREOF, Licensor and Licensee have duly executed this Twelfth Amendment as of the Effective Date.

LICENSOR

/s/ Brian Taylor

By: Brian Taylor
Title: Executive VP of Biopharma Solutions

LICENSEE

/s/ Keith Gottesdiener

By: Keith Gottesdiener
Title: President and CEO

Schedule A

Start	End	License Fee
4/15/2023	12/14/2023	**$706,000.00**
12/15/2023	3/14/2024	**$706,400.00**
3/15/2024	4/14/2024	**$728,000.00**
4/15/2024	3/15/2025	**$734,240.00**

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-3 (No. 333-275321) and on Form S-8 (No. 333-270400, and No. 333-267953) of Prime Medicine, Inc. of our report dated March 1, 2024 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 1, 2024

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Keith Gottesdiener, certify that:

1. I have reviewed this Annual Report on Form 10-K of Prime Medicine, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2024

By: /s/ Keith Gottesdiener

Keith Gottesdiener
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Allan Reine, certify that:

1. I have reviewed this Annual Report on Form 10-K of Prime Medicine, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2024

By: /s/ Allan Reine

Allan Reine
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with this Annual Report of Prime Medicine, Inc. (the "Company") on Form 10-K for the period ending December 31, 2023 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

1. The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 1, 2024

By: /s/ Keith Gottesdiener

Keith Gottesdiener
Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with this Annual Report of Prime Medicine, Inc. (the "Company") on Form 10-K for the period ending December 31, 2023 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

1. The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 1, 2024

By: /s/ Allan Reine

Allan Reine
Chief Financial Officer
(Principal Financial Officer)

PRIME MEDICINE, INC.

COMPENSATION RECOVERY POLICY

Adopted as of September 15, 2023

Prime Medicine, Inc., a Delaware corporation (the "Company"), has adopted a Compensation Recovery Policy (this "Policy") as described below.

1. Overview

The Policy sets forth the circumstances and procedures under which the Company shall recover Erroneously Awarded Compensation from current and former Executive Officers of the Company in accordance with rules issued by the United States Securities and Exchange Commission (the "SEC") under the Securities Exchange Act of 1934 (the "Exchange Act") and the Nasdaq Stock Market. Please refer to Section 3 below for definitions of capitalized terms used and not otherwise defined herein.

2. Compensation Recovery Requirement

In the event the Company is required to prepare a Material Financial Restatement, the Company shall reasonably promptly recover all Erroneously Awarded Compensation with respect to such Material Financial Restatement, and each Covered Person shall be required to take all actions necessary to enable such recovery.

3. Definitions

a. "Applicable Recovery Period" means with respect to a Material Financial Restatement, the three completed fiscal years immediately preceding the Restatement Date for such Material Financial Restatement. In addition, in the event the Company has changed its fiscal year: (i) any transition period of less than nine months occurring within or immediately following such three completed fiscal years shall also be part of such Applicable Recovery Period and (ii) any transition period of nine to 12 months will be deemed to be a completed fiscal year.

b. "Applicable Rules" means any rules or regulations adopted by the Exchange pursuant to Rule 10D-1 under the Exchange Act and any applicable rules or regulations adopted by the SEC pursuant to Section 10D of the Exchange Act.

c. "Board" means the Board of Directors of the Company.

d. "Committee" means the Compensation Committee of the Board or, in the absence of such committee, a majority of independent directors serving on the Board.

e. A "Covered Person" means any Executive Officer. A person's status as a Covered Person with respect to Erroneously Awarded Compensation shall be determined as of the time of receipt of such Erroneously Awarded Compensation regardless of their current role or status with the Company (e.g., if a person began service as an Executive Officer after the beginning of an Applicable Recovery Period, that person would not be considered a Covered Person with respect to Erroneously Awarded Compensation received before the person began service as an Executive Officer, but would be considered a Covered Person with respect to Erroneously Awarded Compensation received after the person began service as an Executive Officer where such person served as an Executive Officer at any time during the performance period for such Erroneously Awarded Compensation).

f. "Effective Date" means October 2, 2023.

g. "Erroneously Awarded Compensation" means, with respect to a Material Financial Restatement, the amount of any Incentive-Based Compensation received by a Covered Person on or after the Effective Date during the Applicable Recovery Period that exceeds the amount that otherwise would have been received by the Covered Person had such compensation been determined based on the restated amounts in the Material Financial Restatement, computed without regard to any taxes paid. Calculation of Erroneously

Awarded Compensation with respect to Incentive-Based Compensation based on stock price or total shareholder return, where the amount of Erroneously Awarded Compensation is not subject to mathematical recalculation directly from the information in a Material Financial Restatement, shall be based on a reasonable estimate of the effect of the Material Financial Restatement on the stock price or total shareholder return upon which the Incentive-Based Compensation was received, and the Company shall maintain documentation of the determination of such reasonable estimate and provide such documentation to the Exchange in accordance with the Applicable Rules.

h. "Exchange" means The Nasdaq Stock Market LLC.

i. An "Executive Officer" means any person who served the Company in any of the following roles, received Incentive-Based Compensation after beginning service in any such role (regardless of whether such Incentive-Based Compensation was received during or after such person's service in such role) and served in such role at any time during the performance period for such Incentive-Based Compensation: the president, the principal financial officer, the principal accounting officer (or, if there is no such accounting officer, the controller), any vice president in charge of a principal business unit, division or function (such as sales, administration or finance), any other officer who performs a policy making function, or any other person who performs similar policy making functions for the issuer. Executive officers of parents or subsidiaries of the Company may be deemed executive officers of the Company if they perform such policy making functions for the Company.

j. "Financial Reporting Measures" mean measures that are determined and presented in accordance with the accounting principles used in preparing the Company's financial statements, any measures that are derived wholly or in part from such measures (including, for example, a non-GAAP financial measure), and stock price and total shareholder return.

k. "Incentive-Based Compensation" means any compensation provided, directly or indirectly, by the Company or any of its subsidiaries that is granted, earned, or vested based, in whole or in part, upon the attainment of a Financial Reporting Measure. Incentive-Based Compensation is deemed received, earned or vested when the Financial Reporting Measure is attained, not when the actual payment, grant or vesting occurs.

l. A "Material Financial Restatement" means an accounting restatement of previously issued financial statements of the Company due to the material noncompliance of the Company with any financial reporting requirement under applicable securities laws, including any required accounting restatement to correct an error in previously issued financial statements that is material to the previously issued financial statements or that would result in a material misstatement if the error were corrected in the current period or left uncorrected in the current period.

m. "Restatement Date" means, with respect to a Material Financial Restatement, the earlier to occur of: (i) the date the Board, a committee of the Board or the officer or officers of the Company authorized to take such action if Board action is not required, concludes, or reasonably should have concluded, that the Company is required to prepare the Material Financial Restatement or (ii) the date a court, regulator or other legally authorized body directs the Company to prepare the Material Financial Restatement.

4. Exception to Compensation Recovery Requirement

The Company may elect not to recover Erroneously Awarded Compensation pursuant to this Policy if the Committee determines that recovery would be impracticable, and one or more of the following conditions, together with any further requirements set forth in the Applicable Rules, are met: (i) the direct expense paid to a third party to assist in enforcing this Policy would exceed the amount to be recovered, and the Company has made a reasonable attempt to recover such Erroneously Awarded Compensation; or (ii) recovery would likely cause an otherwise tax-qualified retirement plan to fail to be so qualified under applicable regulations.

5. Tax Considerations

To the extent that, pursuant to this Policy, the Company is entitled to recover any Erroneously Awarded Compensation that is received by a Covered Person, the gross amount received (i.e., the amount the Covered Person received, or was entitled to receive, before any deductions for tax withholding or other payments) shall be returned by the Covered Person.

6. Method of Compensation Recovery

The Committee shall determine, in its sole discretion, the method for recovering Erroneously Awarded Compensation hereunder, which may include, without limitation, any one or more of the following:

a. requiring reimbursement of cash Incentive-Based Compensation previously paid;

b. seeking recovery of any gain realized on the vesting, exercise, settlement, sale, transfer or other disposition of any equity-based awards;

c. cancelling or rescinding some or all outstanding vested or unvested equity-based awards;

d. adjusting or withholding from unpaid compensation or other set-off;

e. cancelling or setting-off against planned future grants of equity-based awards; and/or

f. any other method permitted by applicable law or contract.

Notwithstanding the foregoing, a Covered Person will be deemed to have satisfied such person's obligation to return Erroneously Awarded Compensation to the Company if such Erroneously Awarded Compensation is returned in the exact same form in which it was received; provided that equity withheld to satisfy tax obligations will be deemed to have been received in cash in an amount equal to the tax withholding payment made.

7. Policy Interpretation

This Policy shall be interpreted in a manner that is consistent with the Applicable Rules and any other applicable law and shall otherwise be interpreted (including in the determination of amounts recoverable) in the business judgment of the Committee. The Committee shall take into consideration any applicable interpretations and guidance of the SEC in interpreting this Policy, including, for example, in determining whether a financial restatement qualifies as a Material Financial Restatement hereunder. To the extent the Applicable Rules require recovery of Incentive-Based Compensation in additional circumstances besides those specified above, nothing in this Policy shall be deemed to limit or restrict the right or obligation of the Company to recover Incentive-Based Compensation to the fullest extent required by the Applicable Rules. This Policy shall be deemed to be automatically amended, as of the date the Applicable Rules become effective with respect to the Company, to the extent required for this Policy to comply with the Applicable Rules.

8. Policy Administration

This Policy shall be administered by the Committee. The Committee shall have such powers and authorities related to the administration of this Policy as are consistent with the governing documents of the Company and applicable law. The Committee shall have full power and authority to take, or direct the taking of, all actions and to make all determinations required or provided for under this Policy and shall have full power and authority to take, or direct the taking of, all such other actions and make all such other determinations not inconsistent with the specific terms and provisions of this Policy that the Committee deems to be necessary or appropriate to the administration of this Policy. The interpretation and construction by the Committee of any provision of this Policy and all determinations made by the Committee under this policy shall be final, binding and conclusive.

9. Compensation Recovery Repayments not Subject to Indemnification

Notwithstanding anything to the contrary set forth in any agreement with, or the organizational documents of, the Company or any of its subsidiaries, Covered Persons are not entitled to indemnification for Erroneously Awarded

Compensation recovered under this Policy and, to the extent any such agreement or organizational document purports to provide otherwise, Covered Persons hereby irrevocably agree to forego such indemnification.