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Delivering on the promise
of Prime Editing

Corporate Presentation

November 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 potential of PM359 to correct the causative mutation of CGD; the anticipated release of initial clinical data from the ongoing Phase 1/2 clinical trial of PM359 expected in 2025; the timing, progress, and results of our Wilson’s Disease program, including the timing of the release of updated data and the opening of an IND and/or CTA application; 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; the ability of the modularity of the platform to accelerate and de-risk ongoing programs and rapidly generate new product candidates; the potential of Prime Editing to address more than 90% of genetic diseases and to address non-genetic diseases; our ability to pursue our areas of focus and any 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 collaboration with Bristol Myers Squibb and the intended and potential benefits thereof, including the receipt of potential milestone and royalty payments from commercial product sales, if any; the potential of Prime Editors to reproducibly correct disease-causing genetic mutations across different tissues, organs and cell types, and the capacity of our Prime Editing and PASSIGE technology to edit CAR-T cells for the treatment of certain cancers and immune diseases; 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 scope of protection we are able to establish and maintain for intellectual property rights covering our Prime Editing technology; 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 current and future product candidates; 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; our estimates of our expenses, capital requirements, and needs for additional financing; and our expectations regarding the anticipated timeline of our cash runway and future financial performance. 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.

Information regarding our estimated cash, restricted cash, cash equivalents, and investments as of September 30, 2024 is based on preliminary unaudited estimates prepared by and is the responsibility of management. Our independent registered public accounting firm has not audited, reviewed or performed any procedures with respect to such preliminary estimates and accordingly does not express an opinion or any other form of assurance with respect thereto. During our financial closing process our estimates can differ materially from our initial estimates presented herein based on our receipt of updated information.

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.

Prime Medicine is the Leader in Gene Editing Positioned to Create Sustainable Value Through Pipeline Execution and External Partnerships

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The Leader in Prime Editing	• Potential to address more than 90% of genetic diseases and opportunities in non-genetic diseases • Pre-clinical efficacy across variety or target tissues leveraging various types of Prime Editing • Comprehensive intellectual property position
Platform Modularity Oriented for Growth	• Fully integrated modular platform - pre-clinical, clinical, manufacturing, regulatory • Proprietary modular delivery systems within target tissues • Advancing Prime Editing regulatory paradigms - streamlined development
Pipeline Positioned for Value Creation	• First clinical data for a Prime Editing program (PM359 for p47^{phox} CGD) expected in 2025 • Wilson's Disease IND and/or CTA expected in H1'26, emerging *in vivo* data to be presented Q4'24 and H1'25 • Strategically focused on high-value programs with clear path to value inflection
Partnerships and BD Potential	• BMS partnership to develop Prime Edited *ex vivo* CAR-T products • Cystic Fibrosis Foundation relationship and funding to advance Prime Editors for Cystic Fibrosis • Additional business development to accelerate and expand pipeline

Pro-forma cash, cash equivalents, investments and restricted cash of $244.6M*, cash runway into H1'26

*Including $55M equity investment received in September 2024 and $55M up-front consideration received in October 2024 from BMS

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

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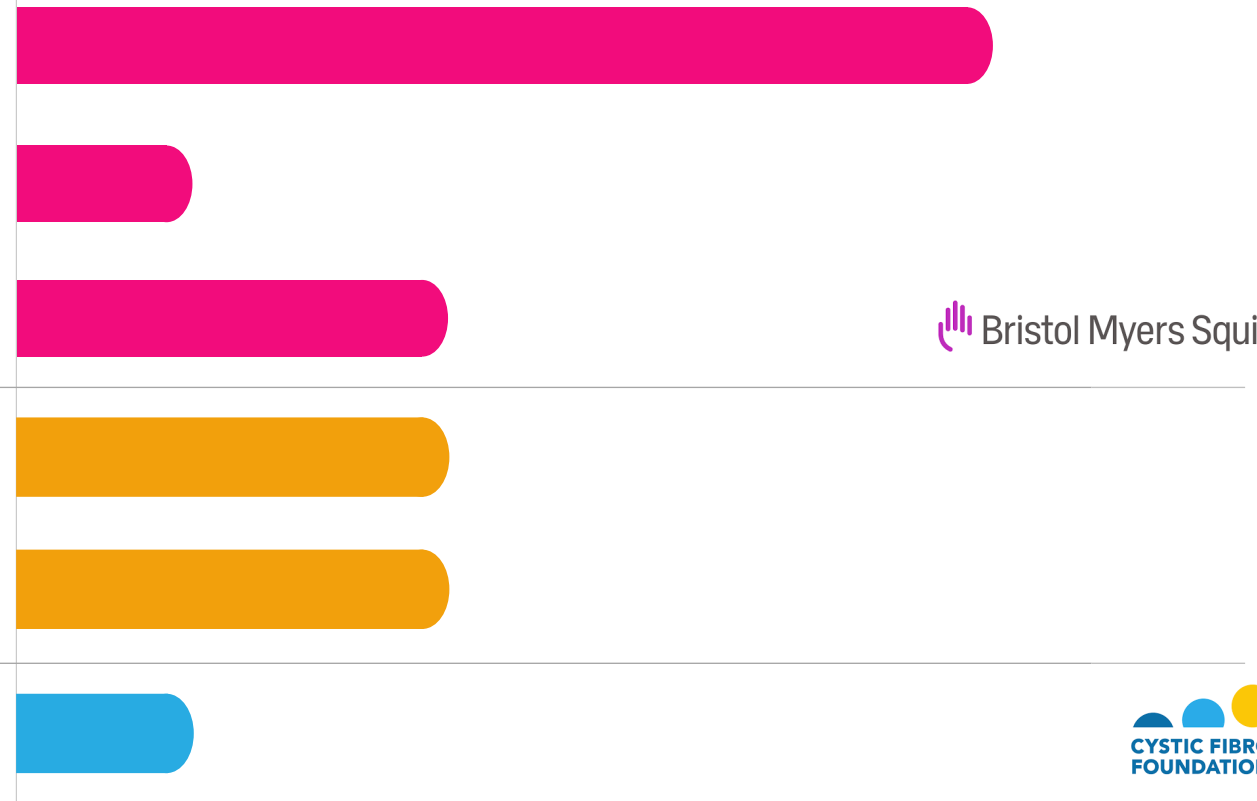
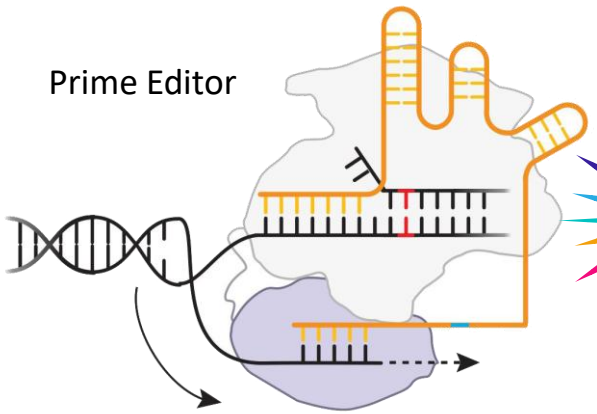
Modular Platform	Indication	Delivery
HEMATOLOGY, IMMUNOLOGY & ONCOLOGY	p47^{phox} Chronic Granulomatous Disease (CGD)	*ex vivo*
	X-linked CGD (with PASSIGE™)	*ex vivo*
	Ex vivo CAR-T[1] (with PASSIGE™)	*ex vivo*
LIVER	Wilson's Disease	LNP
	Undisclosed Program	LNP
LUNG	Cystic Fibrosis[2]	LNP/AAV

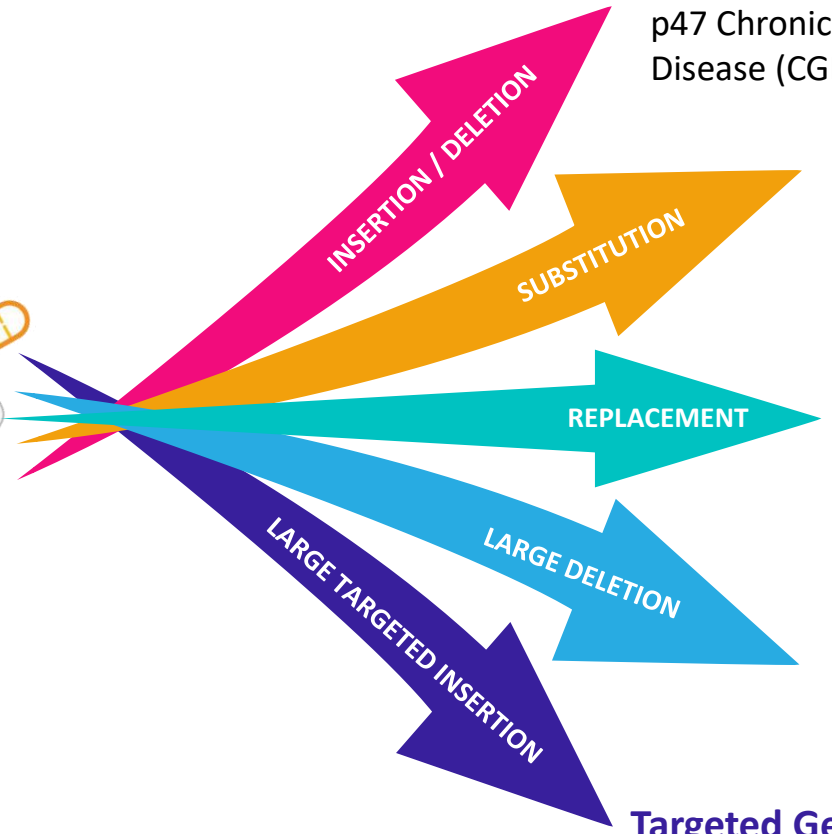


Prime Medicine is identifying opportunities to advance its other programs, including neurological diseases, cell therapy, ocular diseases and hearing loss, in partnership or through internal efforts in the future.

[1] In September 2024, entered into a strategic research collaboration and license agreement with Bristol Myers Squibb to develop and commercialize multiple *ex vivo* T cell products in immunology and oncology.
[2] In January 2024, entered into an agreement with CF Foundation for up to $15 million to support development of Prime Editors for Cystic Fibrosis.

We Believe Prime Editing is the Only Gene Editing Technology That Can Edit, Correct, Insert and Delete DNA Sequences in Any Target Tissue





Deletion / Insertion Correction
p47 Chronic Granulomatous Disease (CGD)

Point Mutation Correction
Wilson's Disease

Hotspot Correction
Cystic Fibrosis, Retinitis Pigmentosa (RHO adRP)

Repeat Excision
Friedreich's Ataxia

Targeted Gene Insertion (PASSIGE™)
XCGD, CAR-T, Cystic Fibrosis

Broad and versatile editing capabilities unlock opportunities across **thousands of indications,** including genetic diseases, infectious diseases, cancers and immunological diseases

Prime Editing is Designed with a Wide Range of Genome Editing Capabilities

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Flexibility to select right approach for each indication based on editing need

Prime Editing Approach	**Small edits** (e.g., all 12 bp swaps, 1-bp to 20-bp ins or del, combinations thereof)	**Mid-sized edits** (e.g., hotspot corrections, del up to 1-kb, ins up to 250 bp)	**Large deletions** (e.g., multi-kb repeat excision, exon del)	**Large insertions or inversions** (e.g., targeted multi-kb gene integration)
Short Flap Prime Editing	✓ +++			
Dual Flap Prime Editing	✓ ++	✓ +++	✓ +++	
Long Flap Prime Editing	✓ ++	✓ +++	✓ ++	
PASSIGE		✓ +	✓ +	✓ +++

✓ = capable of the edit

+/++/+++ = how fit Prime Medicine believes the technology is for making the edit, based on Prime Medicine's internal assessment

BP = base pair; KB = kilobase

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

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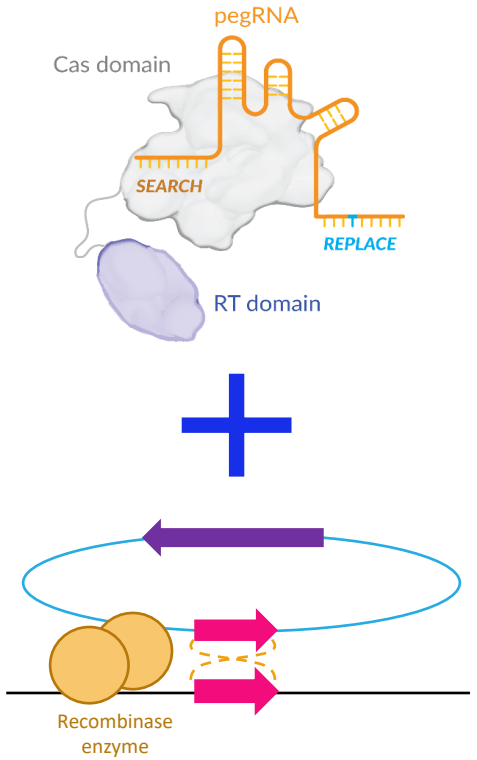
PASSIGE: Prime-Assisted Site-Specific Integrase Gene Editing:
One step non-viral multi-kilobase-size gene editing approach with no double-stranded breaks



Where we are working today:

- **Non-viral, multiplex-edited CAR-T therapies**
  BMS collaboration (e.g., oncology and autoimmune diseases)
- **X-Linked Chronic Granulomatous Disease (XCGD)**
- **Cystic Fibrosis**

Areas of opportunity:*

- **Targeted whole gene replacement for bone marrow diseases**
  (e.g., Hereditary anemias, such as Fanconi Anemia)
- **Targeted whole gene replacement for rare liver diseases**
  (e.g., Phenylketonuria, Tyrosinemia)
- **Correct inversion mutations**
  (e.g., Hemophilia A)
- ***In vivo* protein factory**
  (e.g., GLA enzyme for Fabry's disease)

*Not part of Prime Medicine's current pipeline

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

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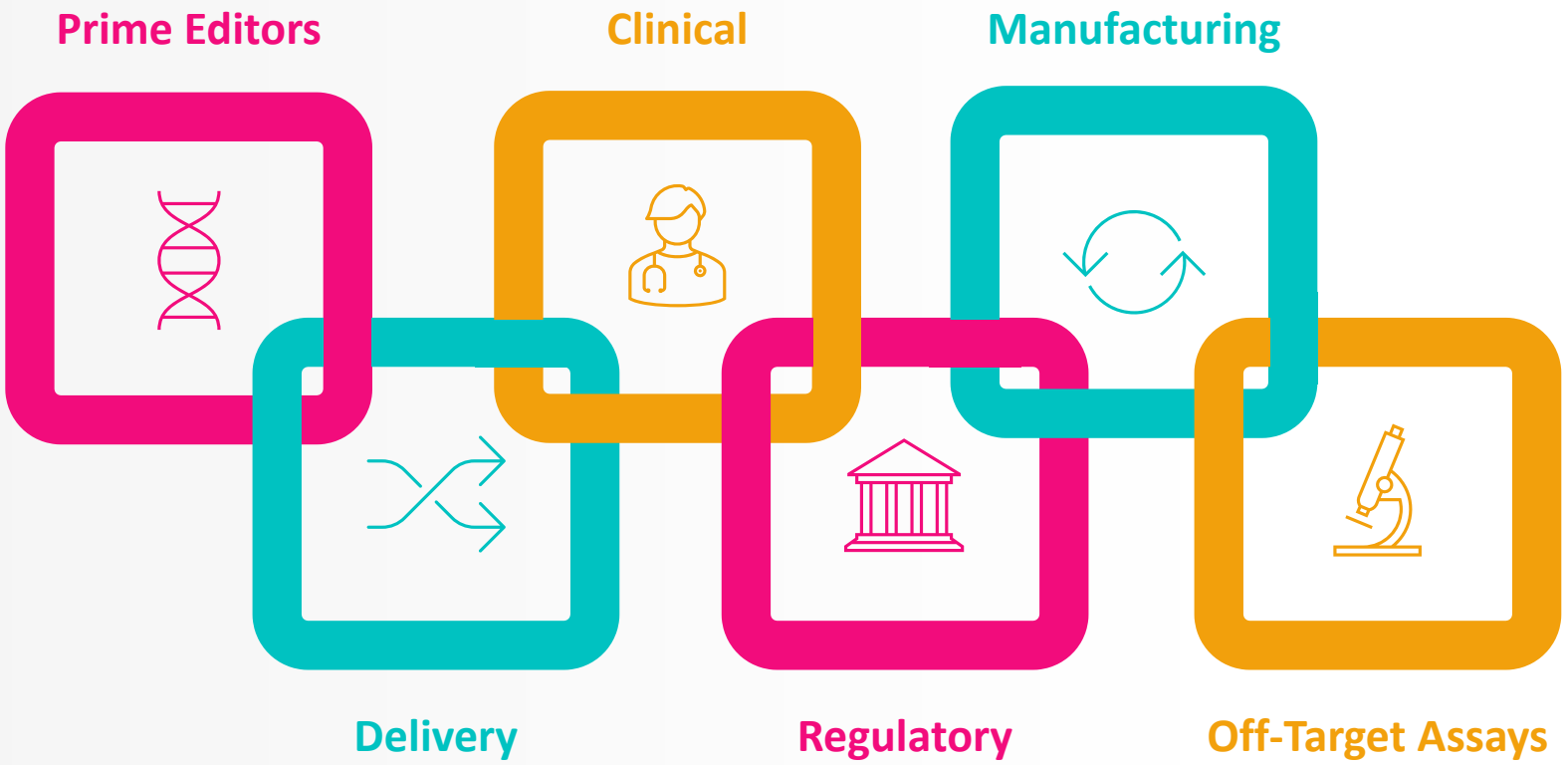
Core components can be readily leveraged to accelerate pipeline growth, efficiency and execution



Prime Editing Can Be Delivered with High Efficiency, Correcting Pathogenic Mutations at Levels Expected to Reverse Disease

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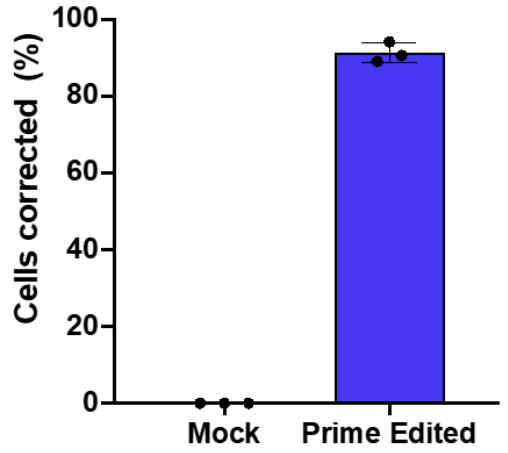
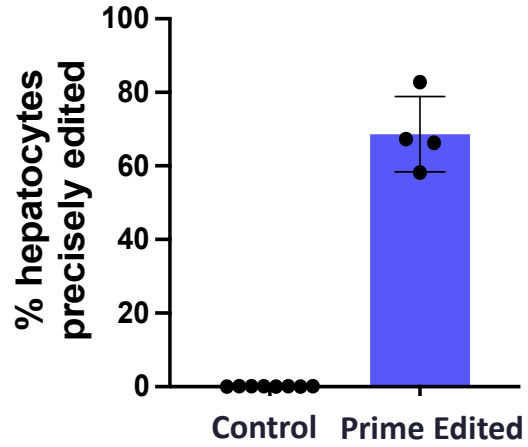
1 Ex Vivo (Human CD34+ Cells)



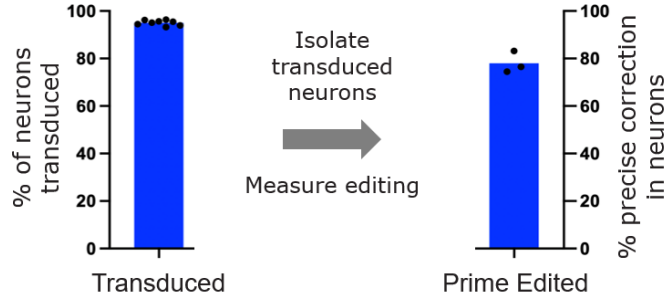
>90% editing of CD34+ cells *ex vivo* via electroporation

2 In Vivo – LNP (NHP Liver)



Up to ~83% of hepatocytes precisely edited in NHPs[1]

3 In Vivo – AAV (Mouse Brain and Eye)



>80% precise editing in mouse CNS

>70% precise editing in mouse photoreceptors

Proof-of-concept in initial indications have accelerated development of subsequent programs

NHP = non-human primate; CNS = central nervous system; [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).

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

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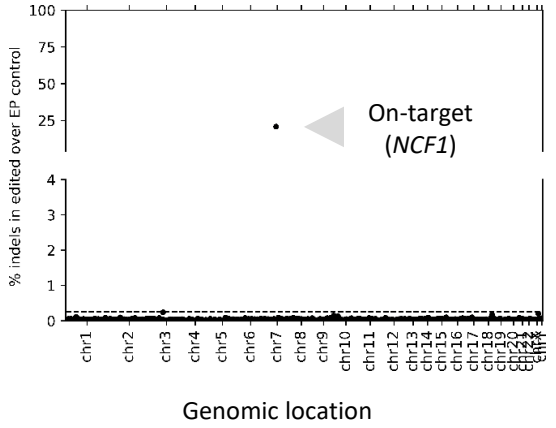
Prime Editing has been evaluated across comprehensive suite of robust, IND-ready assays for off-target discovery

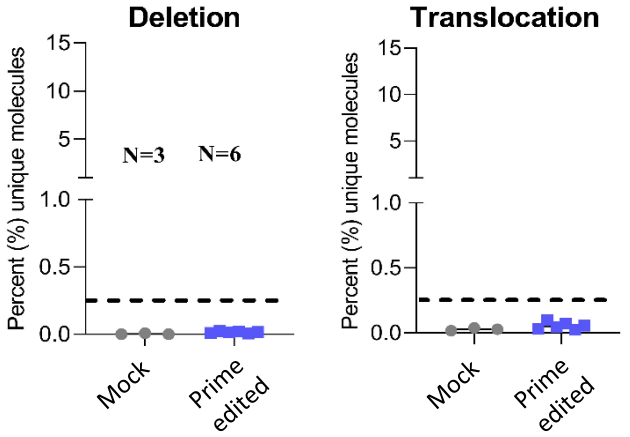
- ☑ **No** detectable double strand breakage
- ☑ **No** detectable off-target edits
- ☑ **No** detectable bystander edits
- ☑ **No** detectable off-target deletions, chromosomal translocations or rearrangements

Examples from CGD Program that have been used to support IND/CTA filings:

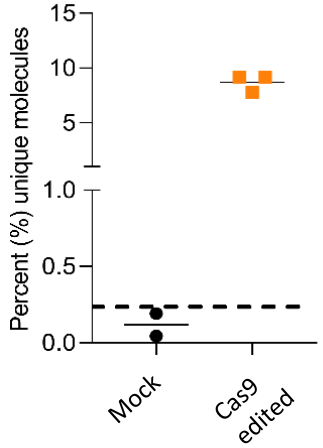
No off-target editing detected in healthy human donor CD34+ cells[1]



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



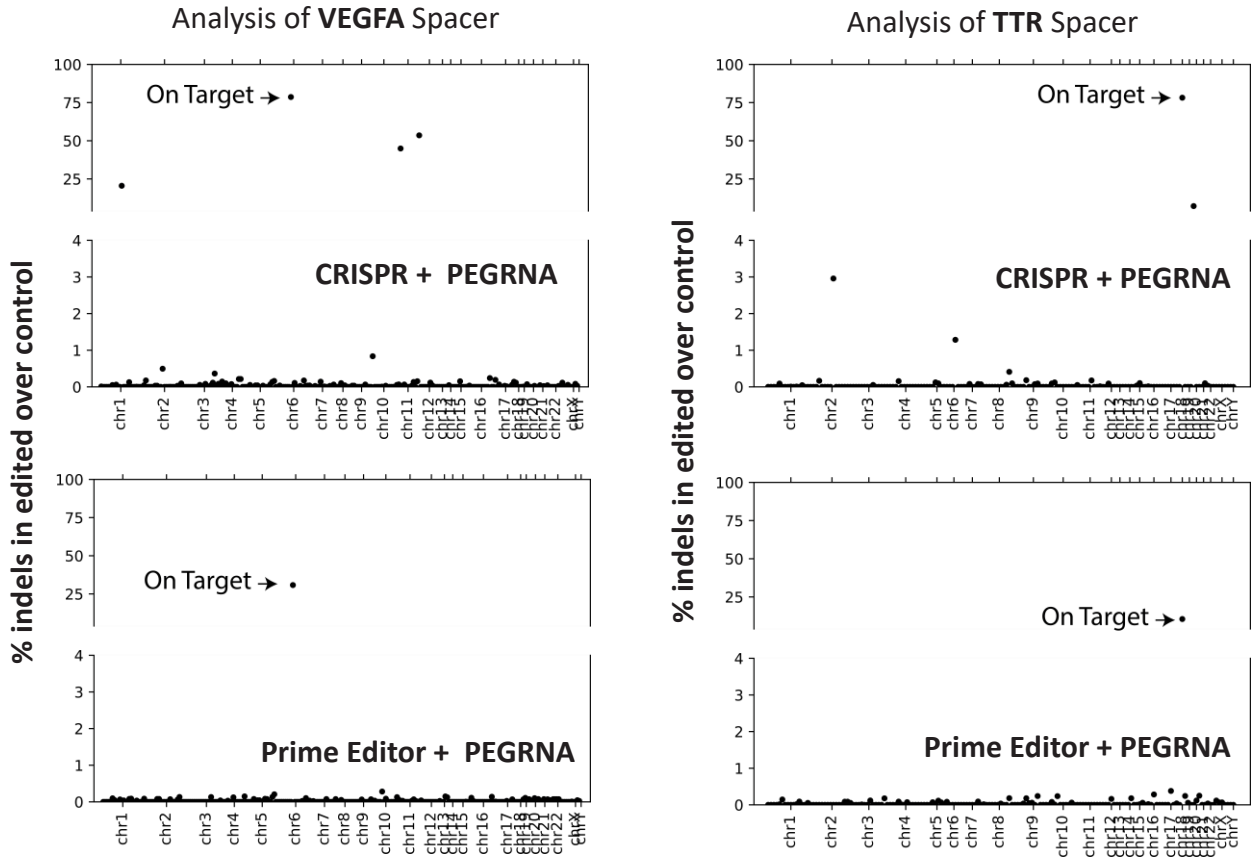
Translocation positive control: **Cas9 nuclease-edited** cells[3]

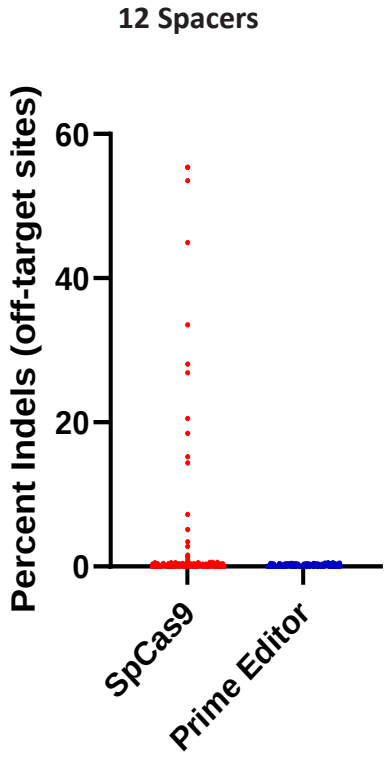


[1]Analysis of edited CD34+ cells from CGD program: Targeted *in vitro* Analysis of 550 potential off-target sites of off-target editing. [2]Data from *in vivo* analysis from mouse bone marrow harvested 16 weeks after engraftment was complete. [3]Positive control generated by transfecting HEK293T with sgRNA targeting *NCF1* and SpCas9 mRNA. HSC = hematopoietic stem cell; IND = investigational new drug; CTA = clinical trial application

Direct Comparisons of Prime Editors to CRISPR Showed Substantially Fewer Off-Target Edits Detected with Prime Editing

Examples from evaluation of potential off-target sites in Prime Edited or CRISPR-edited cells by deep sequencing





In silico and biochemical tools can be used to define potential off-target sites for Prime Editors

Hematology, Immunology and Oncology

Chronic Granulomatous Disease

$p47^{phox}$ CGD and XCGD

Advancing Prime Editors for Chronic Granulomatous Disease (CGD), 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 at least 40 years
- 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 is only curative option: complicated by GvHD, graft failure, limited availability

We believe Prime Editing is uniquely well-suited to address multiple forms of CGD

HSCT = hematopoietic stem cell transplant; GvHD = graft vs. host disease

Prime Medicine's CGD Franchise Covers Vast Majority of Patient Population

Leveraging modular elements from across the PM359 program, including the IND filing, CMC work and clinical trial, to accelerate advancement of XCGD program

	PM359 for p47^{phox} CGD	X-linked CGD Program
Current Status	**Initial data from Phase 1/2 clinical trial expected in 2025**	**Preclinical development ongoing**
Rapidly Advancing	**IND cleared in April 2024, within 30 days of submission**	**Leveraging modular elements of PM359 program to inform and accelerate advancement**
Targeted Mutations	delGT mutation in NCF1	Greater than 90% of mutations in the CYBB gene
Approach	Short Flap Prime Editing	PASSIGE
Opportunity	Approximately 25% of CGD Patients	Approximately 66% of CGD Patients

PM359: Preclinical Data Support Advancement for the Treatment of Chronic Granulomatous Disease

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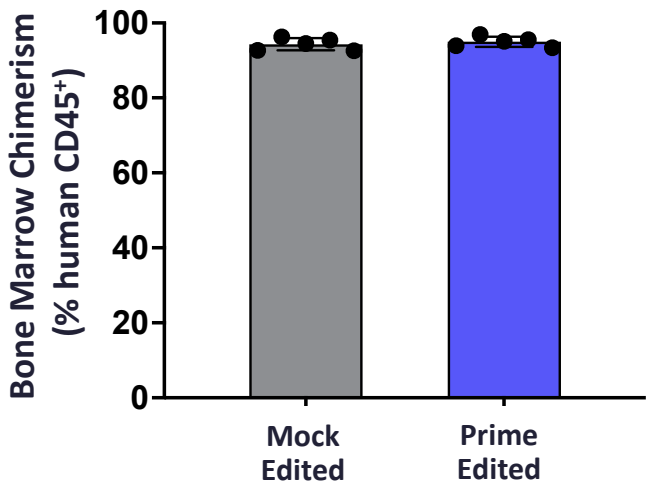
Maintenance of >85% of corrected patient long-term HSCs with complete restoration of NADPH oxidase in neutrophils observed

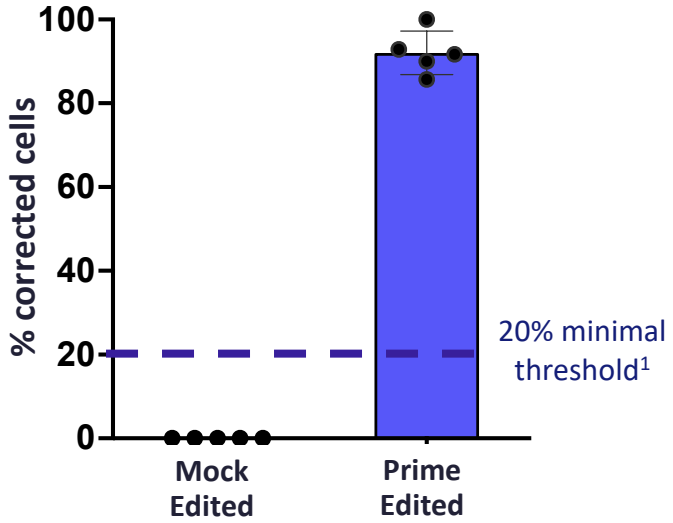
Engraftment

Prime Edited LT-HSCs showed complete engraftment in vivo



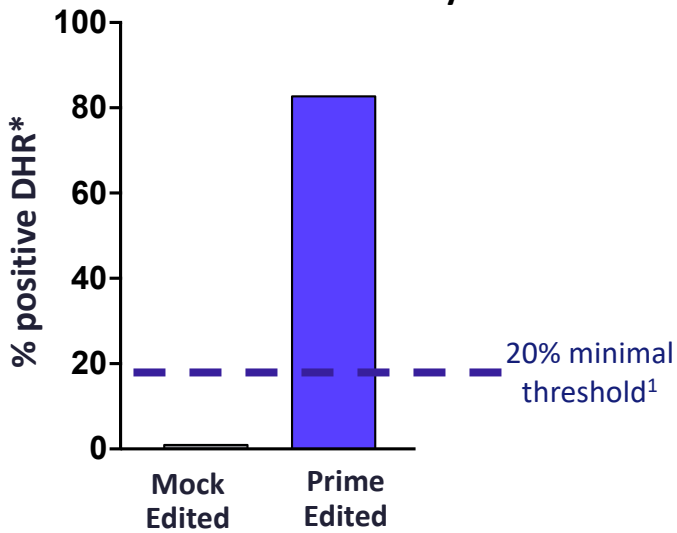
Editing Efficiency

Long-term engrafted HSCs carried precise correction of *NCF1*



Phenotypic Correction

Human neutrophils showed full correction of NADPH oxidase activity ex vivo

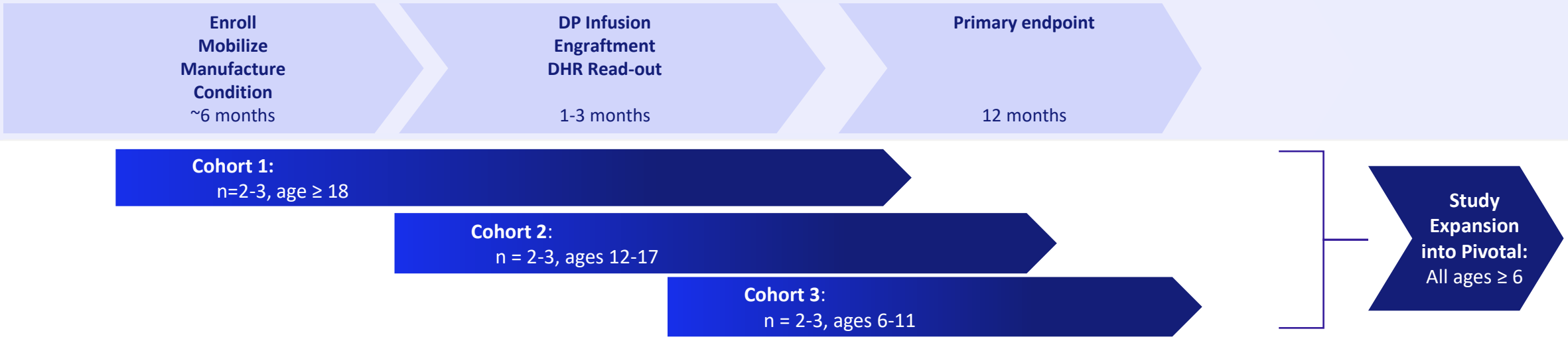


- Full immune system reconstitution by Prime Edited LT-HSCs
- Edited LT-HSC derived neutrophils had normal enzymatic activity (NADPH oxidase)

HSC = hematopoietic stem cell; LT-HSC = long term HSC; DHR = dihydrorhodamine; * normalized to healthy donor control. [1]Minimal threshold for patient benefit per Marciano BE, Zerbe CS, Falcone EL, et al. X-linked carriers of chronic granulomatous disease: Illness, lyonization, and stability. *J Allergy Clin Immunol*. 2018;141(1):365-371. doi:10.1016/j.jaci.2017.04.035.
Data presented at ASGCT and ESGCT 2023

PM359: Prime Medicine Poised to Deliver Initial Clinical Data in 2025

PM359 is comprised of autologous HSCs modified *ex vivo* using Prime Editing



Key eligibility criteria

- delGT mutation in *NCF1* gene
- Dihydrorhodamine (DHR) combined with 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

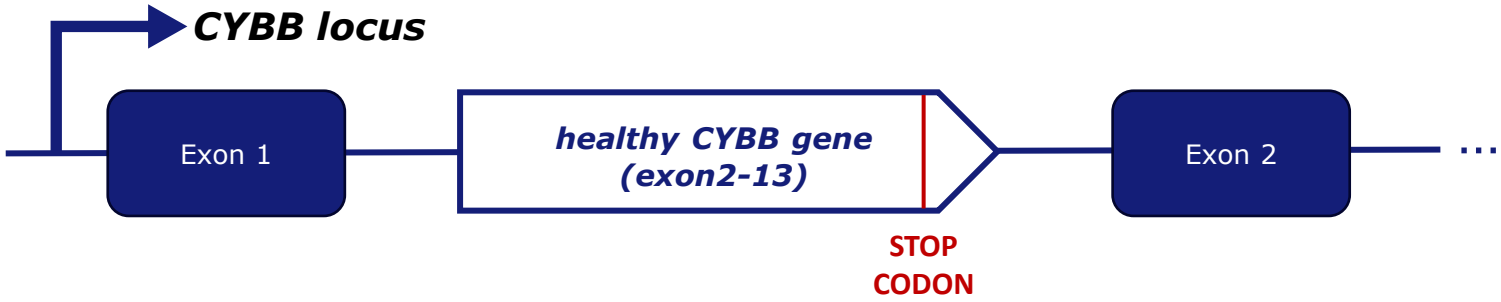
IND cleared April 2024
First clinical data expected in 2025

DP = drug product; GMP = good manufacturing practice; QC = quality control; IND = investigational new drug

PASSIGE has Potential to Treat X-linked CGD (XCGD)

'All in one' delivery of PASSIGE reagents for *CYBB* gene replacement in CD34+ cells has potential to treat >90% of XCGD patients

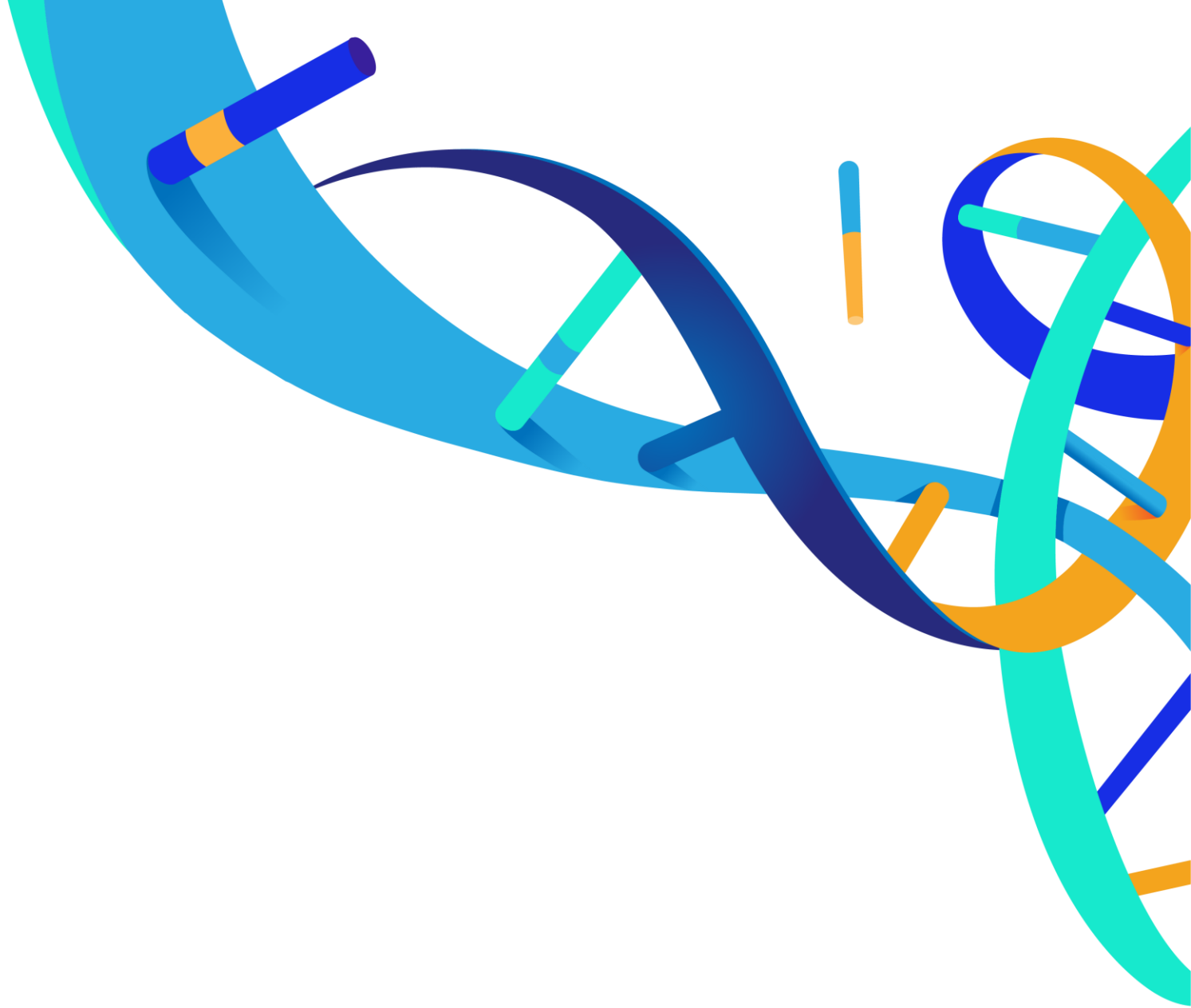
PASSIGE reagents designed to precisely insert healthy CYBB gene sequence at prespecified site in the patient's CYBB locus



- **PASSIGE demonstrated high multiplex editing efficiency**
- **Potential synergies to accelerate leveraging p47^{phox} CGD program**
  - **Validated CGD assays and HSC models** established for PM359 are applicable to X-CGD
- **Healthy CYBB gene sequence under control of the endogenous CYBB regulatory elements**
- **Predicted low risk** of off-target editing

Ex vivo CAR-T

BMS Collaboration



Strategic License and Broad Collaboration Agreement with Bristol Myers Squibb (BMS) to Develop Prime Edited *ex Vivo* CAR-T Products

First broad, multi-target collaboration advancing Prime Editing for the treatment of complex oncology and autoimmune indications

Leadership in Prime Editing; PASSIGE technology may enable one-step, non-viral, multi-kilobase-size editing approach with no double-stranded breaks

Global leader in cell therapy for hematology, immunology and oncology

- $110 million upfront
- >$3.5 billion in potential milestones, including:
  - $185 million in preclinical milestones
  - $1.2 billion in development milestones
  - More than $2.1 billion in commercial milestones
  - Royalties on net sales
- Multiple targets in immunological diseases and cancer, beyond rare genetic diseases in Prime Medicine's internal pipeline

Prime Medicine retains rights to advance certain target reagents designed under this collaboration for applications beyond *ex vivo* T cell products, including *in vivo* T cell and other cell therapy applications

CAR-T: PASSIGE and Multiplex Prime Editing is the Foundation of Prime Medicine's Collaboration with BMS

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Platform modularity 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 of CAR, 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

TRAC = T-cell receptor alpha constant; Data presented at ASH, December 2022, ASGCT, May 2023 and ASH, December 2023

Beyond Precisely Inserting a Chimeric Antigen Receptor, We Can Simultaneously and Efficiently Multiplex Edit CAR-T Cells

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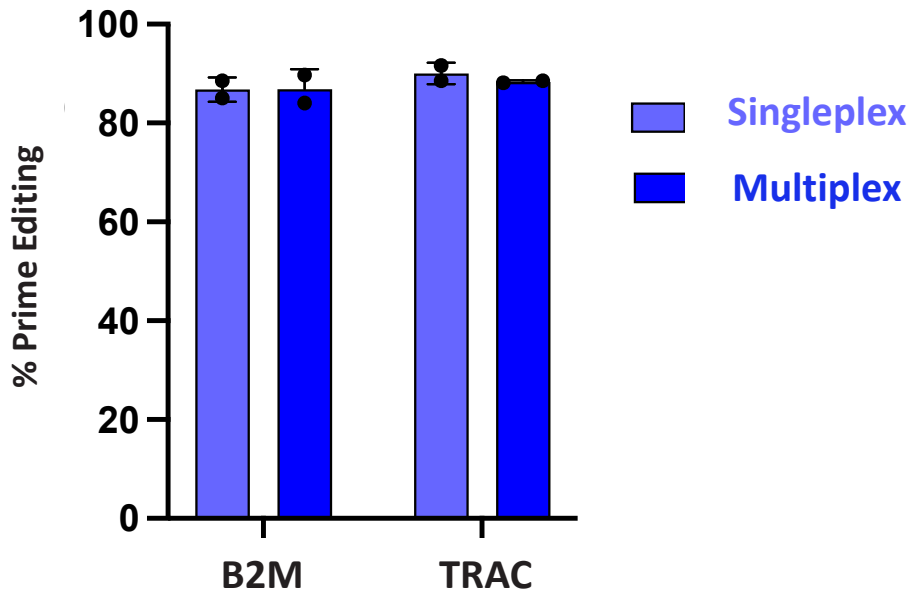
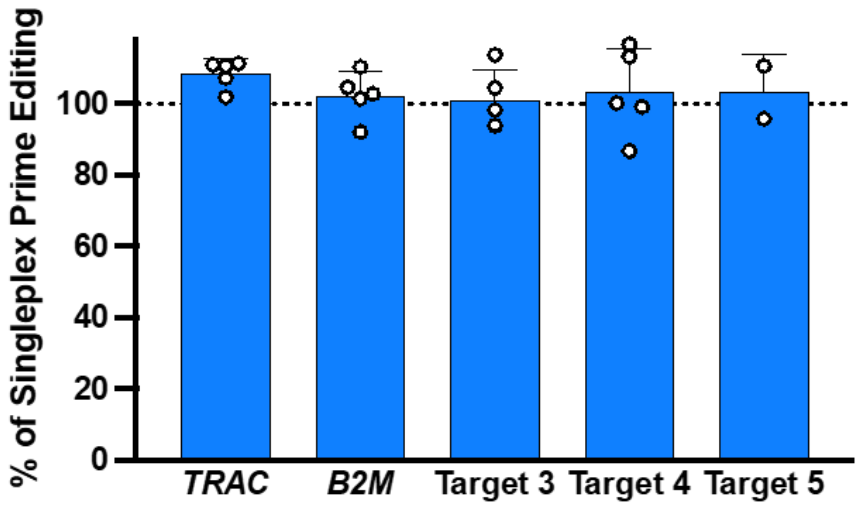
Prime Editors can be multiplexed to introduce multiple genomic modifications in CAR-T cells

High efficiency multiplex editing of B2M and TRAC

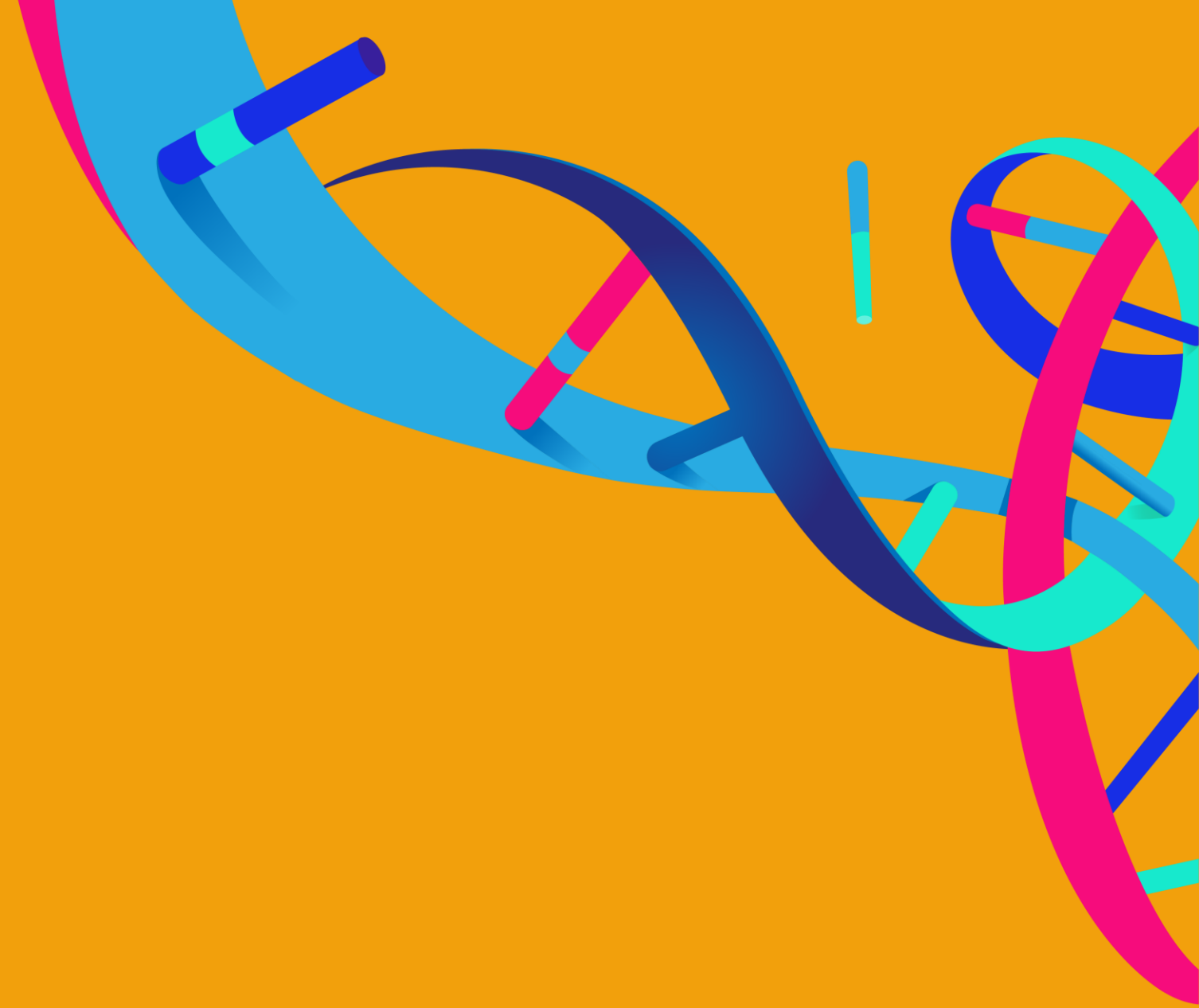


Maintained efficiency with five multiplex edits



B2M = b2 microglobulin
TRAC = T-cell receptor alpha constant

Liver



Advancing Prime Editors for Multiple Mutations Within Wilson's Disease By Leveraging Our Proprietary Universal LNP

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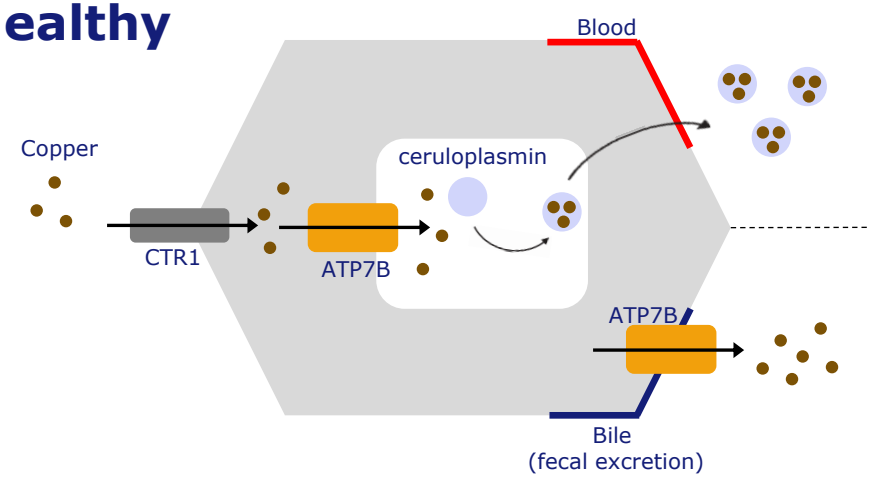
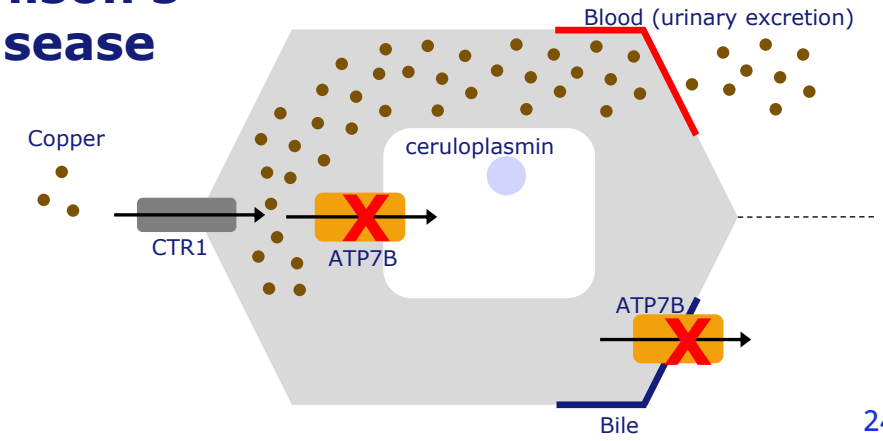
Large genetically defined disease well suited for Prime Editing

- **Disease severity and opportunity**
  - Common liver and systemic disease presenting in teens to 20s
  - Leads to liver failure, neurocognitive decline and premature death
  - Greater than 20,000 patients in US and Europe, 30-50% harboring H1069Q mutation
  - R778L is the predominant mutation in Asian population
- **Unmet need**
  - Many patients die without liver transplant
  - No approved disease modifying therapies
  - Current standard of care aims to prevent copper accumulation; options include chelating agents and low copper diet
- **Human biology**
  - Autosomal recessive due to loss of function mutations in ATP7B
  - Affects copper homeostasis, leading to toxic accumulation of copper in liver and brain
  - Correction of 20-30% of hepatocytes may be curative

Healthy



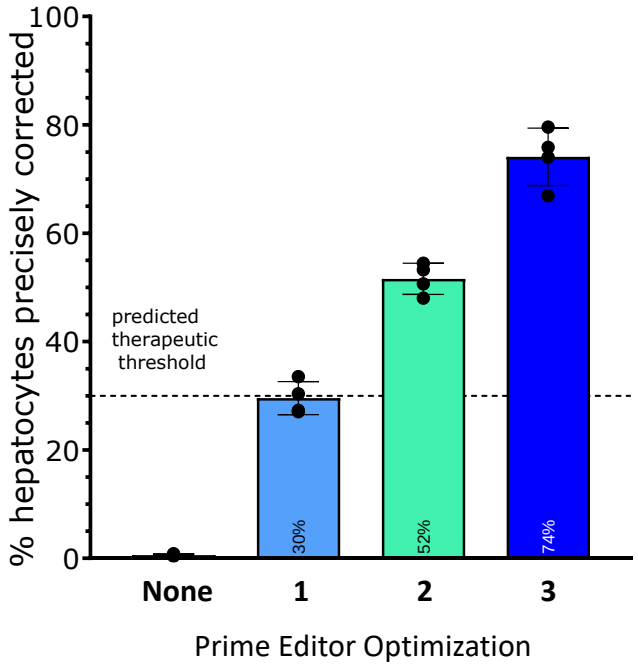
Wilson's disease



Prime Editors Efficiently Correct the H1069Q Mutation *In Vivo*

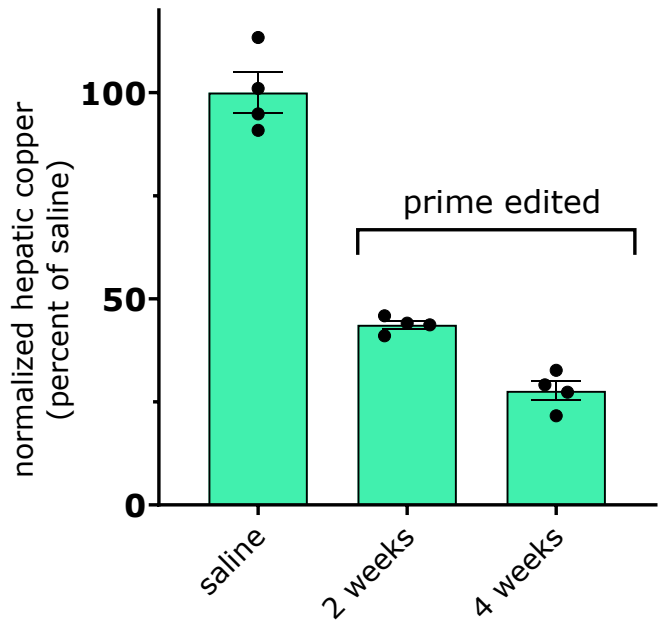
Editing efficiency and copper reduction in fully humanized homozygous p.H1069Q ATP7B mouse model

Prime Editors corrected the H1069Q transversion mutation



Optimizations to the PE enzyme, gRNAs and mRNA improved prime editor editing efficiency

PE optimization #2 yielded a 75% reduction in copper accumulation in the liver



Additional liver copper studies ongoing with optimized Prime Editors

Up to 51% Precise Editing Achieved with Universal LNP-Formulated Surrogate H1069Q Prime Editor *In Vivo* (NHP)

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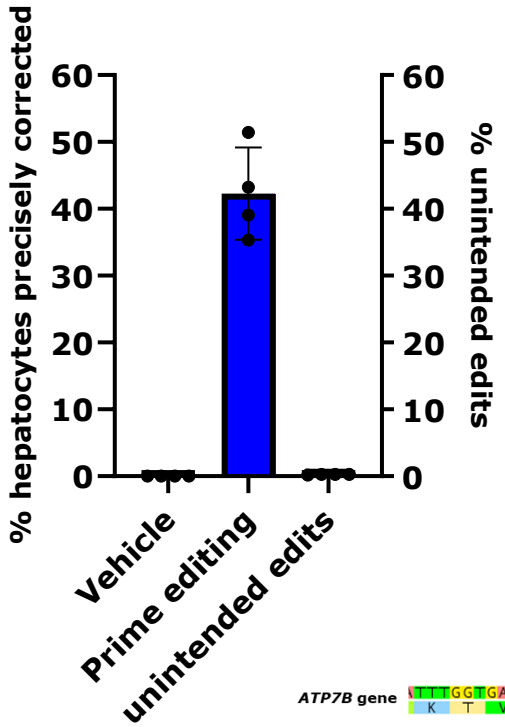
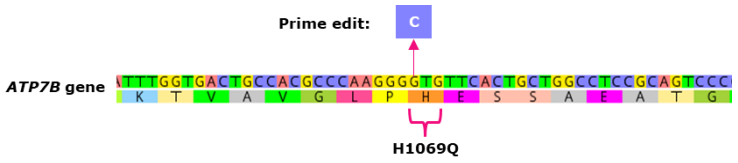
ATP7B H1069 Prime Editing in NHP



Up to 51% editing in liver hepatocytes achieved with un-optimized surrogate NHP Prime Editor

No detectable off-target edits or unintended edits at the target site



Prime Medicine's modular LNP dosed in cynomolgus monkey (NHP) with no safety concerns

- Well-tolerated with no acute reactions, clinical observations, or body weight changes
- Minimal transient LFT elevations
- No change in platelets, coagulation or blood count
- No change in blood biochemistry
- Minimal changes in IL6 levels
- No other cytokine changes
- No change in liver histopathology (H&E)
- Animals healthy at 44 weeks
- Benchmarked against other LNPs in clinical development

Proprietary LNP-formulated Prime Editor is a Complex Multi-Component Drug Product Designed to Support Current and Future Liver Programs

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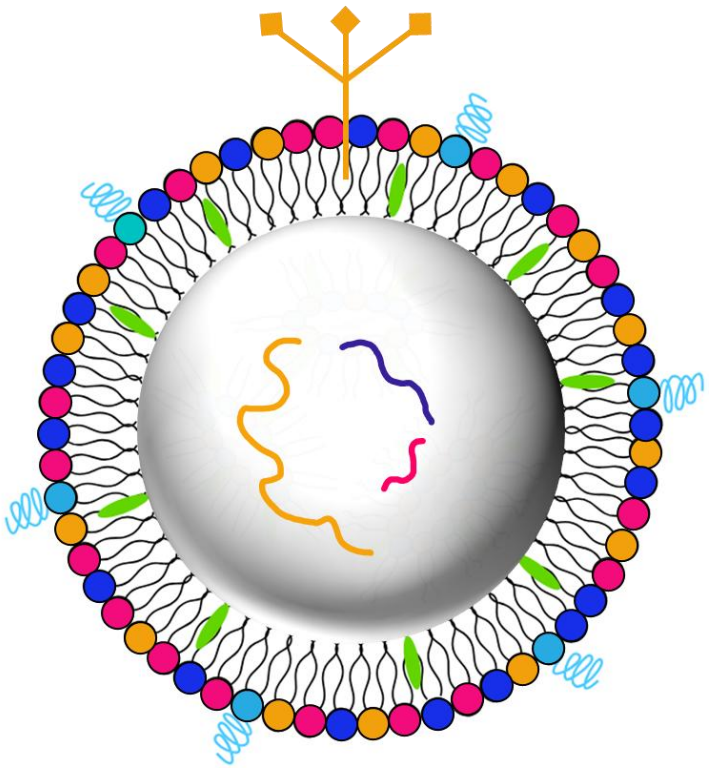
LNP Modularity:

6 out of 8 components in the LNP are the same for liver programs



Ionizable Lipid	• Nucleic acid encapsulation and endosomal escape
Helper Lipid	• Stabilize and improve LNP pharmacokinetics • Facilitate membrane fusion and endosomal escape
PEG Lipids	• Control particle size and stability • Stealth coating reduces serum interactions and increases half-life
Cholesterol	• Improve intracellular delivery • Increase LNP stability
Targeting Ligand	• Proprietary GalNAc formulation to improve biodistribution of LNPs to hepatocytes
PE mRNA	• Prime editor enzyme
pegRNA	• pegRNA is disease & mutation specific
ngRNA	• ngRNA is disease & mutation specific; usage is dependent on the Prime Editing strategy applied

Lung

In January, Entered into Agreement with CF Foundation for Up to $15 Million to Support Development of Prime Editors for CF

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Funding accelerates development of potentially curative therapies for cystic fibrosis (CF) Progressing two distinct strategies:

- **Hotspot editing:** potential to address numerous mutations at mutational hotspots with a small number of Prime Editors
- **PASSIGE:** potential to address nearly all CF patients with a single superexon insertion strategy
- **Funding will also accelerate ongoing LNP delivery efforts to the lung**

With infrastructure support and foundational guidance, CF Foundation brings a world-class research lab with established assays, animal models, reagents, patient samples, as well as deep clinical experience and important patient and advocacy efforts

CF impacts close to **40,000** people in the United States.

There is no cure and existing treatments are ineffective for, or not tolerated by, approximately **15%** of patients.

Prime Medicine believes Prime Editing-based approaches could eventually benefit **more than 93%** of all people with CF.

With CF Foundation's support, Prime Medicine has the potential to deliver a one-time, non-viral therapy that offers first cure to all patients living with CF

CF = Cystic Fibrosis

With Hotspot Editing, Prime Editors Corrected "High Unmet Need" CF Mutations, Including the Prevalent G542X (null) Mutation

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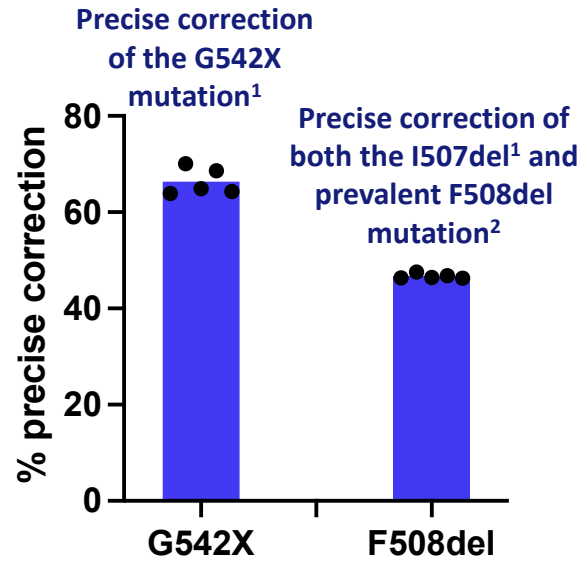
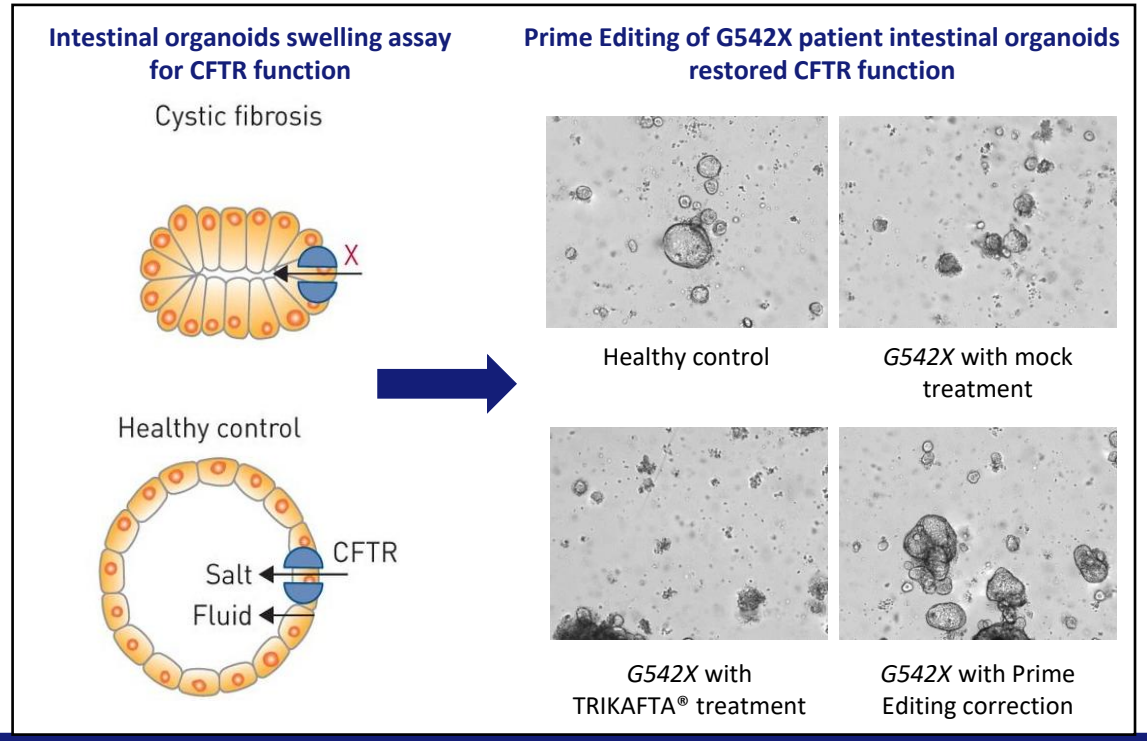
Eight hotspot Prime Editors could address the "high unmet need" mutations;
These **same** eight hotspot Prime Editors could address >93% of **all** CF patients

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 under endogenous control

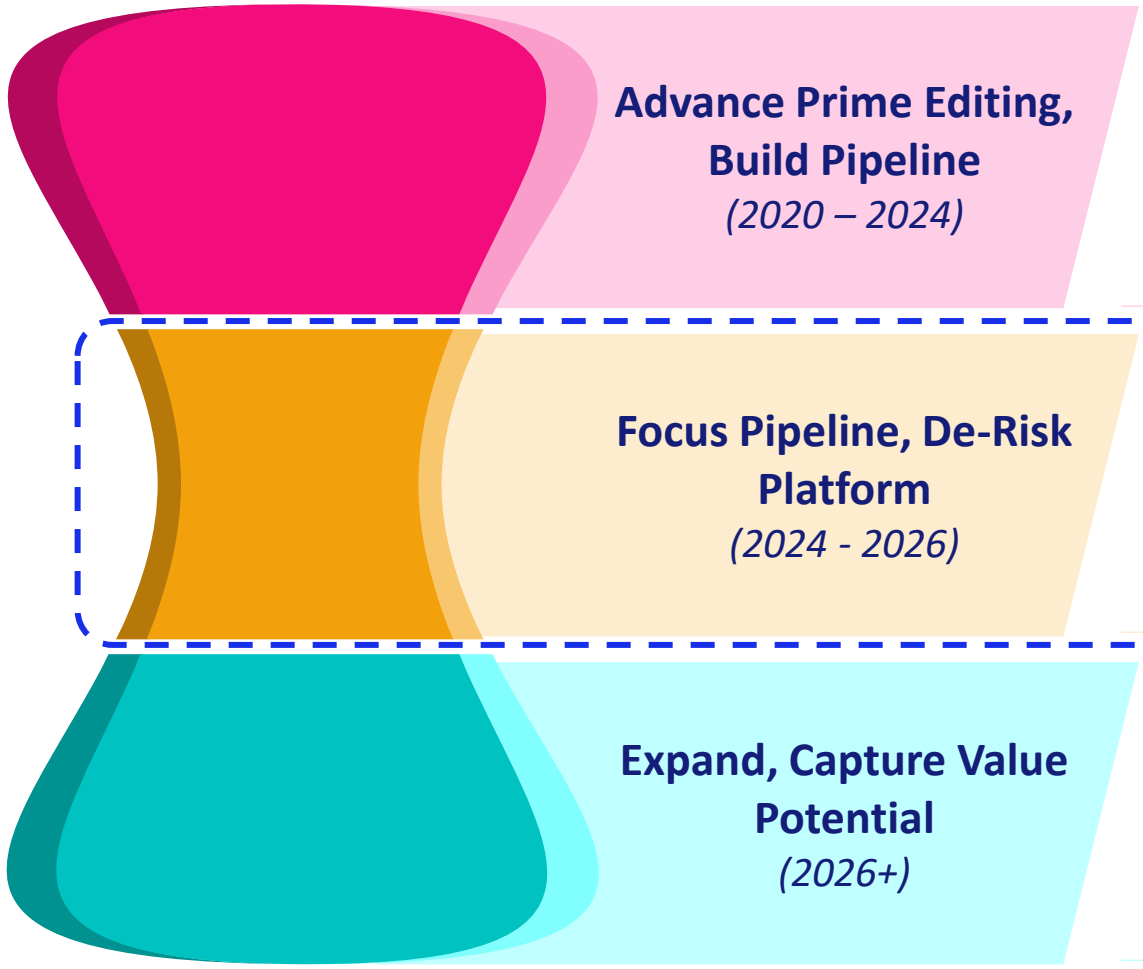
- LNP delivered Prime Editors efficiently corrected patient Human Bronchial Epithelial (HBE) progenitors *in vitro*
- Identified early LNP formulations to deliver Prime Editors to lung basal cells *in vivo*

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 induced pluripotent stem cells. Each dot shows a different Prime Editor

Corporate

Prime Medicine is Entering a Phase of Focused Execution

Focused pipeline to enable future expansion into other high value areas



Advance Prime Editing, Build Pipeline
(2020 – 2024)

- ✓ Prime Medicine began operations in 2020
- ✓ First Prime Editor IND accepted for PM359 in p47phox CGD
- ✓ 18 programs advancing through preclinical development
- ✓ BMS partnership formed to leverage PASSIGE™ / capabilities

Focus Pipeline, De-Risk Platform
(2024 - 2026)

- Continue to leverage BD to build & accelerate pipeline
- First-in-human clinical data expected for prime editor program in $p47^{phox}$ CGD
- Advance Wilson's disease to expected IND in H1 2026
- Multiple high value programs advance towards clinic

Expand, Capture Value Potential
(2026+)

- Expand pipeline within priority focus areas and beyond
- Prepare for first potential clinical launch of Prime Editor therapeutic

Our Pipeline: Focused on Significant Opportunities with High Value Potential

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Prime Medicine's focused pipeline emphasizes significant opportunities with clear path to value inflection

Value Framework

- **Unmet medical need**
- **Commercial potential**
- **Pipeline and platform modularity**
- **Clinical development pathway**
- **Regulatory considerations**
- **Competition**

Selection of Prioritized Investments & Rationale

CGD	• High unmet medical need, potential fast path to registration in p47^{phox} CGD • XCGD Program using PASSIGE, leveraging modular platform, insights from p47^{phox} CGD and other potential synergies (e.g., manufacturing, regulatory)
Wilson's Disease	• Multi-billion-dollar opportunity, early clinical de-risking via clearly defined biomarkers • Uses Prime's universal LNP which can be leveraged for future liver programs • Advance regulatory framework for Wilson's Disease and follow-on liver programs
Cystic Fibrosis	• Multi-billion-dollar opportunity • Prime Editing allows for precise transcriptional control • Up to $15 million funding from Cystic Fibrosis Foundation accelerates lung delivery efforts
CAR-T (BMS)	• Broad strategic deal with BMS, extends reach in immunological diseases and cancer • Combines novel multiplex gene editing capabilities including PASSIGE technology with BMS's broad expertise in development and commercialization of cell therapies

CGD = chronic granulomatous disease; XCGD = x-linked CGD; LNP = lipid nanoparticle

Beyond BMS, Business Development Will Continue to Play a Critical Role in Building Prime Medicine

Prime Medicine plans to remain active in sell-side business development, with the goal of accelerating our pipeline, bolstering our financial resources

Current Relationships

BMS

Develop Prime Edited CAR-T products leveraging PASSIGE and platform

CF Foundation

Funding to accelerate the development of Prime Editors for Cystic Fibrosis

Enabled by scientific leadership in gene editing and program advancement

Partnering Strategy

Within Our Core

Outside Our Core

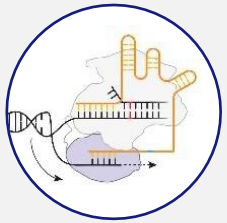
Access Enabling Innovation

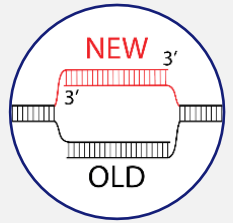
Prime Medicine Holds Extensive Intellectual Property for Prime Editing Technologies

- ***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 pipeline programs

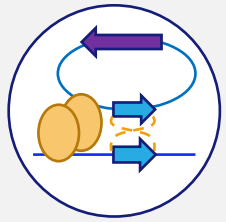
Prime Medicine holds 5 US and 3 ex-US issued patents

- Numerous Prime-owned and in-licensed patent applications with broad coverage filed worldwide
- Pursuing aggressive filing strategy to cover technological advances


Seminal Prime Editing Publication

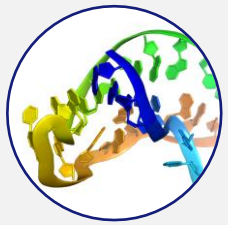


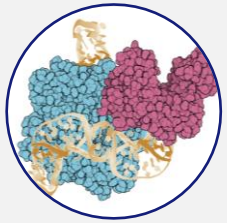
Dual Flap Prime Editing

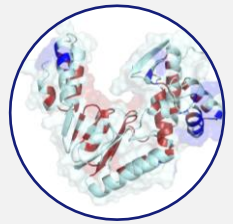

PASSIGE System

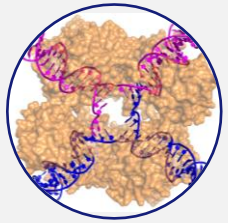
PE4, PE5, PEmax

Engineered pegRNAs


pegRNA Enhancements


Novel PE Proteins


Novel RT Proteins


Improved recombinases

Prime Medicine is the Leader in Gene Editing Positioned to Create Sustainable Value Through Pipeline Execution and External Partnerships

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The Leader in Prime Editing	• Potential to address more than 90% of genetic diseases and opportunities in non-genetic diseases • Pre-clinical efficacy across variety or target tissues leveraging various types of Prime Editing • Comprehensive intellectual property position
Platform Modularity Oriented for Growth	• Fully integrated modular platform - pre-clinical, clinical, manufacturing, regulatory • Proprietary modular delivery systems within target tissues • Advancing Prime Editing regulatory paradigms - streamlined development
Pipeline Positioned for Value Creation	• First clinical data for a Prime Editing program (PM359 for p47^{phox} CGD) expected in 2025 • Wilson's Disease IND and/or CTA expected in H1'26, emerging *in vivo* data to be presented Q4'24 and H1'25 • Strategically focused on high-value programs with clear path to value inflection
Partnerships and BD Potential	• BMS partnership to develop Prime Edited *ex vivo* CAR-T products • Cystic Fibrosis Foundation relationship and funding to advance Prime Editors for Cystic Fibrosis • Additional business development to accelerate and expand pipeline

Pro-forma cash, cash equivalents, investments and restricted cash of $244.6M*, cash runway into H1'26

*Including $55M equity investment received in September 2024 and $55M up-front consideration received in October 2024 from BMS