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

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

January 8, 2024
Date of Report (Date of earliest event reported)

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

Delaware	001-41536	84-3097762
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

21 Erie Street Cambridge, MA	02139
(Address of principal executive offices)	(Zip Code)

(617) 564-0013
(Registrant's telephone number, including area code)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value $.00001 per share	PRME	The Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule12b-2 of the Securities Exchange Act of 1934 (§250.12b-2 of this chapter).

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. ☐

Item 7.01 Regulation FD Disclosure.

Prime Medicine, Inc. (the "Company") will be conducting meetings with participants attending the 42nd Annual J.P. Morgan Healthcare Conference (the "Conference") during the week of January 8, 2024. A copy of the slides to be presented by the Company at the Conference is furnished as Exhibit 99.1 to this Current Report on Form 8-K, which is incorporated herein by reference.

The information in this Item 7.01, including Exhibit 99.1 attached hereto, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Presentation at 42nd Annual J.P. Morgan Healthcare Conference, dated January 2024, furnished herewith.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: January 8, 2024

Prime Medicine, Inc.

By: /s/ Keith Gottesdiener
Name: Keith Gottesdiener, M.D.
Title: President and Chief Executive Officer

Exhibit 99.1

prime medicine

Delivering on the promise
of Prime Editing

JP Morgan Healthcare Conference

January 2024

Forward Looking Statements

This presentation contains forward-looking statements of Prime Medicine, Inc. ("Prime", "we" or "our") within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. These forward-looking statements contain information about our current and future prospects and our operations, which are based on currently available information. All statements other than statements of historical facts contained in this presentation, including statements regarding our strategy, projects and plans are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue" "could," "design," "due," "estimate," "expect," "goal," "hope," "intend," "may," "might," "objective," "opportunity," "plan," "predict," "positioned," "possible," "potential," "project," "seek," "should," "strategy," "target," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, express or implied statements about Prime's beliefs and expectations regarding: the initiation, timing, progress and results of our research and development programs, preclinical studies and future clinical trials, and the release of data related thereto; our ability to demonstrate, and the timing of, preclinical proof-of-concept in vivo for multiple programs; our ability to pursue our four strategic indication categories: immediate target indications, differentiation target indications, "blue sky" indications and "march up the chromosome" approaches; our ability to quickly leverage programs within our initial target indications and to progress additional programs to further develop our pipeline; the potential of Prime Editors to reproducibly correct disease-causing genetic mutations across different tissues, organs and cell types, and the capacity of our PASSIGE technology to edit CAR-T cells for the treatment of certain cancers and immune diseases; the timing of our regulatory filings, including our anticipated initial IND submission for CGD as early as 2024 with additional filings anticipated in 2025; our ability to demonstrate superior off-target profiles for Prime Editing programs; the further advancement of Prime Editors to maximize their versatility, precision and efficiency; the continued development and optimization of various non-viral and viral delivery systems, including our universal liver-targeted LNP delivery approach; the expansion of Prime Editing's therapeutic potential to extend the reach and impact of Prime Editing to areas beyond our current areas of focus; the potential of Prime Editing to offer curative genetic therapies for a wide spectrum of diseases; the scope of protection we are able to establish and maintain for intellectual property rights covering our Prime Editing technology; developments related to our competitors and our industry; our ability to leverage the clinical, regulatory, and manufacturing advancements made by gene therapy and gene editing programs to accelerate our clinical trials and approval of product candidates; the research collaboration with Cimeio to combine our and Cimeio's respective technologies, including our Prime Editing platform and Cimeio's SCIP platform, and the goals of such collaboration, the potential benefits of such collaboration and technology thereunder, including the ability to cure various diseases and replace existing treatments such as transplantation; the implementation of our strategic plans for our business, programs and technology, including our ability to identify and enter into future license agreements and collaborations; regulatory developments in the United States and foreign countries; our ability to attract and retain key scientific and management personnel; and our estimates of our expenses, capital requirements, and needs for additional financing as well as our cash runway into 2024. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make due to a number of risks and uncertainties. These and other risks, uncertainties and important factors are described in the section entitled "Risk Factors" in our most recent Annual Report on Form 10-K, as well as any subsequent filings with the Securities and Exchange Commission. Any forward-looking statements represent our views only as of the date of this presentation and we undertake no obligation to update or revise any forward-looking statements, whether as a result of new information, the occurrence of certain events or otherwise subject to any obligations under applicable law. 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. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party studies, publications, surveys and other data to be reliable as of the date of this presentation, we have not independently verified, and make no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, no independent source has evaluated the reasonableness or accuracy of our internal estimates or research and no reliance should be made on any information or statements made in this presentation relating to or based on such internal estimates and research.

“The age of human therapeutic gene editing isn’t just coming. It’s already here.”*

* David Liu, Ph.D., Co-Founder of Prime Medicine

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FDA allows first pivotal trial of an in vivo gene editing treatment from Intellia

Lei Lei Wu
News Reporter

The FDA cleared Intellia Therapeutics to run a Phase III study of its CRISPR-based therapy for transthyretin (ATTR) amyloidosis with cardiomyopathy, paving the way for the first pivotal study of an *in vivo* gene editing treatment in the US.

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Panel Says That Innovative Sickle Cell Cure Is Safe Enough for Patients

The decision by an advisory committee may lead to Food and Drug Administration approval of the first treatment for humans that uses the CRISPR gene-editing system.

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New Gene Editing Treatment Cuts Dangerous Cholesterol in Small Study

The trial involved only 10 patients, but it suggests cholesterol can be permanently reduced with a single treatment for patients at risk of heart disease.

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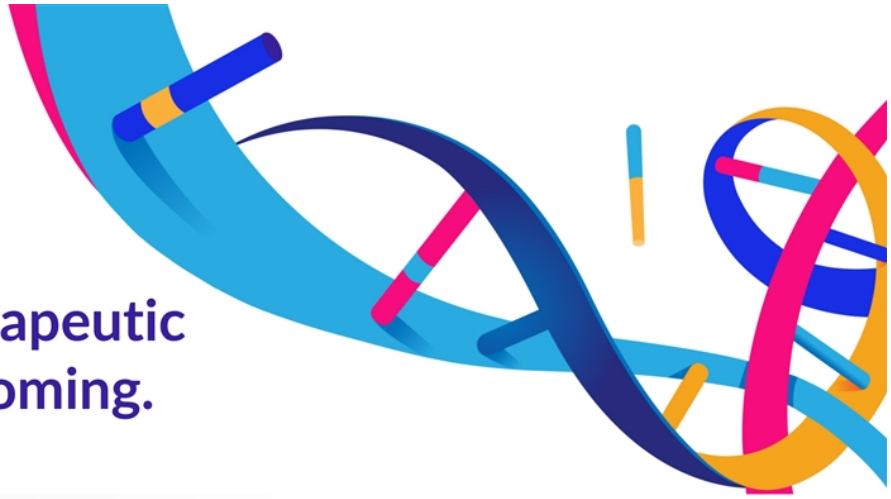

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F.D.A. Approves Sickle Cell Treatments, Including One That Uses CRISPR

People with the genetic disease have new opportunities to eliminate their symptoms, but the treatments come with obstacles that limit their reach.

* David Liu, Ph.D., Co-Founder of Prime Medicine

Now is *our* moment:

Prime Medicine brings together the **right people** and the **right technology** at the **right time**

we are building on decades of progress to deliver the promise of one-time, curative genetic therapies to address the widest spectrum of diseases

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- OPERATIONAL EXECUTION
- BROAD OPPORTUNITY TO ADDRESS LARGE MARKETS
- DIFFERENTIATED SAFETY PROFILE
- PLATFORM MODULARITY
- ENTERING THE CLINIC
- STRATEGIC PIPELINE ALIGNED TO FOUR CORE PILLARS

Consistent **Operational Execution** Sets Strong Foundation For Transition to Clinical-Stage Biotech Company in 2024

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Platform Gestation

- Transferred technology from founding academic lab and reproduced data
- Developed initial strategic pipeline programs
- Executed on key early hires to build out and scale operations
- Completed initial financing round

Platform Industrialization

- Developed high throughput computational pegRNA and PE screening systems
- Established universal assays for off-target activity and PE safety
- Built delivery, CMC and platform innovation capabilities
- Robust and experienced management team in place
- Accessed public markets via IPO

Platform Translation: Entering the Clinic

- First IND / CTA, with several more to follow, and first-in-human data on the horizon
- Robust infrastructure for CMC, Clinical and Regulatory execution
- Preparation for late-stage product development of lead programs
- Platform modularity begins to enable rapid product cycles

PE = Prime Editing; IPO = initial public offering; IND = investigational new drug; CTA = clinical trial application, CMC = chemistry, manufacturing and controls; pegRNA = Prime Editing guide RNA

Prime Editing's Versatility Can Unlock Broad Opportunity Across Wide Spectrum of Diseases

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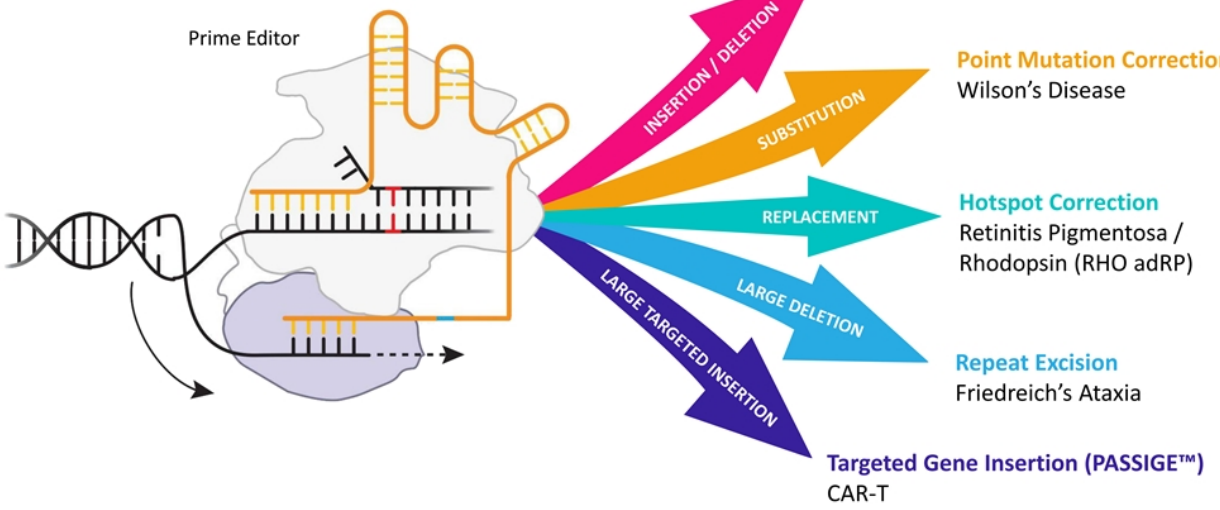
Prime Editing is the only gene editing technology with the capability to edit, correct, insert and delete DNA sequences in any target tissue



Deletion / Insertion Correction
Chronic Granulomatous Disease (CGD)

Point Mutation Correction
Wilson's Disease

Hotspot Correction
Retinitis Pigmentosa / Rhodopsin (RHO adRP)

Repeat Excision
Friedreich's Ataxia

Targeted Gene Insertion (PASSIGE™)
CAR-T

PASSIGE™ Technology Enables Prime Editing to Insert Gene Sized Sequences Precisely, Potentially Addressing Large Markets

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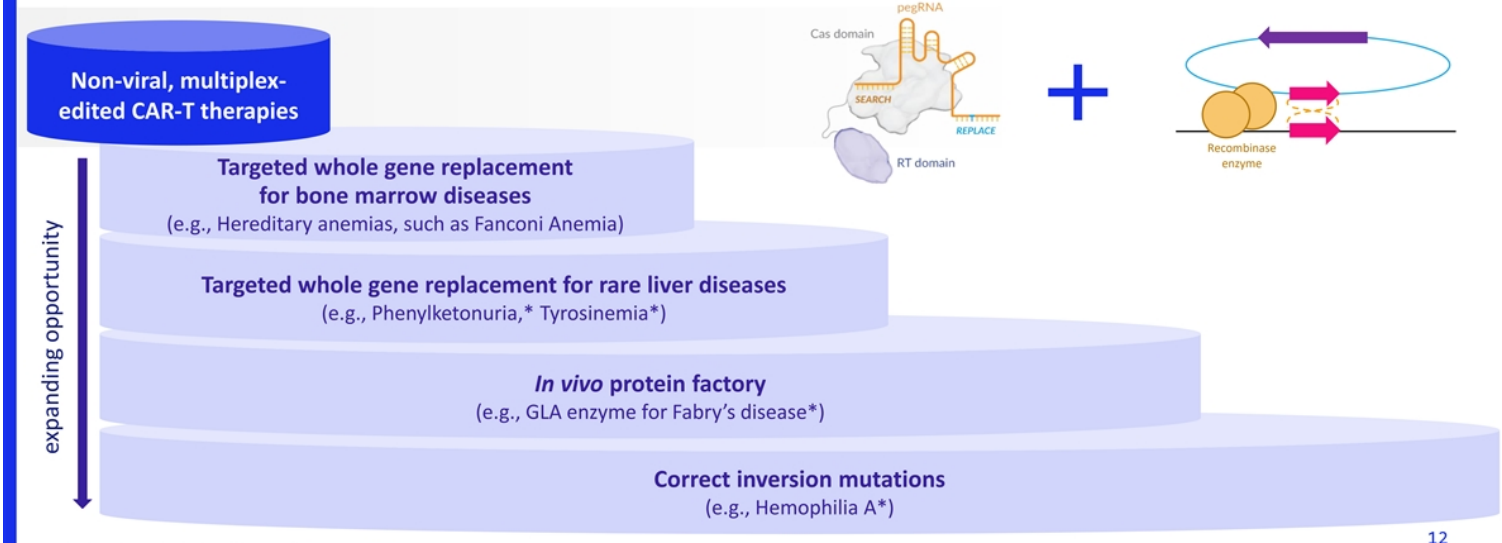
PASSIGE: Prime-Assisted Site-Specific Integrase Gene Editing:
One step non-viral multi-kilobase-size gene editing approach with no double-stranded breaks



*Not part of Prime Medicine's current pipeline

Prime Editing Has Highly Differentiated Safety Profile: No Off-Target Activity Detected in Any Lead Program*

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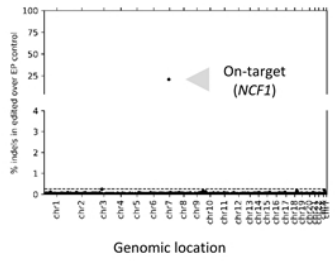
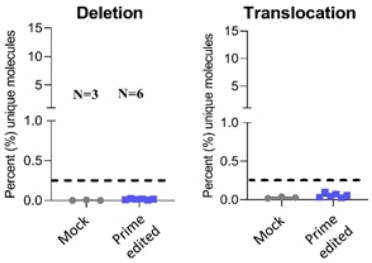
Prime Medicine uses a comprehensive suite of robust, IND-ready assays to evaluate Prime Editor safety risks

Examples from CGD Program that are being used to support IND/CTA filings:

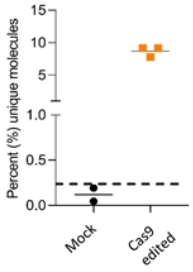
No off-target editing detected in healthy human donor CD34+ cells[1]



No large deletions or translocations in bone marrow engrafted **Prime-Edited** LT-HSCs[2]



Translocation positive control: **Cas9 nuclease-edited** cells[3]



- **No detectable off-target activity in programs* for:**
  - Wilson's Disease
  - CGD
  - Glycogen Storage Disease 1b (GSD1b)
  - RHO
- **No** double strand breakage
- **No** detectable off-target edits
- **No** detectable large deletions, chromosomal translocations or rearrangements

[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 generated by transfecting HEK293T with sgRNA targeting *NCF1* and SpCas9 mRNA. HSC = hematopoietic stem cell; IND = investigational new drug; CTA = clinical trial application

Platform Modularity Accelerates and De-Risks Ongoing Efforts and Enables Rapid Generation of New Product Candidates

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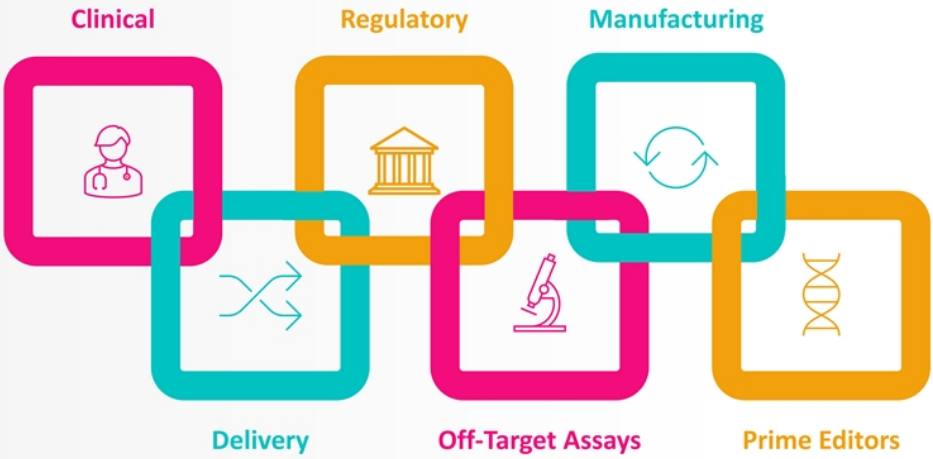
Core components can be readily leveraged to drive pipeline acceleration, efficiency and execution



Prime Medicine is **Entering the Clinic** at the Right Time: Evolving Landscape Favors Innovation in Cell and Gene Therapy

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Positive regulatory interactions in U.S. and globally set stage for near-term clinic entry

In 2023, FDA:

- ☑ Established **Office of Therapeutic Products** under Dr. Nicole Verdun
  Introduced novel initiatives for expediting development of genetic medicines
  - **Platform designation**: allows companies to leverage data across programs using modular components
  - **START program**: increased regulatory feedback for therapies targeting rare diseases with morbidity in first decade of life
- ☑ Allowed **first clinical trials of base editing-** and ***in vivo* CRISPR-based therapies** to proceed
- ☑ Approved **first BLA of CRISPR-based therapy** in Vertex's exa-cel

In 2023, Prime Medicine:

- ☑ Engaged in **multiple formal and informal interactions** with global regulatory agencies on PM359 program and Prime Editing platform
  - INTERACT and pre-IND meetings with the FDA
  - Highly positive interactions with one ex-U.S. agency to-date; two additional pending for early 2024
- ☑ **Prime Medicine has aligned with FDA recommendations** regarding:
  - Preclinical data
  - Toxicology
  - CMC
  - Off-target
  - Clinical development plans

On-track to file first IND in 1H 2024

BLA = biologics license application; IND = investigational new drug

Prime Medicine is Focused Internally on **Four Pillars**, Each with Demonstrated High Efficiency, Precise *in Vivo* Editing

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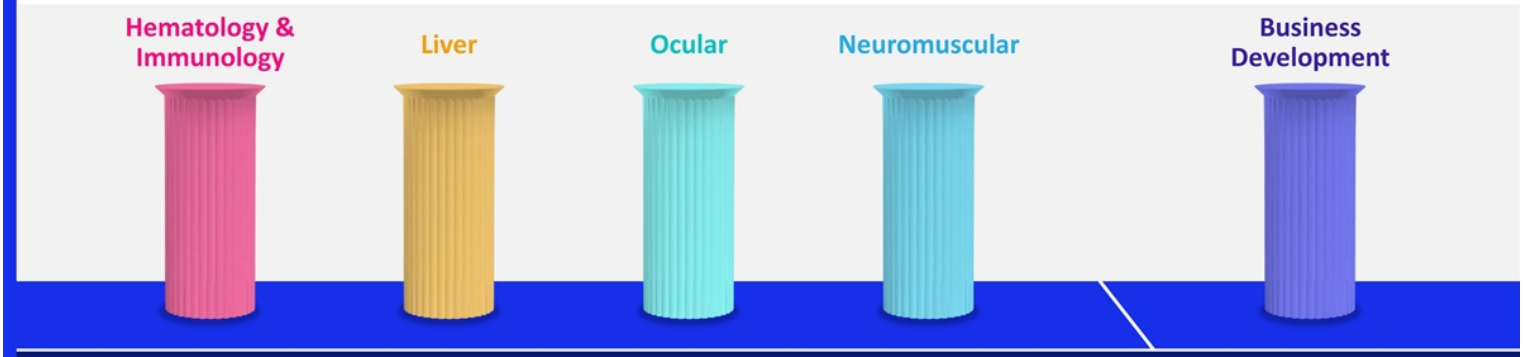
Business development can extend reach and impact, bolstering our financial resources and maximizing the potential of Prime Editing



Strong company foundation

- ☑ Expert at designing guide RNAs, mRNA and vector genome sequence
- ☑ Clinical and Regulatory know-how
- ☑ CMC expertise

Our Pipeline: Aligned to Four Core Modular Platforms, With Additional Programs Advancing as Potential Partnership Opportunities

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Strategic pillar	Indication	Delivery	Discovery	Lead optimization	IND-enabling	Phase 1/2
HEMATOLOGY & IMMUNOLOGY	Chronic Granulomatous Disease	*ex vivo*				
	Other programs in discovery: Fanconi Anemia, Cell Shielding					
LIVER	Wilson's Disease	LNP				
	Glycogen Storage Disease 1b	LNP				
	Undisclosed	LNP				
OCULAR	Retinitis Pigmentosa/Rhodopsin	AAV				
	Other programs in discovery: Retinitis Pigmentosa/Usher Syndrome, Fuchs' Endothelial Corneal Dystrophy					
NEURO	Friedreich's Ataxia	AAV				
	Other programs in discovery: Amyotrophic Lateral Sclerosis, Huntington's Disease, Fragile X Syndrome					
MUSCULAR	Myotonic Dystrophy Type 1	viral/non-viral				
	Other programs in discovery: Oculopharyngeal Muscular Dystrophy, Duchenne Muscular Dystrophy					
ADDITIONAL PROGRAMS *Advancing as potential partnership opportunities*	Cystic Fibrosis (lung)	LNP				
	CAR-T (oncology/autoimmune)	*ex vivo*				
	Other programs in discovery: Usher Syndrome (Type 3) (ear); Non-Syndromic Hearing Loss – GJB2 (ear)					

Advancing PM359 to the Clinic for Chronic Granulomatous Disease, A Disease of Significant Unmet Need

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Rare genetic disease, characterized by defective neutrophil function

- Serious life-threatening disease presents in childhood; life expectancy ~40 years
- Caused by mutation in the p47^{phox} protein[1]
  - Found globally; 100's of patients in U.S. alone[2]
- Results in recurrent, life-threatening infections
  - Difficult to eradicate
  - Frequent hospitalizations, IV antibiotics
  - Potentially deadly infections from normal exposures (gardening, swimming)
- Causes ongoing autoimmunity and inflammation
  - Deteriorating lung function
  - Inflammatory bowel-like syndromes
  - Urinary and gastrointestinal obstruction
- Current treatment options
  - Lifelong anti-microbial therapy: ultimately fails due to evolution of antimicrobial resistance
  - Allogeneic HSCT, only curative option: complicated by GvHD, graft failure, limited availability

We believe Prime Editing is uniquely well-suited to initially address this form of CGD

NCF1 gene encodes the p47^{phox} protein; HSCT = hematopoietic stem cell transplant; [1]P47^{phox} mutation in 25% of patients [2]Prevalence 1:100K-200K

With PM359, Prime Medicine is Set to Become a Clinical-Stage Company Poised to Deliver Data in Near-Term

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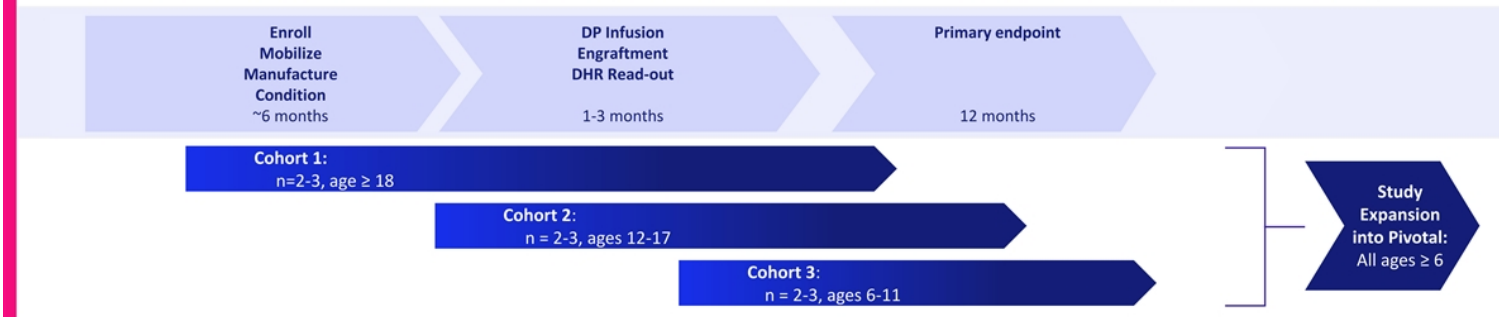
PM359 is comprised of autologous hematopoietic stem cells modified *ex vivo* using Prime Editing



Key eligibility criteria

- delGT mutation in *NCF1* gene
- Dihydrorhodamine (DHR) c/w CGD
- Recent or on-going infectious/inflammatory CGD complications

Key outcome measures

- DHR > 20% normal neutrophil function
- Resolution pre-existing infectious/inflammatory CGD complications
- Frequency new infectious/inflammatory CGD complications

- ✓ DP manufacturing site GMP ready
- ✓ Prime Editing components GMP manufactured, QC tested and ready-for-use to make PM359
- ✓ Global trial sites selected to maximize access to patients, expedite enrollment

IND 1H 2024[1]
First clinical data expected in 2025

DP = drug product; [1]On-track to file first IND/CTA in 1H 2024

Cell Shielding and *In Vivo* Delivery or Targeting Has Potential to Expand HSC Platform Beyond Rare Diseases

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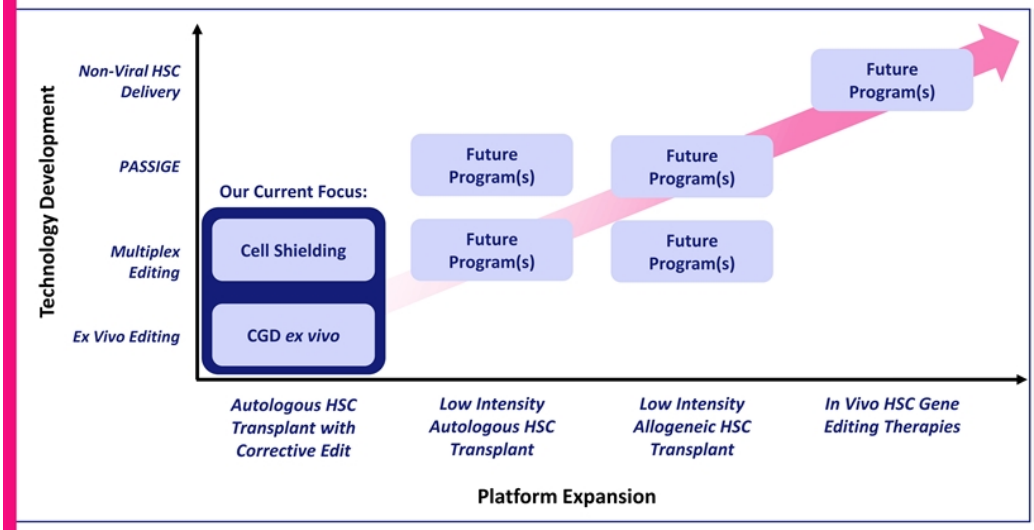
Current efforts lay the foundation for wider range of rare and non-rare indications: benign conditioning with CD117 cell shielding enables **non-toxic bone marrow transplant**



Conditioning toxicity is major bottleneck to HSC transplant. Combining Prime Editing with Cell Shielding:

- To improve safety and effectiveness of HSC transplant, significantly improving:
  - ✓ Accessibility
  - ✓ Eligibility
  - ✓ Outcomes
- To enable selection of *in vivo* edited HSCs, allowing for treatment of genetic diseases without transplant

HSC = hematopoietic stem cell

Proprietary LNP Platform is Advancing Toward the Clinic for the Treatment of Liver Diseases

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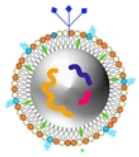
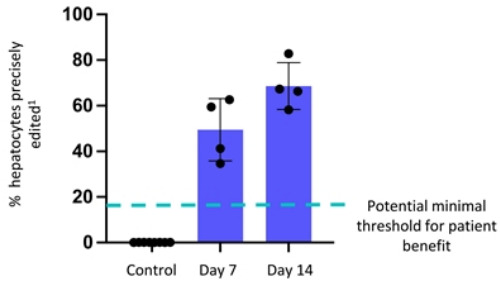


Universal targeted LNP

LNP delivery mechanism shown to precisely correct disease-causing mutations in the liver of NHPs

LNP delivered Prime Editors achieved high levels of precise editing in the livers of NHPs



- Precise and efficient editing of up to 83% of hepatocytes in NHPs
- Separately, no off-target editing detected in patient-derived iPSCs
- Additional data showed repeat dosing of NHPs was generally well tolerated, and led to at least equal levels of precise editing

Proof-of-concept in GSD1b may accelerate development of all liver programs, including Wilson's Disease and other undisclosed programs in rare and non-rare liver diseases

[1]% Hepatocytes precisely edited is calculated from NGS of whole liver biopsy, factored for 60% of cells in liver are hepatocytes (Based on PK/PD relationships and qualifications of cell types in liver: Wang et al Sci. Rep. (2021) 11:19396; MacParland et al Nat Commun. (2018) 9:4383; Hansel et al, Curr Protoc Toxicol (2014) 62:14.12.1; Kmiec, Adv Anat Embryol Cell Biol. (2001) 161:III–XIII. 1–151). Data presented at ESGCT 2023, October 2023. NHP = non-human primate

Early Data with Proprietary Dual-AAV System: Key Step Toward Unlocking Opportunities in Retinal Diseases and Larger Indications

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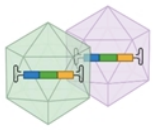
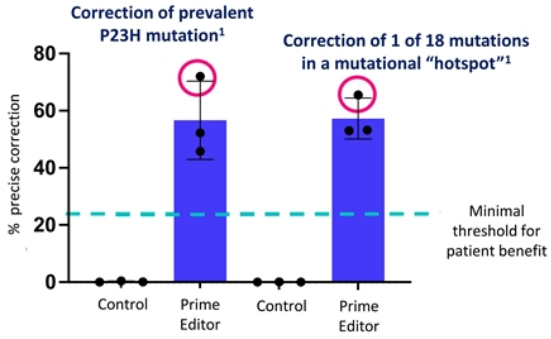
Proof-of-concept achieved: demonstrated ability to correct pathogenic mutations in the eye with high efficiency and no off-target edits detected



Proprietary dual AAV

In RHO adRP, Prime Editors efficiently corrected a prevalent RHO mutation and all mutations in a mutational "hotspot"



- Precise and efficient correction of prevalent *RHO* mutations: up to ~65-70% precise correction in photoreceptors *in vivo*
- Prime Editors prevented degeneration of retina *in vivo*
- Separately, no off-target editing detected in human photoreceptors
- No detectable evidence of viral vector integration into retina cells

Proof-of-concept in RHO adRP potentially accelerates development of all retina programs, including Retinitis Pigmentosa/Usher Syndrome program, as well as other ophthalmological diseases

[1]Editing within transduced area of mouse retina; 25% is predicted to be therapeutically beneficial based on Cideciyan et al., 1998. PNAS 95, 7103-7108. Mutations in RHO p.P23H and the two hotspot mutations p.V345L/p.P347L affect approximately 60% of patients with RHO adRP. Single Prime Editor corrects 18 different pathogenic mutations within single hotspot. Data presented at RD2023, October 2023

Early *In Vitro* and *In Vivo* Data Suggest Potential for Prime Editing To Address Many Neuromuscular Repeat Expansion Diseases

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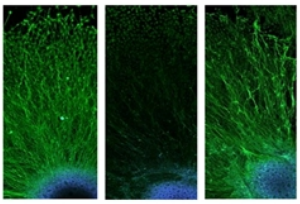
Prime Editors offer genetic correction in patient-derived neurons and muscle

Friedreich's Ataxia

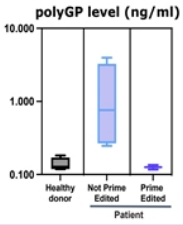
PE restored sensory neuron function



Amyotrophic Lateral Sclerosis

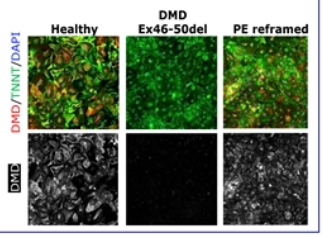
PE restored motor neuron function

- toxic RNA foci resolved
- RAN peptides resolved
- C9ORF72 level restored



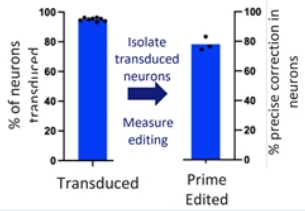
Duchenne Muscular Dystrophy

PE restored dystrophin and cardiomyocyte function



Delivery

PE efficiently edited rodent neurons *in vivo* delivered by dual AAV



- Prime Editors offer a potential curative therapeutic approach for repeat expansion diseases and other neuromuscular diseases
- Prime Medicine is leading with Friedreich's ataxia and amyotrophic lateral sclerosis
- Efficient Prime Editing of neurons by local delivery to the CNS observed in mice
- Current focus on modular AAV delivery system to CNS in large animal studies

PE = Prime Editing; CNS = central nervous system

Business Development Remains Core Focus for Building Prime Medicine

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Prime Medicine will remain active in both sell-side and buy-side business development, with the goal of accelerating our pipeline, bolstering our financial resources, and maximizing the potential of Prime Editing

Recent accomplishments have built a strong foundation to facilitate execution of a multi-pronged business development strategy in 2024 and beyond

- ✓ NHP proof-of-concept achieved
- ✓ Murine proof-of-concept achieved across several programs and delivery modalities
- ✓ Expected first IND/CTA application following positive regulatory discussions
- ✓ Industrialization of Prime Editing platform, enabling the exploitation of modularity to rapidly develop product candidates
- ✓ Foundational patents issued

NHP = non-human primate; IND = investigational new drug; CTA = clinical trial application

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

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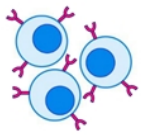

Modularity of platform has potential to accelerate development of additional CAR-T programs

	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 ✓ **No detectable off-target** edits, translocations, or unintended structural abnormalities
Manufacturing / Cost of Goods	✗ Dependence on viral components ✗ Complicated by multi-step engineering	✓ **Entirely non-viral** manufacturing process ✓ **Single-step** editing and integration

Data presented at ASH, December 2022, ASGCT, May 2023 and ASH, December 2023

Prime Editors Correct "High Unmet Need" CF Mutations, For Example, the Prevalent G542X (null) Mutation

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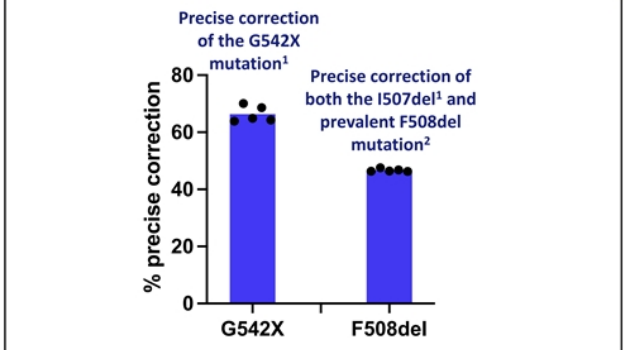
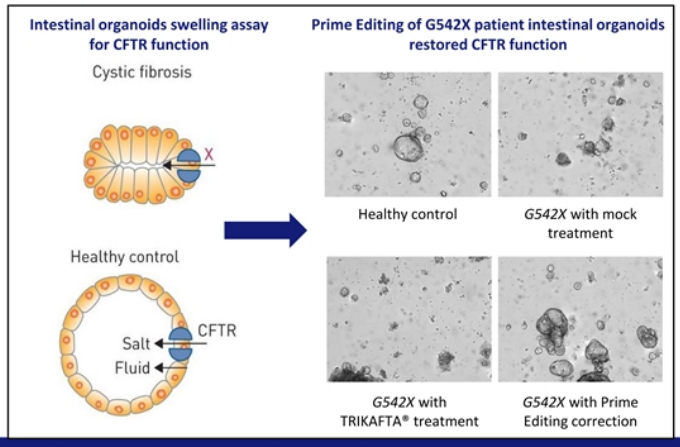
Eight hotspot Prime Editors could address the "high unmet need" mutations;
These **same** eight hotspot Prime Editors could address >98% of **all** CF patients

Prime Editors efficiently corrected the G542X mutation and mutations in the I507del/F508del "hotspot"





One-time, non-viral delivery to patient intestinal organoids restored CFTR function

- LNP delivered Prime Editors efficiently corrected patient Human Bronchial Epithelial (HBE) progenitors *in vitro*
- Identified early LNP formulations to deliver Prime Editors to lung basal cells *in vivo*

Van Mourik et al., 2019. Actual time course: 24 hours. TRIKAFTA® is a registered trademark of Vertex Pharmaceuticals, Incorporated.
[1]G542X and I507del are "high unmet need" mutations; F508del is one of the most prevalent CF mutations; [2]data show correction in patient iPSCs. Each dot shows a different Prime Editor

Prime Medicine Holds Extensive Intellectual Property for Prime Editing Technologies

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Prime Medicine's IP includes:

- ***Multiple configurations*** of RNA-templated gene editing
  - Prime Editor protein configurations: fusion, separate and split configurations
  - pegRNA configurations: fusion, split, separate and engineered configurations
  - Dual flap and dual guide RNA editing systems
- ***Broad diversity*** of RNA-templated gene editing systems
  - Large variety of nucleic acid programmable DNA binding proteins
  - Extensive range of RNA-dependent DNA polymerases (reverse transcriptases)
- ***PASSIGE™***: System using Prime Editing and recombinase to insert gene-sized DNA at chosen target location in genome
  - PASSIGE systems include various gene editing configurations and recombinases
- ***Additional gene editing technology*** including DNA-dependent DNA polymerase editing
- ***Program-specific patent filings*** for all pipeline programs

Prime Medicine has 3 issued US patents and 1 allowed US application

- Numerous pending applications worldwide with broad coverage
- Aggressive filing strategy covering technological advances

Key Upcoming Events will Drive Prime Medicine Forward, Support Our Maturation into a Clinical-Stage Company

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Summary of key ongoing activities and planned next steps for Prime Medicine in 2024-2025

Pipeline

Hematology & Immunology
- Open IND and/or CTA for Phase 1/2 study in Chronic Granulomatous disease in 1H 2024, with anticipated initial clinical data in 2025
- Advance Shielded HSC and Immunotherapy Pairs (SCIP) technology, establish proof-of-concept in HSC and immunotherapy, and identify first clinical program(s) with this approach in 2024
- Advance Prime Medicine's differentiated CAR-T program (using PASSIGE™) into lead optimization

Liver
- Continue to advance preclinical studies for our 3 liver programs, and initiate IND-enabling activities for at least one in 2024, leading to an IND/CTA in 2H 2025/1H 2026

Ocular
- Nominate development candidate for Retinitis Pigmentosa / Rhodopsin (RHO) in 2024 and initiate IND-enabling activities in 2024

Neuromuscular
- Continue to advance Friedreich's Ataxia, and advance one other program into lead optimization in 2024

Platform

Delivery
- Nominate first development candidate using Prime Medicine's liver-targeted universal LNP platform in 2024
- In large animal studies, establish AAV delivery platform and a route of administration for neuromuscular programs in 2024

Regulatory
- Advance discussions with Regulatory agencies on platform strategy for streamlined development

As of September 30, 2023, Prime Medicine had cash, cash equivalents, and investments of $165.3 million, excluding restricted cash, or $178.8 million, including restricted cash

IND = investigational new drug; CTA = clinical trial application; HSC = hematopoietic stem cell


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Delivering on the promise
of Prime Editing
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Our Pipeline: Aligned to Four Core Modular Platforms, With Additional Programs as Potential Partnership Opportunities

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Strategic pillar	Indication	Delivery	Discovery	Lead optimization	IND-enabling	Phase 1/2
HEMATOLOGY & IMMUNOLOGY	Chronic Granulomatous Disease	*ex vivo*				
	Fanconi Anemia	*ex vivo*				
LIVER	Wilson's Disease	LNP				
	Glycogen Storage Disease 1b	LNP				
	Undisclosed	LNP				
OCULAR	Retinitis Pigmentosa/Rhodopsin	AAV				
	Retinitis Pigmentosa/Usher Syndrome	AAV				
	Fuchs' Endothelial Corneal Dystrophy	viral/non-viral				
NEURO	Friedreich's Ataxia	AAV				
	Amyotrophic Lateral Sclerosis	viral/non-viral				
	Huntington's Disease	viral/non-viral				
	Fragile X Syndrome	viral/non-viral				
MUSCULAR	Myotonic Dystrophy Type 1	viral/non-viral				
	Oculopharyngeal Muscular Dystrophy	LNP				
	Duchenne Muscular Dystrophy	AAV				
ADDITIONAL PROGRAMS *Advancing as potential partnership opportunities*	Cystic Fibrosis (lung)	LNP				
	Usher Syndrome Type 3 (ear)	AAV				
	Non-Syndromic Hearing Loss – GJB2 (ear)	AAV				
	CAR-T (oncology / autoimmune)	*ex vivo*				