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

March 3, 2026
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.)**
60 First Street **Cambridge, MA**		**02141**
(Address of principal executive offices)		**(Zip Code)**

(617) 465-0013

(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 2.02 Results of Operations and Financial Condition.

On March 3, 2026, Prime Medicine, Inc. (the "Company") issued a press release announcing its financial results and business highlights for the year ended December 31, 2025. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information contained in Item 2.02 of this Current Report on Form 8-K, 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 (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 (the "Securities Act") or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 7.01 Regulation FD Disclosure.

On March 3, 2026, the Company posted an updated corporate presentation to its website at https://investors.primemedicine.com/news-events. A copy of the corporate presentation is furnished as Exhibit 99.2 to this Current Report on Form 8-K, which is incorporated herein by reference. Reference to the Company's website is for inactive textual reference only and the content of the website should not be deemed incorporated by reference into this Current Report on Form 8-K.

The information in this Item 7.01, including Exhibit 99.2 attached hereto, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of 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 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	Press Release, dated March 3, 2026, furnished herewith.
99.2	Corporate Presentation, dated March 2026, 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: March 3, 2026

Prime Medicine, Inc.

By: /s/ Allan Reine

Name: Allan Reine, M.D.

Title: Chief Executive Officer

Prime Medicine Reports Full Year 2025 Financial Results and Provides Business Updates

-- On track to file IND and/or CTA for Wilson Disease and AATD programs in 1H 2026 and mid-2026, respectively; initial clinical data for both expected in 2027 --

-- Ongoing engagement with FDA for PM359 in CGD; plan to submit BLA following final alignment --

-- Prime Medicine reported cash, cash equivalents, investments, and restricted cash of $191M providing cash runway into 2027 --

Cambridge, Mass., March 3, 2026 – Prime Medicine, Inc. (Nasdaq: PRME), a biotechnology company committed to delivering a new class of differentiated one-time curative genetic therapies, today reported financial results for the full year ended December 31, 2025 and provided a business update.

"We are shaping the future of genetic medicine by advancing a platform that is rapidly emerging as the predominant gene editing technology. With Prime Editing, we have the opportunity to permanently and safely correct disease-causing mutations across a broad range of indications, supported by our comprehensive IP estate," said Allan Reine, M.D., Chief Executive Officer of Prime Medicine. "With this foundation, our vision is bold and unwavering: to strategically deliver on the promise of Prime Editing and ensure patients have access to transformative therapies capable of delivering durable, and potentially lasting cures. This begins with PM359, our *ex vivo* Prime Edited autologous HSC product for CGD, for which we announced breakthrough data in 2025, which we believe supports an accelerated approval in the United States."

Dr. Reine continued, "We are also intensely focused on R&D execution. We are progressing toward key regulatory milestones for our two liver-focused programs – in Wilson Disease and Alpha-1 Anti-trypsin Deficiency – including planned IND and CTA submissions and the initiation of Phase 1/2 clinical trials. In parallel, we continue to generate compelling preclinical data across our portfolio, including for our program for Cystic Fibrosis; to further optimize our modular delivery and manufacturing approaches; and to explore additional collaborations that could expand the reach of our platform. These near- and mid-term milestones position us to deliver important additional clinical validation of Prime Editing, as we accelerate our path toward bringing meaningful, life-changing therapies to patients."

Prime Medicine's Pipeline:

Prime Medicine is advancing *in vivo* gene editing programs aimed at treating two of the most significant genetic liver disorders: Wilson Disease (WD) and Alpha-1 Antitrypsin Deficiency (AATD). Prime Medicine anticipates submitting an investigational new drug (IND) and/or clinical trial application (CTA) for its anchor WD program (targeting the H1069Q mutation) in the first half of 2026, and plans to leverage the modularity of the Prime Editing platform to subsequently advance follow-on programs targeting other mutations, which collectively address a majority of WD patients. Prime Medicine expects to file an IND and/or CTA for its AATD program in mid-2026, and to report initial clinical data from both WD and AATD programs in 2027.

Following positive proof-of-concept data from the first two patients treated in its Phase 1/2 study of PM359 for the treatment of Chronic Granulomatous Disease (CGD), Prime Medicine is actively working to ensure this transformative therapy is available for patients in need.

Prime Medicine is also progressing an in vivo Cystic Fibrosis (CF) program with support from the Cystic Fibrosis Foundation, and anticipates generating preclinical proof of concept data in 2026. Additionally, its efforts to develop Prime Edited CAR-T products for hematology, immunology and oncology continue in partnership with Bristol Myers Squibb.

Recent Business Updates:

- Prime Medicine continues to engage with the U.S. Food and Drug Administration (FDA) to explore ways to make PM359 available to patients with CGD. Based on recent interactions, Prime Medicine believes clinical data generated to-date may be sufficient to support an accelerated approval of PM359. The Company is working towards final alignment with the FDA, and intends to submit a Biologics License Application (BLA).
- In December 2025, Prime Medicine announced the publication of Phase 1/2 clinical data with PM359 in the New England Journal of Medicine (NEJM). The data, which were also presented in a poster session at the 67th American Society of Hematology (ASH) Annual Meeting, showed rapid neutrophil and platelet engraftment, as well as durable restoration of NADPH oxidase activity and early clinical benefit, without any safety concerns.

Full Year 2025 Financial Results

- **Research and Development (R&D) Expenses:** R&D expenses were $160.6 million for the year ended December 31, 2025, as compared to $155.3 million for the year ended December 31, 2024. The increase in R&D expenses is driven primarily by license and intellectual property costs and facility related expenses, offset by Prime Medicine's strategic focus on advancing its in vivo liver franchise, deprioritization of its CGD program, and a reduction in R&D personnel resulting from the workforce reduction.
- **General and Administrative (G&A) Expenses:** G&A expenses were $52.3 million for the year ended December 31, 2025, as compared to $50.2 million for the year ended December 31, 2024. The increase in G&A expenses was driven by increases in professional and consultant fees.
- **Net Loss:** Net loss was $201.1 million for the year ended December 31, 2025, as compared to $195.9 million for the year ended December 31, 2024.
- **Cash Position:** As of December 31, 2025, cash, cash equivalents, investments, and restricted cash were $191.4 million, as compared to $204.5 million as of December 31, 2024.

Financial Guidance

Based on its current operating plans, Prime Medicine expects that its cash, cash equivalents and investments as of December 31, 2025 will be sufficient to fund its operating expenses and capital expenditure requirements into 2027.

About Prime Medicine

Prime Medicine is a leading biotechnology company dedicated to creating and delivering the next generation of gene editing therapies to patients. The Company is deploying its proprietary Prime Editing platform, a versatile, precise and efficient gene editing technology, to develop a new class of differentiated one-time curative genetic therapies. Designed to make only the right edit at the right position within a gene while minimizing unwanted DNA modifications, Prime Editors have the potential to repair almost all types of genetic mutations and work in many different tissues, organs and cell types. Taken together, Prime Editing's versatile gene editing capabilities could unlock opportunities across thousands of potential indications.

Prime Medicine is currently progressing a diversified portfolio of investigational therapeutic programs organized around its core areas of focus: hematology, immunology and oncology, liver and lung. Across each core area, Prime Medicine is focused initially on a set of high value programs, each targeting a disease with well-understood biology and a clearly defined clinical development and regulatory path, and each expected to provide the foundation for expansion into additional opportunities. Over time, the Company intends to maximize Prime Editing's broad and versatile therapeutic potential, as well as the modularity of the Prime Editing platform, to rapidly and efficiently expand beyond the diseases in its current pipeline, potentially including additional genetic diseases, immunological diseases, cancers, infectious diseases, and targeting genetic risk factors in common diseases, which collectively impact millions of people. For more information, please visit www.primemedicine.com.

From time to time Prime Medicine may use its website, our X, formerly Twitter, account (@PrimeMedicine) or its LinkedIn profile at https://www.linkedin.com/company/prime-medicine to distribute material information. Its financial and other material information is routinely posted to and accessible on the Investors section of its website, available at www.primemedicine.com. Investors are encouraged to review the Investors section of its website because the Company may post material information on that site that is not otherwise disseminated by the Company. Information that is contained in and can be accessed through the Company's website or its social media is not incorporated into, and does not form a part of, this press release.

Forward Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, implied and express statements about Prime Medicine's beliefs and expectations regarding: the continued development and advancement of PM359, including the significance of data from its Phase 1/2 trial of PM359; the planned regulatory interactions with the FDA based on the data from its Phase 1/2 trial of PM359 and the outcomes of any such interactions; the continued development and advancement of its CF, AATD and WD programs, including the anticipated timing of filing an IND and/or CTA application for its WD program in the first half of 2026 and for its AATD program in mid-2026, and initial clinical data for both programs in 2027; the potential of PM359 to address the unmet medical need for patients with CGD; the potential of Prime Editing to correct the causative mutations of, and to cure, diseases, including AATD, WD, CF and CGD; the potential for its modular universal LNP platform to precisely deliver Prime Editors and enable significant efficiencies in pre-clinical development, manufacturing and clinical development; the ability to demonstrate, and the timing of, preclinical proof-of-concept *in vivo* for multiple programs; the further advancement of Prime Editors to maximize their versatility, precision and efficiency; the collaboration with Bristol Myers Squibb and the Cystic Fibrosis Foundation and the intended and potential benefits thereof; the initiation, timing, progress, and results of its research and development programs, preclinical studies and future clinical trials, including the release of data related thereto; the modularity of the Prime Editing platform and the benefits thereof; the potential for Prime Editors to more precisely and effectively achieve genetic modification; the potential for Prime Editors to repair genetic mutations and offer curative genetic therapies for a wide spectrum of diseases; the expansion of Prime Editing's therapeutic potential and the creation of value through strategic business development to extend the reach and impact of Prime Editing to areas beyond Prime Medicine's current pipeline; its expectations regarding the breadth of Prime Editing technology and the implementation of its strategic plans for its business, programs, and technology; the potential of Prime Editing to unlock opportunities across thousands of potential indications; and its expected cash runway. The words "may," "might," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "expect," "estimate," "seek," "predict," "future," "project," "potential," "continue," "target" and similar words or expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks associated with: uncertainties related to Prime Medicine's product candidates entering clinical trials; the authorization, initiation, and conduct of preclinical and IND-enabling studies and other development requirements for potential product candidates, including uncertainties related to opening INDs and obtaining regulatory approvals; risks related to the development and optimization of new technologies, the results of preclinical studies, or clinical studies not being predictive of future results in connection with future studies; the scope of protection Prime Medicine is able to establish and maintain for intellectual property rights covering its Prime Editing technology; Prime Medicine's ability to identify and enter into future license agreements and collaborations; Prime Medicine's expectations regarding the anticipated timeline of its cash runway and future financial performance; and general economic, industry and market conditions. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Prime Medicine's most recent Annual Report on Form 10-K, as well as any subsequent filings with the Securities and Exchange Commission. In

addition, any forward-looking statements represent Prime Medicine's views only as of today and should not be relied upon as representing its views as of any subsequent date. Prime Medicine explicitly disclaims any obligation to update any forward-looking statements subject to any obligations under applicable law. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

Investor and Media Contacts

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Condensed Consolidated Balance Sheet Data
(unaudited)

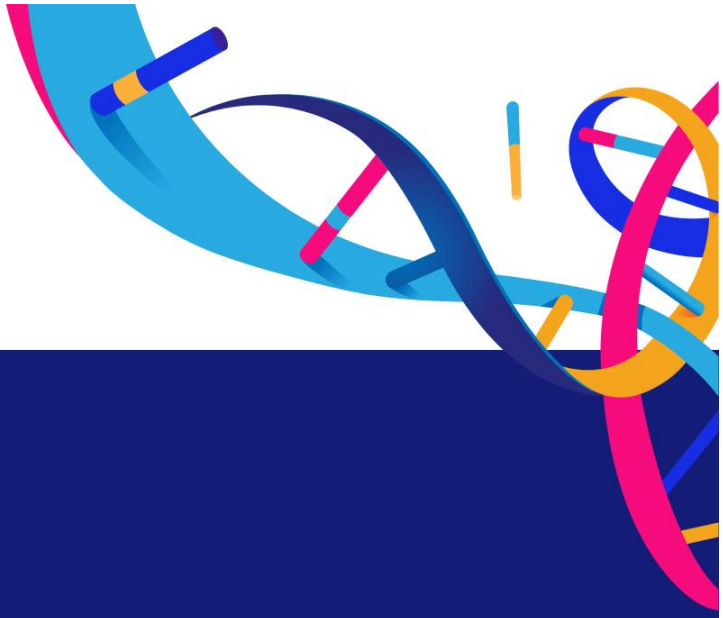
(in thousands)	December 31, 2025	December 31, 2024
Cash, cash equivalents, and investments	$ 177,680	$ 190,442
Total assets	342,733	297,508
Total liabilities	221,865	144,359
Total stockholders' equity	120,868	153,149

Condensed Consolidated Statement of Operations
(unaudited)

(in thousands, except share and per share amounts)	Year Ended December 31, 2025	Year Ended December 31, 2024
Revenue:		
Collaboration revenue — related party	$ 4,586	$ 1,609
Collaboration revenue	46	1,374
Total revenue	4,632	2,983
Operating expenses:		
Research and development	160,636	155,289
General and administrative	52,346	50,161
Total operating expenses	212,982	205,450
Loss from operations	(208,350)	(202,467)
Other income:		
Interest income	4,149	3,522
Accretion (amortization) of investments	2,479	3,507
Change in fair value of short-term investment — related party	432	(485)
Other income, net	148	41
Total other income, net	7,208	6,585
Net loss attributable to common stockholders	$ (201,142)	$ (195,882)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.35)	$ (1.65)
Weighted-average common shares outstanding, basic and diluted	148,758,527	118,600,381

prime medicine

Delivering on the promise of
Prime Editing



Corporate Presentation

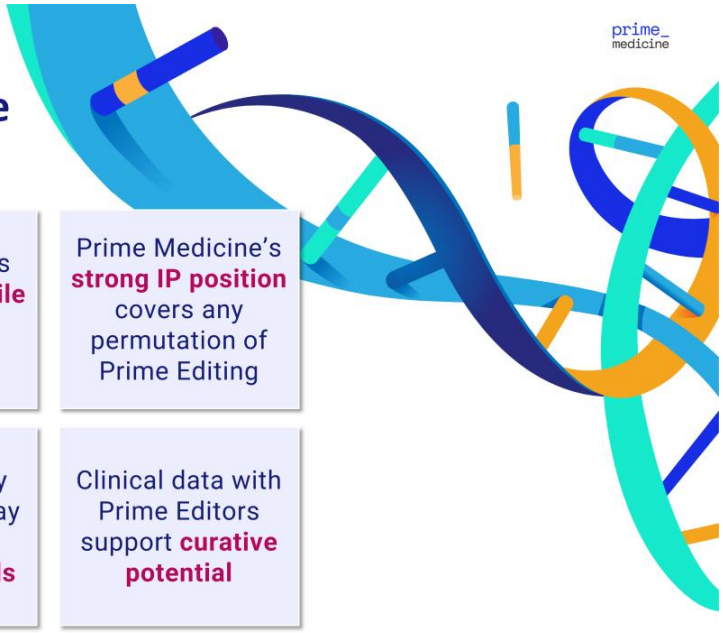
March 2026

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 Prime Editing to correct the causative mutations of diseases, including CGD, Wilson Disease, CF, and AATD; the continued development and advancement of its AATD and Wilson Disease programs, including the timing of the filing of IND and/or CTA applications in mid-2026 and 1H 2026, respectively, and the timing of initial data for both programs in 2027; the initiation, timing, progress and results of our research and development programs, preclinical studies and future clinical trials, including the release of data related thereto; the significance of data from our Phase 1/2 trial of PM359; the regulatory interactions with the FDA based on the data from our Phase 1/2 trial of PM359 and the outcomes of any such interactions; our ability to obtain regulatory approval for PM359; the safety profile of Prime Editing, our modular LNP, and our programs; the timing of, and our ability to achieve, clinical validation and sustained, long-term value creation; the modularity of the Prime Editing platform and the benefits thereof; the 2025 agreement with the Cystic Fibrosis Foundation, its expanded funding pursuant thereto, and the intended and potential benefits thereof; 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; our expectations regarding the breadth of Prime Editing, including the potential of Prime Editing to address more than 90% of genetic diseases and to address non-genetic diseases; the continued development and optimization of various non-viral and viral delivery systems, including our universal liver-targeted LNP delivery approach; the scope of protection we are able to establish and maintain for intellectual property rights covering our Prime Editing technology; the implementation of our strategic plans for our business, programs and technology, including our ability to maintain collaborations or strategic relationships and identify and enter into future license agreements and collaborations; regulatory developments in the United States and foreign countries; developments related to our competitors and our industry; 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.

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 Editing: Emerging as the Predominant Gene Editing Technology



Gene editing **permanently corrects** genetic alterations

Prime Editing is the **most versatile** gene editing technology

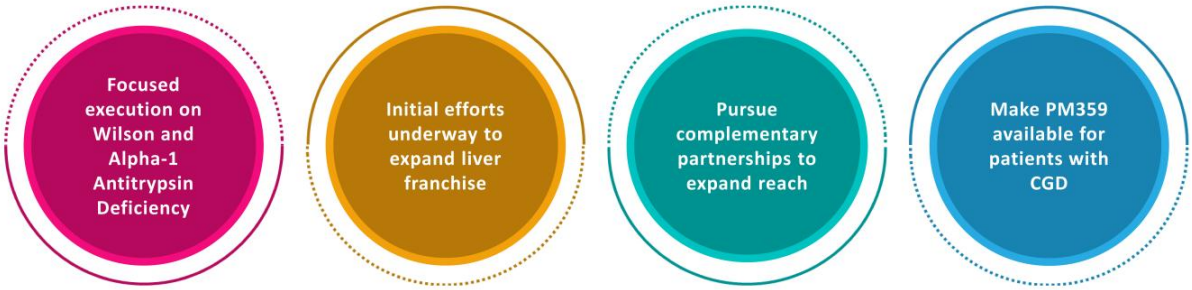
Prime Medicine's **strong IP position** covers any permutation of Prime Editing

Prime Editing **does not cause double-strand breaks or bystander edits**

New regulatory models pave way for **platform-based approvals**

Clinical data with Prime Editors support **curative potential**

Prime Medicine is Strategically Delivering on the Promise of Prime Editing



DISCIPLINED CLINICAL DEVELOPMENT, MAXIMIZE PLATFORM IMPACT AND ENSURE ACCESS TO BREAKTHROUGH THERAPIES

Near-Term, Focused Execution Positions Prime Medicine to Capitalize on the Full Potential of Prime Editing

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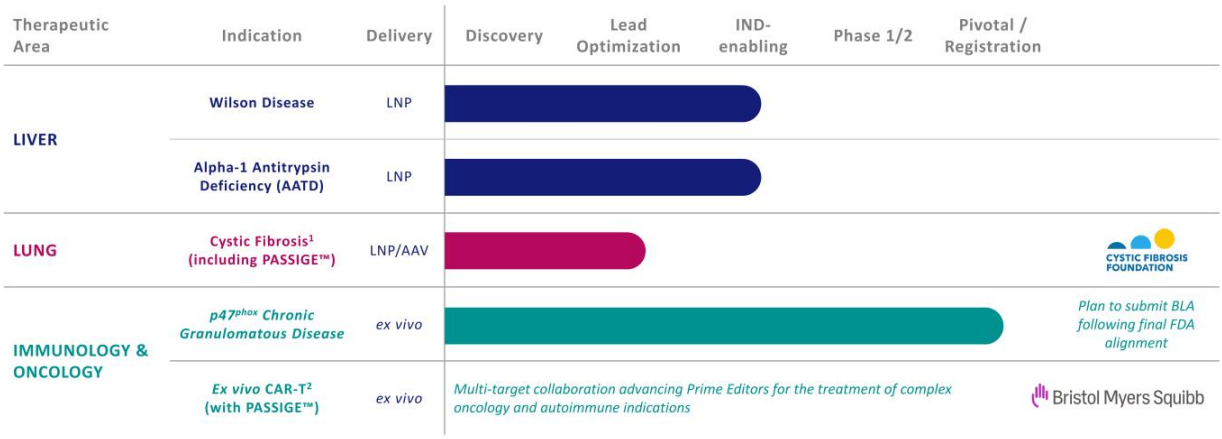
	2026	2027+
WILSON DISEASE	• File PM577 IND and/or CTA in 1H • Initiate Phase 1 clinical trial • Advance follow-on Prime Editors for other common mutations	• Announce PM577 initial clinical data • Capitalize on platform modularity vis-a-vis additional common mutations
AATD	• File PM647 IND and/or CTA mid-year • Initiate Phase 1 clinical trial	• Announce PM647 initial clinical data
OTHER	• Progress towards a BLA filing for CGD • Share *in vivo* proof-of-concept data in CF • Expand pipeline within priority focus areas and beyond	• Initiate IND-enabling studies for CF • Relaunch programs targeting neurological and other large indications

Secure multiple additional strategic partnerships to accelerate our pipeline and bolster our financial resources

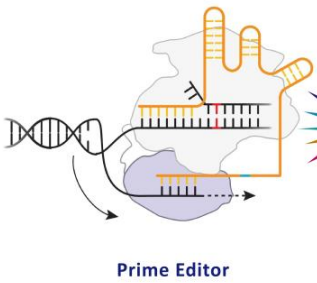
Prime Medicine's Pipeline: Focused on Value Creating Opportunities



Prime Medicine is identifying opportunities to expand the reach of Prime Editing either via organic growth around its liver franchise and / or business development

[1] In January 2024 and July 2025, Prime entered into agreements with the CF Foundation for up to $15 million and $24 million, respectively, to support development of Prime Editors for Cystic Fibrosis.
[2] In September 2024, Prime 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.
LNP = lipid nanoparticle; AAV = adeno-associated virus; CGD = chronic granulomatous disease

We Plan to Leverage the Versatility of Prime Editing to Address a Range of Diseases Across Target Tissues



Prime Editor

INSERTION / DELETION

SUBSTITUTION

REPLACEMENT

LARGE DELETION

LARGE TARGETED INSERTION

Deletion / Insertion Correction
p47 Chronic Granulomatous Disease (CGD)

Point Mutation Correction
Wilson Disease, Alpha-1 Antitrypsin Deficiency

Hotspot Correction
Cystic Fibrosis, Retinitis Pigmentosa (RHO adRP)

Repeat Excision
Repeat expansion diseases

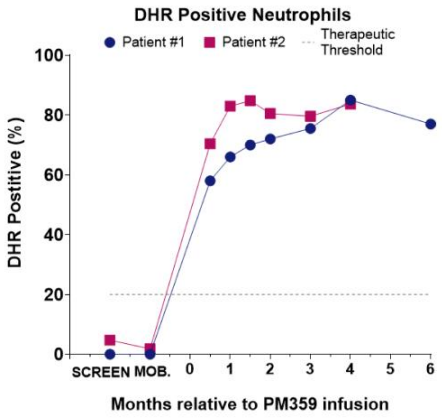
Targeted Full Gene Insertion (PASSIGE™)
CAR-T, Cystic Fibrosis

Prime Editing is designed with a wide range of genome editing capabilities and the ability to make edits of any size, from small base pair swaps to large, multi-kilobase insertions or inversions

Breakthrough Clinical Data with PM359 in CGD Provide Proof-of-Concept for Prime Editing as the Foundation for a New Class of Curative Therapies

prime_ medicine

Observed rapid engraftment, restored DHR positivity and improvement in inflammatory markers, with acceptable safety



- **Successful manufacturing** from single mobilizations
- **Tolerable myeloablative conditioning** at fully therapeutic exposures with expected adverse events (transitory mucositis, pancytopenia)
- **No serious adverse events** attributed to PM359
- **Rapid neutrophil and platelet engraftment** confirmed within 2-3 weeks post transplant, markedly faster than current benchmarks
- **Rapid recovery of NADPH oxidase activity**: ~3-4x therapeutic threshold by day 30, sustained out to six months post infusion
- **Both patients remain free of new CGD-related complications or significant intercurrent illness post-infusion;** patient 2 demonstrated improvement in inflammatory markers of CAC

Prime Medicine plans to submit a BLA following final regulatory alignment

*Source: CASGEVY label, median time to engraftment for neutrophils and platelets observed at days 27 and 35, respectively
Note: patient #1 was an 18 year old male, patient #2 was a 57 year old male
DHR = dihydrorhodamine, an assay to measure NADPH oxidase activity

Prime Medicine Has Not Observed Any Detectable Off-Target Editing, Large Deletions, or Translocations in Any Lead Program

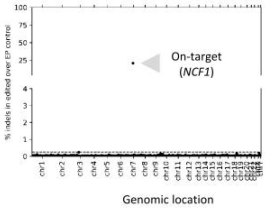
Prime Medicine uses CRISPR-Cas9 editors as a positive control in off-target analyses

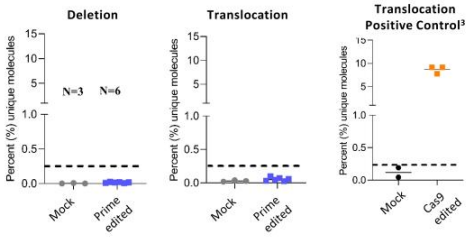
Examples from CGD program used to support IND/CTA filings

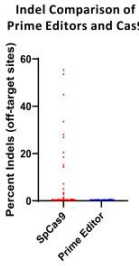
No off-target editing detected in healthy human donor CD34+ cells[1]

No large deletions or translocations observed in Prime-Edited LT-HSCs[2] vs. Cas-9 nuclease edited cells

No off-target edits detected with Prime Editing vs. Cas9



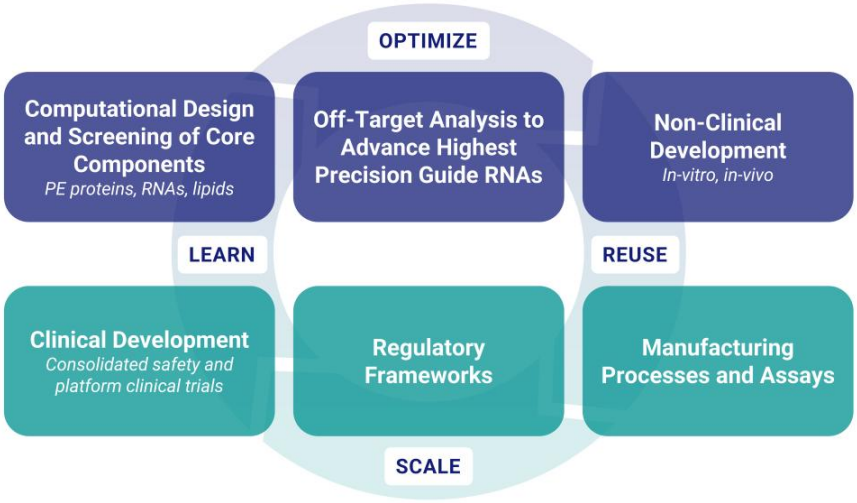




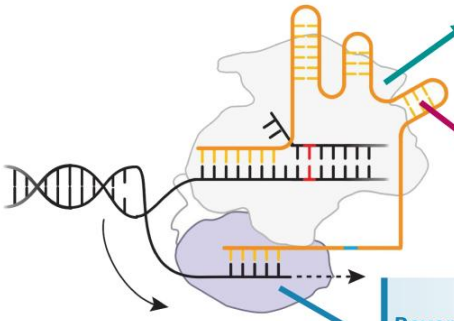
- **No** detectable double strand breakage
- **No** detectable off-target edits
- **No** detectable bystander edits
- **No** detectable deletions, chromosomal translocations or rearrangements

[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]Cas9 nuclease-edited cells, generated by transfecting HEK293T with sgRNA targeting *NCF1* and SpCas9 mRNA.
CGD = chronic granulomatous disease; HSC = hematopoietic stem cell; IND = investigational new drug; CTA = clinical trial application

Modular Prime Editing Platform Flywheel Effect: Industrialized Engine is Reused Across Programs



Prime Medicine Holds Extensive, Foundational Intellectual Property for Prime Editing Technologies



CRISPR-Cas Enzyme
Any programmable nuclease to specifically identify and cut DNA sequences

Guide RNA
Engineered RNAs that locate the exact editing site and provide the template for transcription

Reverse Transcriptase
Converts RNA into complementary DNA

Any combination or permutation of a **CRISPR-Cas enzyme**, template **Guide RNA** with a **Reverse Transcriptase** is **Prime Editing** and is covered by our extensive patent estate

Prime Medicine holds 7 U.S. and 14 ex-U.S. issued patents in an extensive patent estate that protects its breakthrough Prime Editing platform, delivery technologies and therapeutics

Liver

Prime Medicine's Initial Liver Franchise: Aspiring to Cure Two of the Largest Genetic Liver Diseases, Enabled by Platform Modularity

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PM577: Wilson Disease

Opportunity (Patients)

>20,000	US and EU
7,500-15,000+	Japan

IND and/or CTA 1H 2026; data 2027

Initial focus on H1069Q mutation

PM647: AATD

Opportunity (Patients)

200,000	US and EU
20,000-30,000	Diagnosed

IND and/or CTA mid-2026; data 2027

Plan to leverage key learnings, regulatory frameworks and manufacturing synergies from PM577 to accelerate efforts and reduce costs for other Wilson Disease mutations, AATD and future follow-on liver programs

WD = Wilson Disease; AATD = Alpha-1 Antitrypsin Deficiency; IND = investigational new drug; CTA = clinical trial application

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

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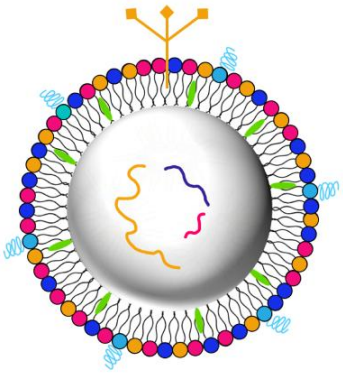
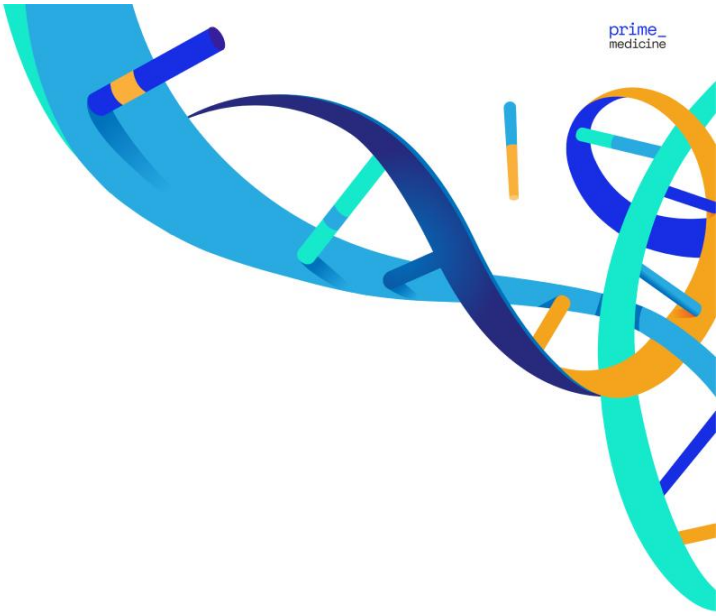
LNP Modularity:

Majority of components in the LNP are the same across 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 and mutation specific
ngRNA	ngRNA is disease and mutation specific; usage is dependent on the Prime Editing strategy applied

Wilson Disease



Advancing Prime Editors for Wilson Disease: Disease Overview

Large genetically defined disease well suited for Prime Editing

Disease Severity and Opportunity

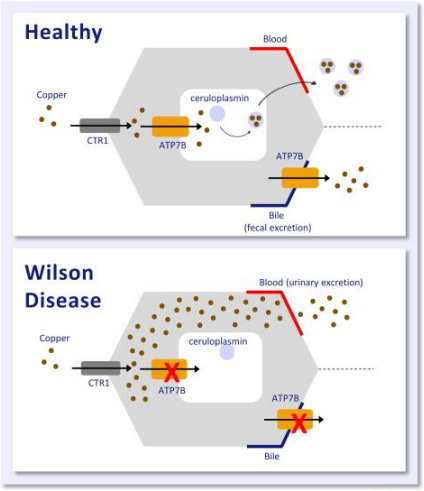
- Common liver and systemic disease presenting in teens to 20s
- Leads to liver failure, neurocognitive decline and premature death
- Greater than 20,000 patients in US and Europe, 30-50% harboring H1069Q mutation
- 7,500 – 15,000+ patients in Japan, R778L is the predominant mutation in the Asian population

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

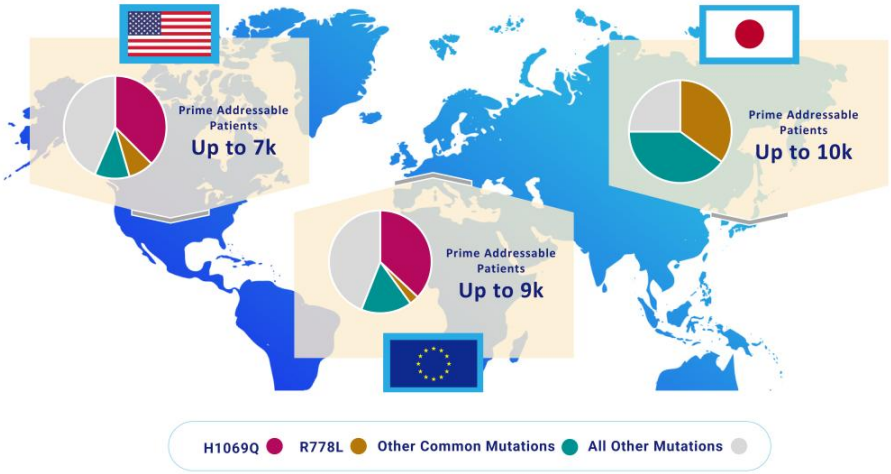
Human Biology

- Autosomal recessive due to loss of function mutations in ATP7B
- Affects copper homeostasis, leading to toxic accumulation of copper in liver and brain



Prime Medicine's Wilson Disease Programs Have Potential to Address Multi-Billion Dollar Market

- **Six most common mutations account for up to 26,000 patients** in addressable markets (US, Europe, Japan) with unique geographic mutational distribution; incidence rate of approximately 300 new patients per year
- **Consistency in disease presentation and management** across mutations and key markets enables Prime Medicine to establish an anchor with PM577 (H1069Q) to provide leverage and read-through to other mutations



Prime Editors Efficiently and Precisely Corrected the Two Most Prevalent Disease-Causing Mutations in Wilson Disease

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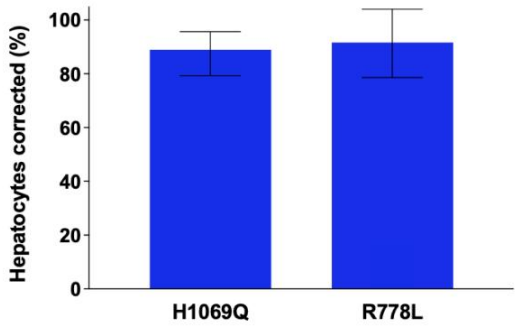
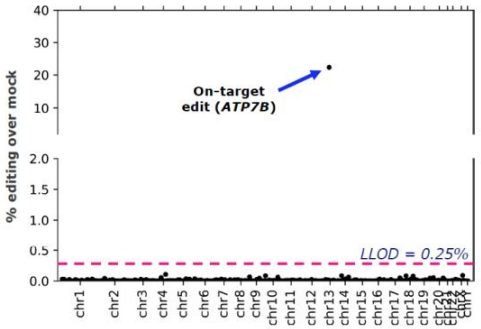
Efficient correction of the H1069Q and R778L mutations in fully humanized mouse models



No detectable off-target editing identified in patient-derived cells for PM577



Prime Editors delivered with Prime Medicine's universal liver LNP administered at clinically relevant doses

LNP = lipid nanoparticle

PM577 Efficiently Corrects the H1069Q Mutation and Completely Restores Wild-Type Copper Concentration *In Vivo*

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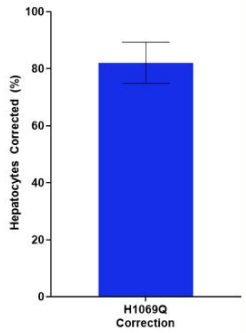
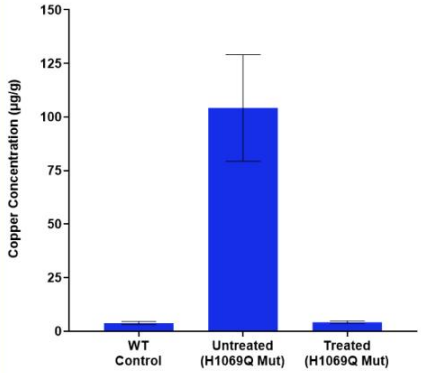
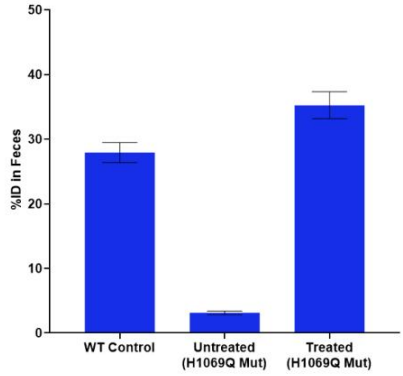
>80% hepatocytes edited



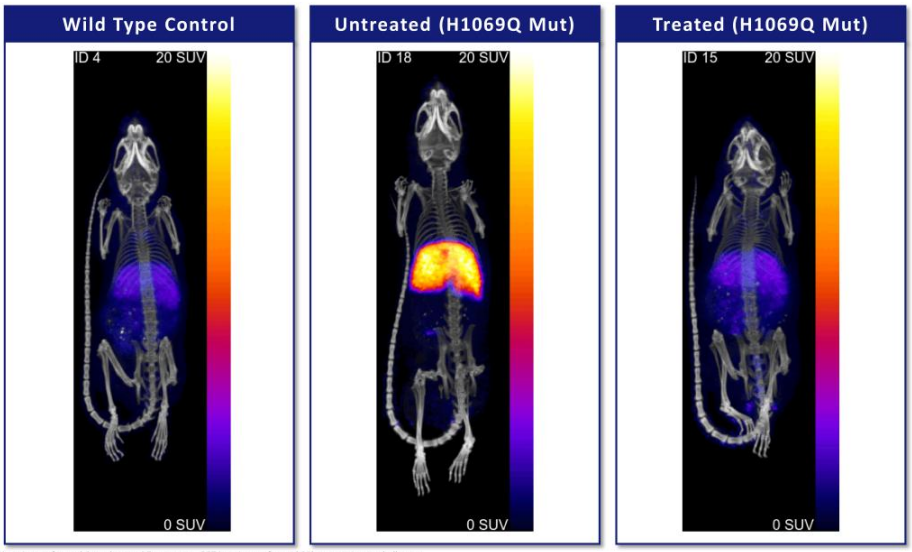
Hepatic copper concentration returns to wild-type levels at eight weeks



Copper excreted normally through the feces at four weeks



Prime Edited Mice Challenged with Radiolabeled Copper Demonstrated Normal Copper Clearance



*Copper challenge and PET imaging performed 4 weeks post PE treatment, PET imaging performed 24hrs post copper challenge

PM577 Clinical Development: On Track for H1'26 IND and/or CTA with Proof-of-Concept Data Anticipated in 2027

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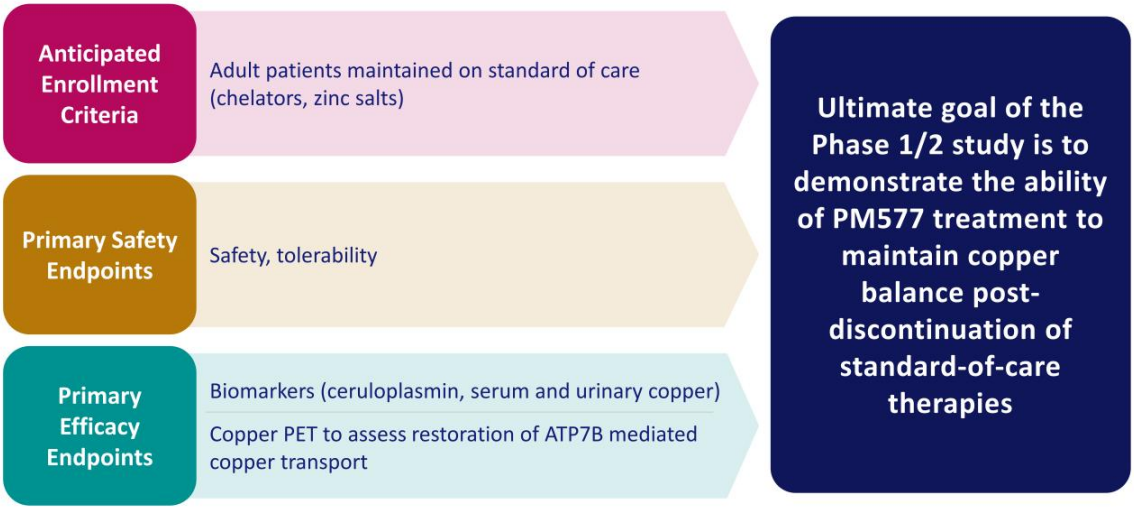

IND = investigational new drug; CTA = clinical trial application

We Plan to Leverage Platform Modularity to Rapidly Advance Prime Editors for a Majority of Wilson Disease Patients

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H1069Q (PM577)

ANCHOR MUTATION:

Large commercial opportunity in U.S. and Europe

- 1H 2026 IND/CTA
- Lead in observational study to potentially expedite patient recruitment

Follow-on programs to leverage same liver-targeted LNP; swap out guide sequence

R778L

Large commercial opportunity in Japan

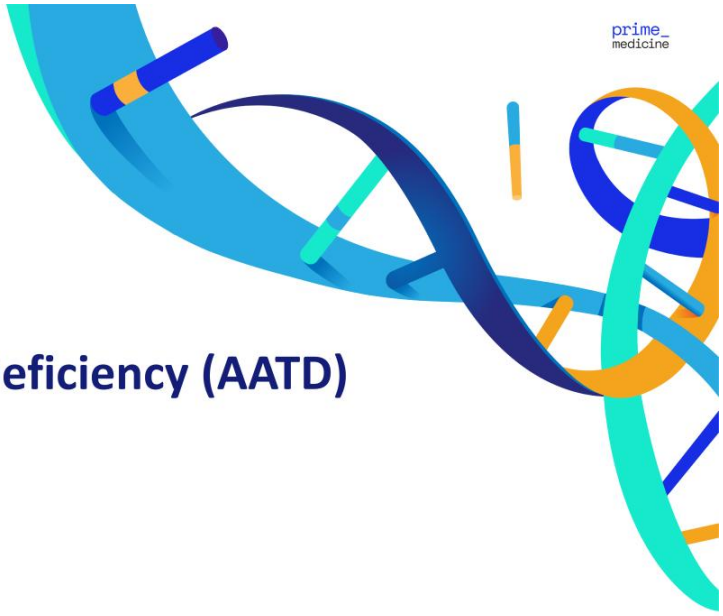
- >90% editing efficiency, minimal preclinical work to formalize DC
- Goal to incorporate into existing regulatory filings; engage PMDA

Other Mutations

Attractive business case to develop follow-on programs

- Fast path to DC (potentially off in vitro data)
- Goal to incorporate into existing regulatory filings

IND = investigational new drug; CTA = clinical trial application; LNP = lipid nanoparticle; DC = development candidate; PMDA = Japan's Pharmaceuticals and Medical Devices Agency



Alpha-1 Antitrypsin Deficiency (AATD)

Advancing Prime Editors for AATD: Disease Overview

Disease Severity and Opportunity

- AATD is an inherited genetic disorder that causes low levels of AAT protein
- Low levels of AAT protein increases the risk of lung disease (emphysema)
- Patients are also at risk of liver disease (cirrhosis) caused by mutant protein aggregation
- Approximately 200,000 patients in the US and EU, ~10-15% of which are diagnosed today

Unmet Need

- Many patients progress to liver failure or severe lung disease, requiring transplant
- Current standard of care includes chronic AAT augmentation therapy for lung disease; no approved curative therapies
- No approved treatments for liver disease

Human Biology

- Autosomal codominant disorder due to mutations in SERPINA1 gene
- Lung: lack of functional AAT leads to unrestricted neutrophil elastase activity, among other pathological changes (loss of function)
- Liver: defective AAT protein misfolding and accumulation (gain of function)
- 20-30% correction in hepatocytes could be curative

We believe Prime Editing is uniquely well-suited to correct mutant AAT protein to wild-type without the risk of bystander edits

AATD = Alpha-1 Antitrypsin Deficiency; A1AT = alpha-1 antitrypsin

AATD Program Objective: Normalize AAT Levels in PiZZ Genotype Patients to Healthy Human Levels

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Program Goals

- Restore SERPINA1 gene to wild type, without bystander or other unwanted edits
- Increase M-AAT levels minimally above protective threshold (~11 µM), ideally into healthy human range (>20 µM)
- Maintain wild-type protein under endogenous control to protect patients during acute episodes (M-AAT levels rise 2-4x)
- Decreasing Z-AAT in the liver may potentially ameliorate the liver manifestations of AATD

*Taken from Vidal R, Blanco I, Casas F, *et al*. Arch Bronconeumol. 2006;42(12):645-59; ** MZ, SZ and ZZ genotype contain Pi*Z mutation; Z-AAT = mutant A1AT protein.

PM647 Efficiently Corrected the Mutation *In Vivo* Resulting in M-AAT Protein Restoration at Clinically Relevant Doses

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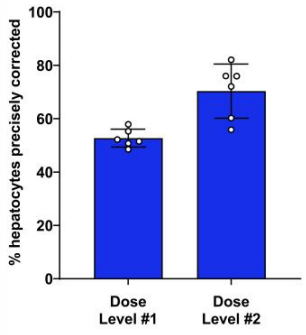
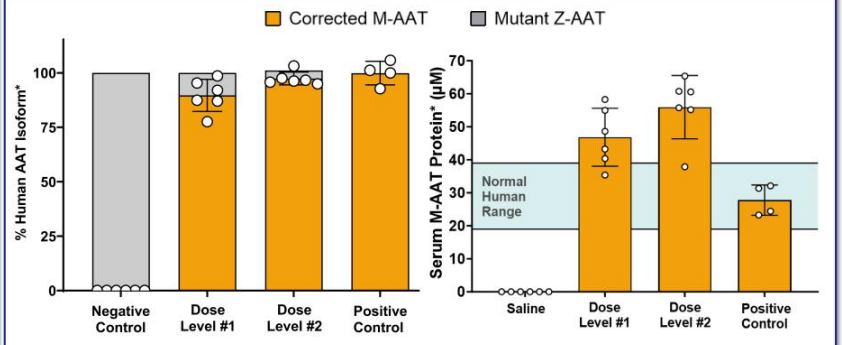
Efficient correction



Restoration M-AAT Protein**



Prime has initiated IND-enabling activities and is on track for mid'26 IND and/or CTA application(s)

M-AAT = healthy A1AT protein; Z-AAT = mutant A1AT protein; IND = investigational new drug; CTA = clinical trial application
*Performed by LC-MS; **Analysis at day 7 positive control = healthy human serum

PM647 Clinical Development: On Track for Mid'26 IND and/or CTA with Proof-of-Concept Data Anticipated in 2027

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Anticipated Enrollment Criteria	Group A: adult patients with pulmonary only disease Group B: adult patients with liver disease with or without pulmonary disease
Primary Safety Endpoints	Safety, tolerability
Primary Efficacy Endpoints	Group A: Measurement of serum AAT levels Group B: Measurement of Z-AAT in liver

Ultimate goal of the Phase 1/2 study is to demonstrate the ability of PM647 treatment to restore wild type (M-AAT) protein levels and potentially ameliorate liver disease

IND = investigational new drug; CTA = clinical trial application

Lung

Advancing Prime Editors for Cystic Fibrosis (CF), a Disease for Which There is No Curative Therapy

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Prime Medicine's efforts in Cystic Fibrosis funded through multiple grants from the Cystic Fibrosis Foundation

Disease Severity and Opportunity

- Progressive, genetic disease that affects the lungs, pancreas and other organs, leading to premature death
- Impacts close to 40,000 people in the United States, ~1,000 new cases diagnosed each year

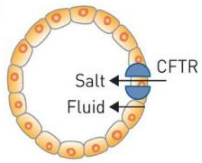
Unmet Need

- Existing treatment options include airway clearance, inhaled medicines, pancreatic enzyme supplements, fitness plans and CFTR modulators for patients with specific mutations
- No cure and existing treatments are ineffective for, or not tolerated by, approximately 15% of patients

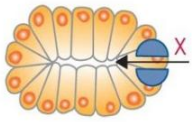
Human Biology

- Autosomal recessive disorder caused by mutations in the CFTR gene, which cause CFTR protein to become dysfunctional
- Dysfunctional CFTR reduces chloride and bicarbonate transport to epithelial lumen

Healthy



Cystic Fibrosis



We believe Prime Editing-based approaches could eventually benefit more than 93% of all people with CF

CFTR = cystic fibrosis transmembrane conductance regulator

Prime Medicine has Made Significant Progress Developing Prime Editors for G542X Mutated Cystic Fibrosis

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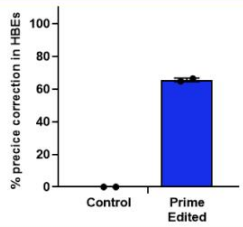
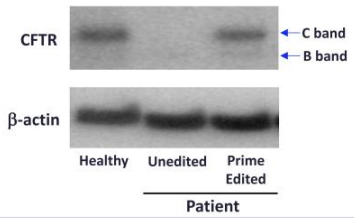
G542X In vitro Prime Editor in Primary HBEs



Phenotypic restoration of G542X mutated CFTR in differentiated ALI culture



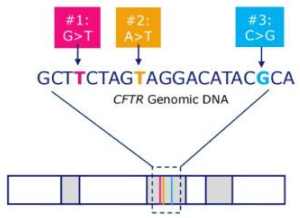
Efforts towards LNP and AAV *in vivo* delivery to humanized mice and large animals ongoing

- We believe primary human lung progenitor data is most predictive of *in vivo* efficacy
- Comprehensive suite of assays in development to enable selection of development candidate and advance to IND enabling studies
- Humanized mouse colonies, ferret and NHP colony established for *in vivo* optimization
- Prime's targeted modular lung LNP as well as alternative delivery system are being applied to accelerate CF hotspot editing *in vivo*

Parallel Prime Editing Approaches to CF: Hotspot and PASSIGE

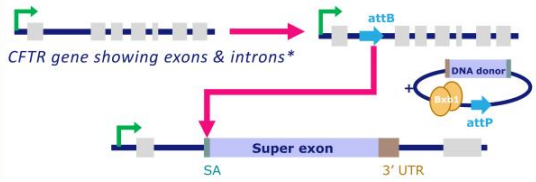
Hotspot

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



PASSIGE

Potential to address nearly all CF patients with a single super exon insertion strategy



Restoring CFTR function in Prime Edited cells under endogenous control

CF = cystic fibrosis; attP = complimentary recognition sequence for attB; SA = splice acceptor; 3' UTR = 3' untranslated region; *Exons in gray introns in black

Immunology and Oncology

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 Editors for the treatment of complex oncology and autoimmune indications

prime medicine	**Leadership in Prime Editing; PASSIGE technology may enable one-step, non-viral, multi-kilobase-size editing approach with no double-stranded breaks**
Bristol Myers Squibb	**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 the genetic diseases in Prime Medicine's internal pipeline

Prime Medicine retains the ability to advance reagents designed under this collaboration in certain *ex vivo* (non-BMS targets) and all *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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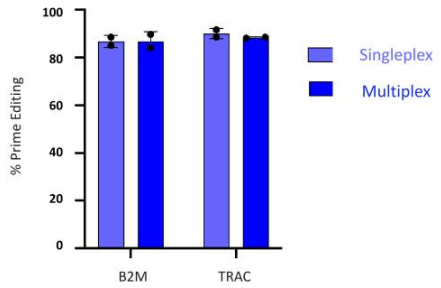
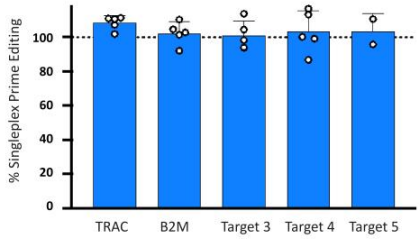
Prime Editors can be multiplexed to introduce multiple genomic modifications in CAR-T cells

High efficiency multiplex editing of B2M and TRAC



Maintained efficiency with five multiplex edits



Corporate

Our Strategy to Maximize the Broad Therapeutic Potential of Prime Editing

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Within Our Core

Partner at the right time to fund, advance and commercialize our wholly owned pipeline programs (e.g., liver, lung)

CYSTIC FIBROSIS FOUNDATION

Funding accelerates the development of Prime Editors for Cystic Fibrosis

Outside Our Core

Form strategic partnerships to access expertise and expand into therapeutic areas beyond our near-term internal focus (e.g., cell therapy, CNS)

Bristol Myers Squibb

Developing Prime Edited CAR-T products leveraging PASSIGE and platform

Enabling Innovation

Access best-in-class enabling technologies to unlock the full potential of Prime Editing (e.g., delivery technologies)

By pairing our internal resources with strategic partners and best-in-class enabling technologies, we aim to accelerate platform development and extend the reach of Prime Editing

Prime Medicine is Leading the Next Generation of Gene Editing

Preeminent Editing Technology

- Permanently corrects genetic alterations, without causing double-strand breaks or bystander edits
- Potential to address approximately 90% of genetic diseases and opportunities in non-genetic diseases
- Prime Medicine's comprehensive IP portfolio covers any permutation of Prime Editing

Platform Modularity Oriented for Growth

- Fully integrated modular platform powers every program and drives leverage
- Proprietary modular delivery systems accelerate follow-on programs within target tissues
- New regulatory models pave way for platform-based approvals

Pipeline Positioned for Value Creation

- Breakthrough data in CGD provides proof-of-concept for curative potential of Prime Editing
- PM577 in Wilson Disease IND and/or CTA expected in H1'26; AATD IND and/or CTA expected in mid-2026
- Focused on programs in large genetic diseases, with clear path to value and multi billion-dollar opportunities

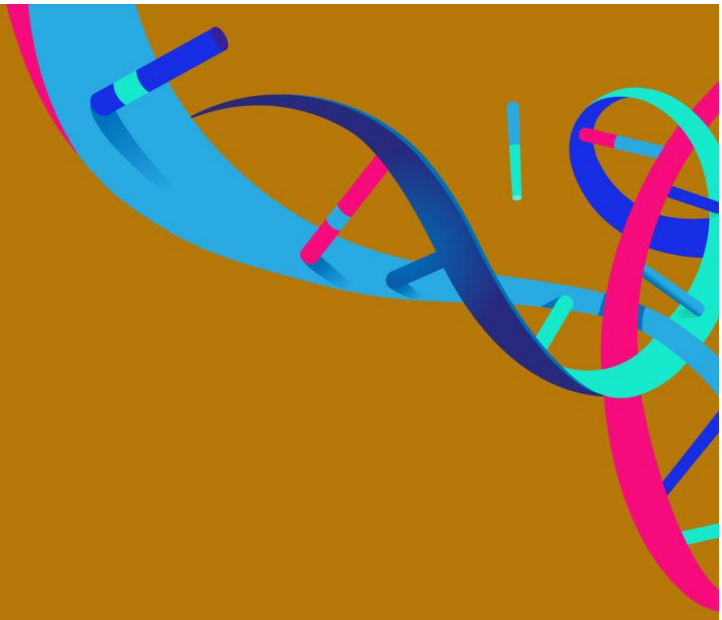
Significant Partnerships and BD Potential

- 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 $191.4M for 12/31/2025, cash runway into 2027

AATD = Alpha-1 Antitrypsin Deficiency; IND = investigational new drug; CTA = clinical trial application

Appendix



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

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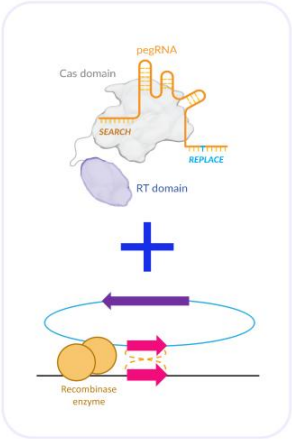
PASSIGE: Prime-Assisted Site-Specific Integrase Gene Editing:
One step non-viral multi-kilobase-size gene editing approach with no double-stranded breaks



Where we are working today:

- **Non-viral, multiplex-edited CAR-T therapies**
  BMS collaboration (e.g., oncology and autoimmune diseases)
- **Cystic Fibrosis**

Areas of opportunity:*

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

*Not part of Prime Medicine's current pipeline