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

September 28, 2024
Date of Report (Date of earliest event reported)

Prime Medicine, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-41536**	**84-3097762**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**
60 First Street **Cambridge, MA**		**02141**
(Address of principal executive offices)		**(Zip Code)**

(617) 564-0013

(Registrant's telephone number, including area code)

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

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

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

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

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

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

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

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

Emerging growth company ☒

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

Item 1.01 Entry into a Material Definitive Agreement.

On September 28, 2024 (the "Effective Date"), Prime Medicine, Inc. (the "Company") entered into a Research Collaboration and License Agreement (the "Collaboration Agreement") with Juno Therapeutics, Inc., a wholly-owned subsidiary of the Bristol-Myers Squibb Company ("BMS"). Under the terms of the Collaboration Agreement, the Company granted to BMS an exclusive worldwide license to certain Prime Editing technology for developing, manufacturing and commercializing ex vivo T-cell therapeutic products directed to select targets. Additionally, on the Effective Date, the Company entered into a Securities Purchase Agreement (the "Purchase Agreement") with BMS, pursuant which the Company agreed to sell and issue shares of its common stock to BMS.

Research Collaboration and License Agreement

Pursuant to the Collaboration Agreement, the Company will design Prime Editing reagents to be used by BMS to develop, manufacture and commercialize ex vivo T-cell therapeutic products directed to specific targets selected by BMS.

Under the Collaboration Agreement, the Company will receive a $55.0 million upfront payment and a $55.0 million equity investment from BMS (as described below). The Company is also eligible to receive more than $3.5 billion in milestones, including up to $185 million in preclinical milestones, up to $1.2 billion in development milestones and more than $2.1 billion in commercialization milestones, along with royalties on net sales.

Unless earlier terminated, the term of the Collaboration Agreement continues until expiration of the last royalty term for the applicable product in the applicable country. The Collaboration Agreement is subject to customary termination provisions, including termination by a party for the other party's uncured, material breach.

The Collaboration Agreement also includes customary representations and warranties, covenants and indemnification obligations.

The foregoing summary of the terms of the Collaboration Agreement is qualified in its entirety by reference to the full text of the Collaboration Agreement, a copy of which the Company intends to file as an exhibit to its Quarterly Report on Form 10-Q for the quarter ended September 30, 2024.

Stock Purchase Agreement

On the Effective Date, the Company entered into the Purchase Agreement with BMS, pursuant to which the Company agreed to issue and sell, and BMS agreed to purchase, in an unregistered offering (the "Offering"), 11,006,163 shares (the "Shares") of the Company's common stock, par value $0.0001 per share (the "Common Stock") for an aggregate purchase price of $55.0 million pursuant to the terms and conditions thereof. The closing of the Offering (the "Closing") is expected to occur on September 30, 2024.

The Purchase Agreement includes lock-up restrictions with respect to the Shares. Pursuant to the terms of the Purchase Agreement, BMS has agreed not to, directly or indirectly, sell or transfer any of the Shares until September 30, 2027 subject to specified conditions and exceptions. In addition, the Company agreed, among other things, to file with the Securities and Exchange Commission a registration statement covering the resale of the Shares and to use commercially reasonable efforts to cause such registration statement to become effective on or prior to ninety (90) calendar days after the Closing.

The foregoing summary of the terms of the Purchase Agreement is qualified in its entirety by reference to the full text of the Purchase Agreement, a copy of which the Company intends to file as an exhibit to its Quarterly Report on Form 10-Q for the quarter ended September 30, 2024.

Amendment No. 4 to The Broad Institute License Agreement

In connection with the Collaboration Agreement, the Company entered into a Letter Agreement (the "Amendment") with The Broad Institute, Inc. ("Broad") on September 27, 2024, which amends that certain License Agreement by and between the Company and Broad, dated as of September 26, 2019 (as amended, the "Broad-Prime License Agreement"), to modify certain obligations of Company and rights of Broad in relation to the Collaboration Agreement as a sublicense under the Broad-Prime License Agreement. The Amendment, among other things, modifies the royalty and certain commercial milestones that the Company is obligated to pay to Broad on net sales of products under the Collaboration Agreement. Except as expressly stated in the Amendment, all other terms and provisions of the Broad-Prime License Agreement shall remain in full force and effect.

The foregoing summary of the Amendment is qualified in its entirety by reference to the full text of the Amendment, a copy of which the Company intends to file as an exhibit to its Quarterly Report on Form 10-Q for the quarter ended September 30, 2024. A summary of the terms of the Broad-Prime License Agreement is set forth in the Company's Annual Report in Form 10-K for the year ended December 31, 2023, which was filed with the Securities and Exchange Commission on March 1, 2024.

Item 3.02 Unregistered Sales of Equity Securities.

The information set forth above in Item 1.01 under the caption "Securities Purchase Agreement" is incorporated herein by reference. The Company expects the Shares to be issued in reliance on the exemption from registration under Section 4(a)(2) of the Securities Act of 1933, as amended (the "Securities Act") and Regulation D under the Securities Act, and corresponding provisions of state securities or "blue sky" laws. The Company is relying on this exemption from registration for private placements based in part on the representations made by BMS, including that it is acquiring the Shares for the purpose of investment and not with a view to the resale or distribution of any part thereof in violation of the Securities Act, and an appropriate legend will be applied to the Shares. The Shares have not been registered under the Securities Act or any state securities laws and may not be offered or sold in the United States absent registration, or an applicable exemption from registration, under the Securities Act and any applicable state securities laws.

Item 7.01 Regulation FD Disclosure.

On September 30, 2024, the Company issued press releases entitled "Prime Medicine Announces Strategic Research Collaboration and License Agreement with Bristol Myers Squibb to Develop and Commercialize Multiple Prime Edited Ex Vivo T-Cell Therapies" and "Prime Medicine Unveils Strategically Focused Pipeline." A copy of each press release is furnished as Exhibit 99.1 and Exhibit 99.2, respectively, to this Current Report on Form 8-K, which is incorporated herein by reference.

A copy of the Company's September 2024 corporate presentation is furnished as Exhibit 99.3 to this Current Report on Form 8-K, which is incorporated herein by reference.

The information in this Item 7.01, including Exhibit 99.1, Exhibit 99.2 and Exhibit 99.3 attached hereto, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act, 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 September 30, 2024, furnished herewith.
99.2	Press Release, dated September 30, 2024, furnished herewith.
99.3	Presentation, dated September 2024, furnished herewith.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

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

Date: September 30, 2024

Prime Medicine, Inc.

By: /s/ Keith Gottesdiener

Name: Keith Gottesdiener, M.D.

Title: President and Chief Executive Officer

Prime Medicine Announces Strategic Research Collaboration and License Agreement with Bristol Myers Squibb to Develop and Commercialize Multiple Prime Edited Ex Vivo T-Cell Therapies

Collaboration Combines Prime Medicine's Precise, Multiplex Gene Editing Capabilities with Bristol Myers Squibb's Broad Expertise in Development and Commercialization of Novel Cell Therapies

Prime Medicine to Receive $110 Million Upfront, with Potential for More Than $3.5 Billion in Milestones, Including $1.4 Billion in Development Milestones and More Than $2.1 Billion in Commercialization Milestones

CAMBRIDGE, Mass., Sept. 30, 2024 – Prime Medicine, Inc. (Nasdaq: PRME) today announced a strategic research collaboration and license agreement with Bristol Myers Squibb (NYSE: BMY) to develop reagents for the next generation of *ex vivo* T-cell therapies. Under the terms of the agreement, Prime Medicine will design optimized Prime Editor reagents for a select number of targets, including reagents that use its Prime Assisted Site-Specific Integrase Gene Editing (PASSIGE™) technology. Bristol Myers Squibb will be responsible for development, manufacturing and commercialization of the next generation cell therapies, with support from Prime Medicine in gene editing strategy and reagent development.

"We are excited to collaborate with Bristol Myers Squibb, a global leader in cell therapy for hematology, immunology, and oncology. Through this effort, we will apply our Prime Editing technology beyond the rare genetic diseases in our internal pipeline, potentially unlocking opportunities in areas of high unmet needs in immunological diseases and cancer," said Keith Gottesdiener, M.D., President and Chief Executive Officer of Prime Medicine. "We are particularly excited that efforts under this collaboration will leverage our PASSIGE technology, that we believe will advance our one-step, non-viral, multi-kilobase-size gene editing approach into the clinic. There is tremendous opportunity for PASSIGE and Prime Editing to revolutionize the field of cell therapy, and we look forward to expanding our reach over time through both internal and partnered efforts."

Prime Medicine's PASSIGE technology combines Prime Editing with an integrase or other site-specific recombinase to introduce large gene-sized cargo into the genome for stable cargo expression. PASSIGE is delivered through an entirely non-viral manufacturing process without introducing double-stranded DNA breaks or off-target edits and may enable more precise and effective genetic modification.

"We are excited to enter this agreement with Prime Medicine as we continue to explore and invest in next generation approaches, including gene editing technologies, that may help unlock the full potential of cell therapy," said Teri Foy, Senior Vice President of Cancer Immunology and Cell Therapy Therapeutic Research Center at Bristol Myers Squibb. "Integrating Prime Medicine's technologies with our internal capabilities has the potential to open new avenues for innovation and we look forward to collaborating with them as we continue to bring the promise of cell therapy to immunology and oncology."

Under the terms of the agreement, Prime Medicine will receive a $55 million upfront payment and a $55 million equity investment from Bristol Myers Squibb. Prime Medicine is also eligible to receive more than $3.5 billion in milestones, including up to $1.4 billion in development milestones and more than $2.1 billion in commercialization milestones, along with royalties on net sales.

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 our 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.

Prime Medicine 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 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 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 potential of Prime Editors to reproducibly correct disease-causing genetic mutations across different tissues, organs and cell types, and the capacity of its Prime Editing and PASSIGE technology to edit CAR-T cells for the treatment of certain cancers and immune diseases; its ability to demonstrate superior off-target profiles for Prime Editing programs; its expectations regarding the breadth of Prime Editing technology and the implementation of its strategic plans for its business, programs, and technology; and the potential of Prime Editing to unlock opportunities across thousands of potential indications. 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: the development and optimization of new technologies; 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; the effect of unfavorable macroeconomic conditions or market volatility resulting from general economic, industry and market conditions, including rising interest rates, inflation, and adverse developments affecting the financial services industry; and Prime Medicine's accumulated deficit and the expectation for continued operating losses and negative operating cash flows for the foreseeable future, including its expectations regarding the anticipated timeline of its cash runway and future financial performance. 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 and Quarterly Report on Form 10-Q for the quarter ended June 30, 2024, 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.

Prime Medicine Contacts:

Investor Contact
Hannah Deresiewicz
Precision AQ
212-362-1200
hannah.deresiewicz@precisionaq.com

Media Contact
Dan Budwick, 1AB
dan@1ABmedia.com

Prime Medicine Unveils Strategically Focused Pipeline

-- Prioritizing Set of High Value Programs in Core Areas of Focus; Modularity of Prime Editing Platform Expected to Allow Prime Medicine to Generate Follow-on Candidates Rapidly and Efficiently --

-- Initial Clinical Data from Phase 1/2 Trial in CGD Expected in 2025 While Advancing Wilson's Disease Program Toward Expected IND Application and/or CTA in 1H 2026 --

-- Today Announced Strategic Research Collaboration and License Agreement with Bristol Myers Squibb to Develop and Commercialize Multiple Prime Edited ex vivo T-cell Therapies --

-- Together with $110 Million Upfront Consideration Received Under Agreement with Bristol Myers Squibb, Anticipated Cost Savings are Expected to Extend Cash Runway into the First Half of 2026 --

Cambridge, Mass., Sept. 30, 2024 – Prime Medicine, Inc. (Nasdaq: PRME), a biotechnology company committed to delivering a new class of differentiated one-time curative genetic therapies, today announced that it is focusing its pipeline 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.

"We founded Prime Medicine with a singular vision: to apply our groundbreaking Prime Editing platform to address the genetic causes of debilitating diseases and provide patients with long-lasting cures," said Keith Gottesdiener, M.D., President and Chief Executive Officer of Prime Medicine. "Over the past four years, we have started to translate this vision into reality, advancing PM359 into the clinic and generating preclinical data that show we can reproducibly and durably correct disease causative mutations in multiple cell types and successfully deliver Prime Editors across target tissues. In addition, we are encouraged by recent commentary from the U.S. Food and Drug Administration, which is increasingly supportive of modular approaches to developing genetic therapies, for which we believe Prime Editing is uniquely suited. We believe that Prime Medicine has the potential to change the treatment paradigm for a wide range of diseases, which collectively impact millions of people."

Dr. Gottesdiener continued, "In order to maximize Prime Editing's reach, we believe now is the time to strategically focus our efforts on a set of high value programs. Importantly, each prioritized program is intended to serve as a beachhead, allowing us to advance our technological leadership across a number of target tissues and cell types, while providing insights into research and development, regulatory strategy, CMC and delivery that will potentially allow us to progress our follow-on programs more rapidly and efficiently. In parallel, we plan to continue to leverage strategic business development, such as the collaboration with Bristol Myers Squibb that we announced this morning, to further extend Prime Editing's reach. We expect to share first-in-human clinical data from our Phase 1/2 trial in CGD in 2025 and new preclinical data for our Wilson's Disease program in the fourth quarter of 2024, as we work to bring this paradigm-shifting technology to patients."

Prime Medicine's Focused Pipeline

Hematology, Immunology & Oncology

Prime Medicine will focus on the development of two programs for the treatment of chronic granulomatous disease (CGD), which together have the potential to address the vast majority of people living with CGD:

- **PM359, an *ex vivo* autologous hematopoietic stem cell (HSC) product for the treatment of p47^{phox} CGD.** Approximately one quarter of patients with CGD present with a mutation in p47^{phox}. In April 2024, the U.S. Food and Drug Administration (FDA) cleared Prime Medicine's investigational new drug (IND) application for PM359, less than one month after the IND filing. The Company has initiated a Phase 1/2 clinical trial to assess the safety, biological activity and preliminary efficacy of PM359 in adult and pediatric patients and continues to

expect initial clinical data from the study in 2025. Once proof-of-concept is established, Prime Medicine expects to advance PM359 rapidly into a pivotal study. PM359 has received rare pediatric drug designation and orphan drug designation from the FDA.

- ***Ex vivo* HSC product for the treatment of X-linked CGD.** Prime Medicine today announced its first follow-on program in hematology and immunology. Building on its efforts in p47^{phox} CGD, Prime Medicine is advancing a program for X-linked CGD, which utilizes its Prime Assisted Site-Specific Integrate Gene Editing (PASSIGE™) technology, and is expected to address over 90 percent of known mutations in the *CYBB* gene with a single approach. Mutations in the *CYBB* gene occur in approximately two thirds of patients with CGD. Prime Medicine intends to leverage modular elements from across the PM359 program, including the IND filing, chemistry, manufacturing and controls (CMC) work and clinical trial, with the aim to accelerate advancement of its X-CGD program.

BMS Collaboration:

- ***Ex Vivo* T-Cell Therapies.** As announced this morning, Prime Medicine entered into a strategic research collaboration and license agreement with Bristol Myers Squibb, a global leader in cell therapy for hematology, immunology, and oncology, to develop and commercialize multiple Prime Edited *ex vivo* T-cell therapies. Under the terms of the agreement, Prime Medicine will design optimized Prime Editor and PASSIGE reagents for a select number of targets in immunological diseases and cancer; Bristol Myers Squibb will be responsible for development, manufacturing and commercialization of the next generation cell therapies, with support from Prime Medicine in gene editing strategy and reagent development. Under the terms of the agreement, Prime Medicine will receive a $55 million upfront payment and a $55 million equity investment from Bristol Myers Squibb. Prime Medicine is also eligible to receive more than $3.5 billion in milestones, including up to $1.4 billion in development milestones and more than $2.1 billion in commercialization milestones, along with royalties on net sales.

Liver

- **Lipid nanoparticle (LNP) Prime Editor for the treatment of Wilson's Disease.** Prime Medicine is focused on advancing its Wilson's Disease program, which targets prevalent mutations in the *ATP7B* gene. Prime Medicine expects to present new preclinical data and initiate IND-enabling activities for this program in the fourth quarter of 2024, and intends to file an IND and/or clinical trial application (CTA) in the first half of 2026. The program will use Prime Medicine's universal LNP, a multi-component and modular delivery system that the Company expects will be used across all liver disease programs, allowing more rapid and cost-efficient expansion into follow-on rare and non-rare liver indications.

Lung

- **LNP / adeno-associated virus (AAV) Prime Editors for the treatment of Cystic Fibrosis (CF).** With funding from the Cystic Fibrosis Foundation, Prime Medicine is continuing to advance two strategies to potentially cure CF: hotspot editing and PASSIGE. Using hotspot editing, the Company aims to address multiple mutations at mutational hotspots with a small number of Prime Editors; using PASSIGE, the Company aims to address nearly all people with CF with a single superexon insertion strategy. Through the Cystic Fibrosis Foundation, Prime Medicine has access to infrastructural support and foundational guidance, including established assays, animal models reagents and patient samples, which may accelerate advancement of the Company's Prime Editors for CF.

Additional Programs

In order to pursue its prioritized high value programs as rapidly as possible, the Company is identifying partnership opportunities to advance its other programs, including those for neurological diseases, cell therapy, ocular diseases and hearing loss. Prime Medicine expects that business development will continue to play a critical role in accelerating and funding its pipeline, allowing the Company to maximize the potential and reach of Prime Editing, including in areas outside its core focus. Prime Medicine may also choose to advance these programs through internal efforts in the future.

Updated Financial Guidance

As a result of this strategic pipeline prioritization, Prime Medicine will streamline its operating expenses and capital expenditures. Together with the $110 million upfront consideration received from Bristol Myers Squibb under the strategic research collaboration and license agreement announced this morning, Prime Medicine expects its cash runway to fund operations into the first half of 2026.

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 our 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.

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 potential of PM359 to correct the causative mutation of CGD; the anticipated maturation into a clinical-stage company by bringing PM359 into clinical development in 2024 with initial clinical data from the ongoing Phase 1/2 clinical trial of PM359 expected in 2025; the initiation, timing, progress, and results of its research and development programs, preclinical studies and future clinical trials, and the release of data related thereto; 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; certain activities and next steps to support the Company's maturation into a clinical-stage company, including opening an IND and/or CTA application, clinical data expectations, establishing proof-of-concept, advancing programs into lead optimization, advancing preclinical studies and initiating IND-enabling activities, and establishing AAV delivery platform and route of administration for neuromuscular programs; 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 potential of Prime Editors to reproducibly correct disease-causing genetic mutations across different tissues, organs and cell types, and the capacity of its Prime Editing and PASSIGE technology to edit CAR-T cells for the treatment of certain cancers and immune diseases; its ability to demonstrate superior off-target profiles for Prime Editing programs; exploring business development opportunities that could accelerate existing work and the benefits thereof; the modularity of the Prime Editing platform and the benefits thereof; 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: the development and optimization of new technologies; 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; the effect of unfavorable macroeconomic conditions or market volatility resulting from general economic, industry and market conditions, including rising interest rates, inflation, and adverse developments affecting the financial services industry; and Prime Medicine's expectations regarding the anticipated timeline of its cash runway and future financial performance. 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 and Quarterly Report on Form 10-Q for the quarter ended June 30, 2024, 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 Contact
Hannah Deresiewicz
Precision AQ
212-362-1200
hannah.deresiewicz@precisionaq.com

Media Contact
Dan Budwick, 1AB
dan@1ABmedia.com

prime medicine

Delivering on the promise
of Prime Editing

Corporate Presentation

September 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 maturation into a clinical-stage company by bringing PM359 into clinical development in 2024 with initial clinical data from the ongoing Phase 1/2 clinical trial of PM359 expected in 2025; the initiation, timing, progress and results of our research and development programs, preclinical studies and future clinical trials, and the release of data related thereto; our ability to demonstrate, and the timing of, preclinical proof-of-concept in vivo for multiple programs; our ability to pursue our 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; certain activities and next steps to support our maturation into a clinical-stage company, including opening an IND and/or CTA application, clinical data expectations, establishing proof-of-concept, advancing programs into lead optimization, advancing preclinical studies and initiating IND-enabling activities, 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 June 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.

Corporate Update

Prime Medicine is Developing One-Time, Curative Genetic Therapies

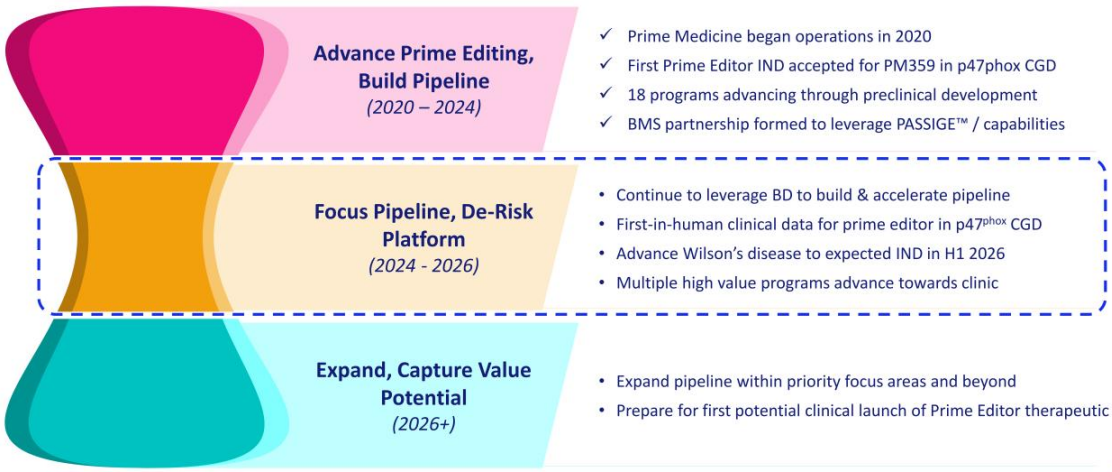
prime_ medicine

Strategic priorities:

- Share first ever clinical data for a Prime Editor (PM359 in CGD) in 2025
- Advance lead liver program (Wilson's Disease) to IND in H1 2026
- Progress other high value programs across focused target tissues
- Continue to build and execute on platform modularity
- Continue to leverage business development
- Streamline regulatory framework for the development of Prime Editing therapeutics

Prime Medicine is Entering a Phase of Focused Execution

Focused pipeline to enable future expansion into other high value areas



Our Pipeline: Focused on Significant Opportunities with High Value Potential

prime medicine

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

Value Framework

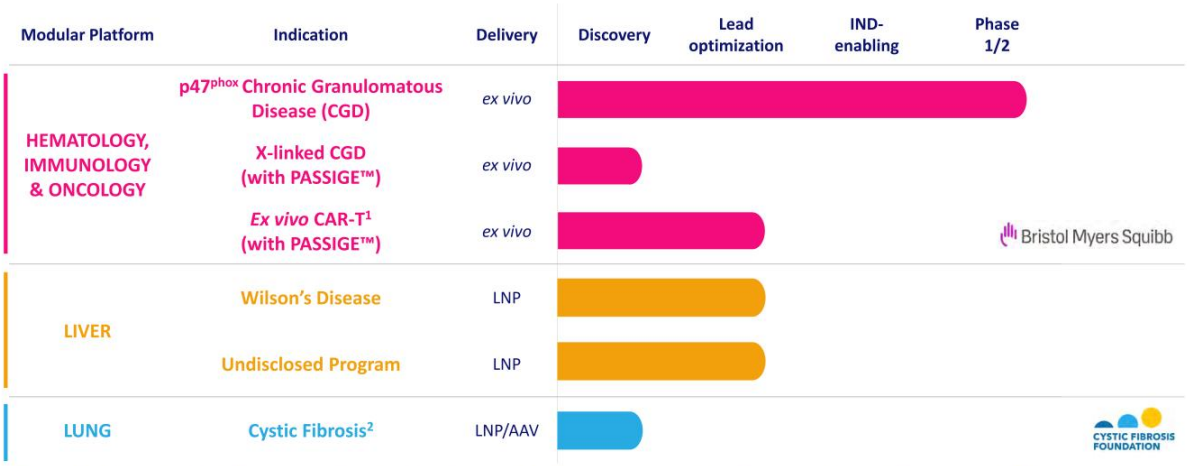
- Unmet medical need
- Commercial potential
- Pipeline and platform modularity
- Clinical development pathway
- Regulatory considerations
- Competition

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

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



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.

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

prime medicine

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

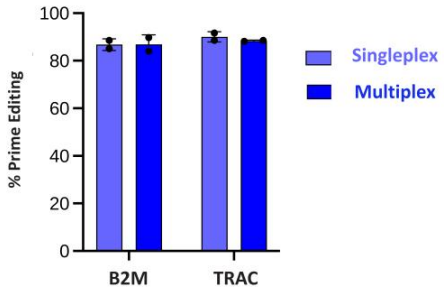
TRAC = T-cell receptor alpha constant; Data presented at ASH, December 2022, ASGCT, May 2023 and ASH, December 2023

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

prime medicine

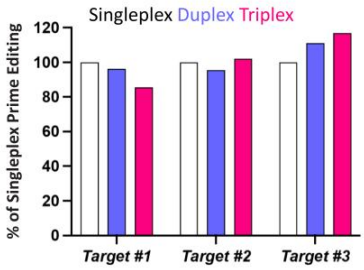
Prime Editors can be multiplexed to introduce multiple genomic modifications in CAR-T cells

β2 microglobulin (B2M) was knocked out by introducing a stop codon precisely in the B2M gene



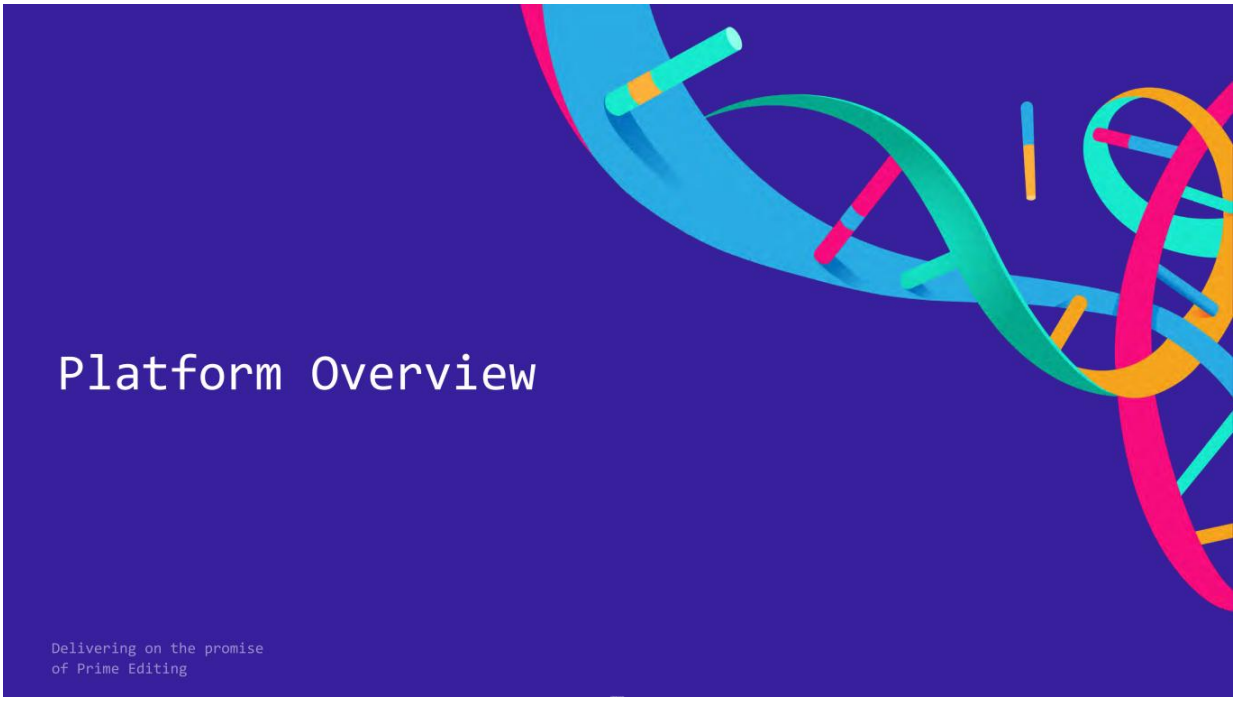
- Knockout with Prime Editing was efficient in T cells and could be done in multiplex B2M knockout leading to immune evasion

Prime Editing efficiency was maintained in multiplex at three target sites



- PASSIGE and multiplex Prime Editing efficiency were maintained in multiplex
- Up to 6 multiplex edits in T cells with high efficiency

Data presented at ASGCT 26th Annual Meeting, May 2023.


Platform Overview
Delivering on the promise
of Prime Editing

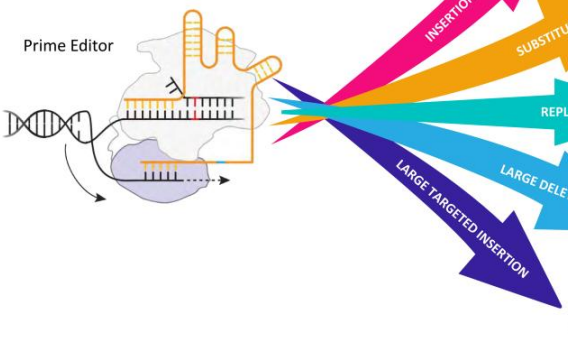
Now is *our* moment:

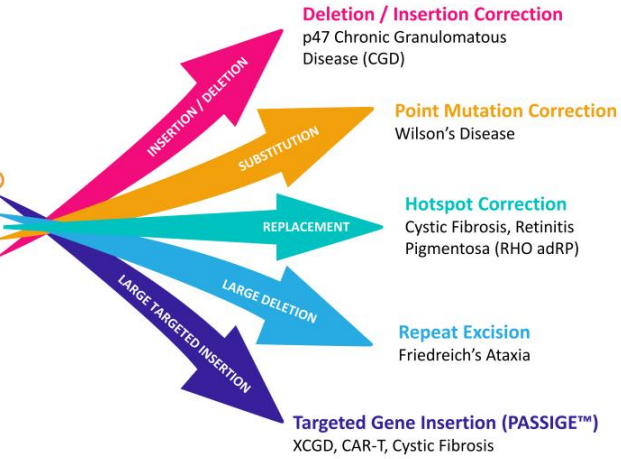
Prime Medicine brings together the **right people** and the **right technology** at the **right time**

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

- **BROAD OPPORTUNITY TO ADDRESS LARGE MARKETS**
- **PLATFORM MODULARITY**
- **EFFICIENT DELIVERY**
- **DIFFERENTIATED SAFETY PROFILE**
- **PIPELINE ALIGNED TO CORE AREAS OF FOCUS**
- **EVOLVING REGULATORY LANDSCAPE FOR GENETIC MEDICINES**

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

prime medicine

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

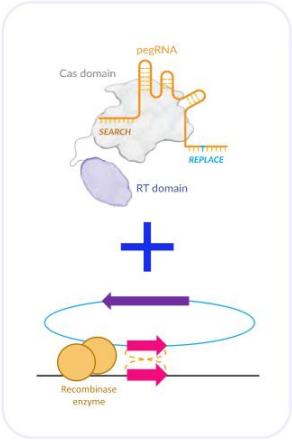
+/++/+++ = how fit Prime Medicine believes the technology is for making the edit, based on Prime Medicine's internal assessment

BP = base pair; KB = kilobase

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

prime medicine

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 Collab (e.g., oncology and autoimmune diseases)
- **X-Linked Chronic Granulomatous Disease (XCGD)**
- **Cystic Fibrosis**

Areas of opportunity:*

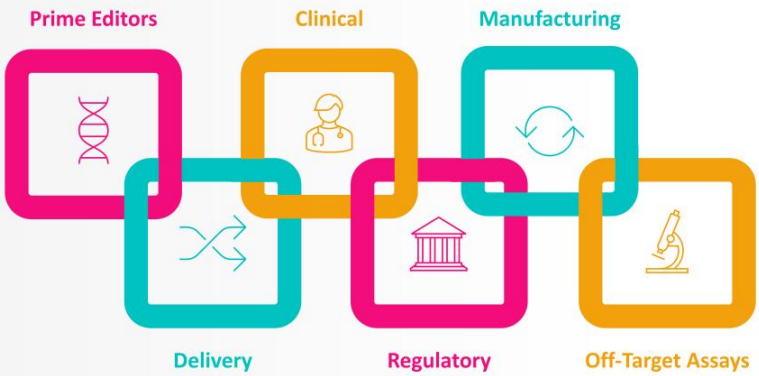
- **Targeted whole gene replacement for bone marrow diseases**
  (e.g., Hereditary anemias, such as Fanconi Anemia)
- **Targeted whole gene replacement for rare liver diseases**
  (e.g., Phenylketonuria, Tyrosinemia)
- **Correct inversion mutations**
  (e.g., Hemophilia A)
- ***In vivo* protein factory**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

prime medicine

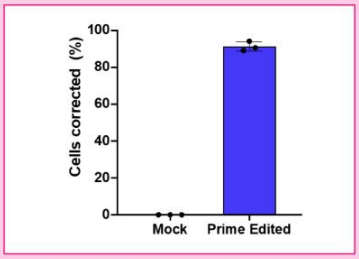
Core components can be readily leveraged to accelerate pipeline growth, efficiency and execution



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

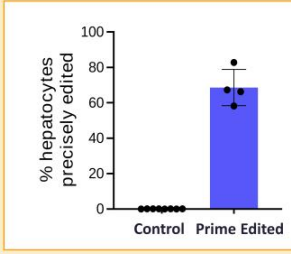
prime_ medicine

1 Ex Vivo (Human CD34+ Cells)



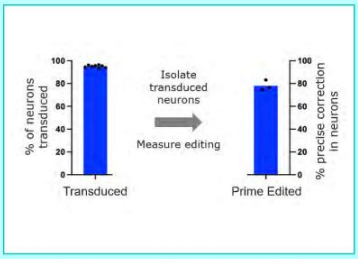
>90% editing of CD34+ cells *ex vivo* via electroporation

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 may accelerate development of subsequent programs within each area of focus

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

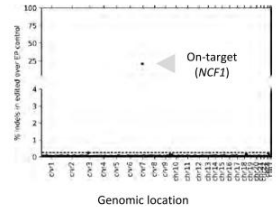
prime medicine

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

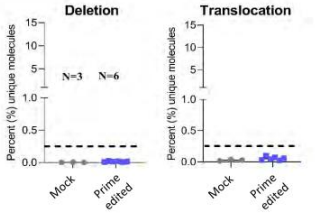
- **No** detectable double strand breakage
- **No** detectable off-target edits
- **No** detectable bystander edits
- **No** detectable off-target deletions, chromosomal translocations or rearrangements

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

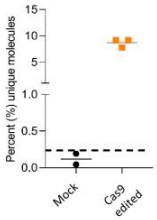
No off-target editing detected in healthy human donor CD34+ cells[1]



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



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

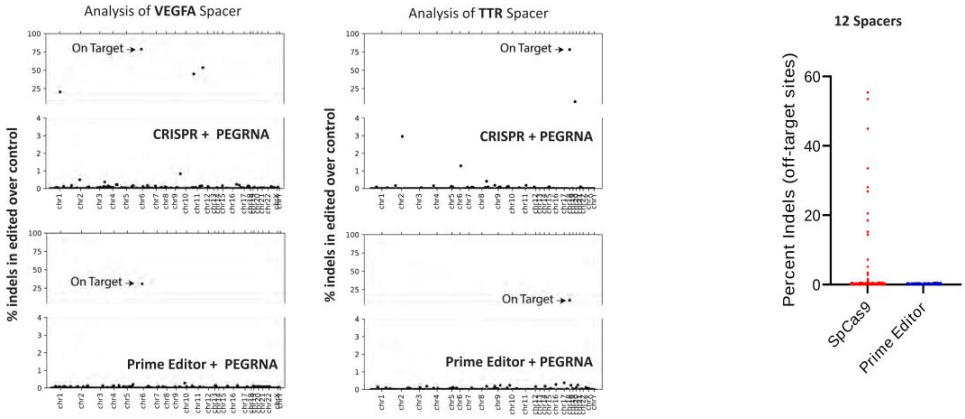


[1]Analysis of edited CD34+ cells from CGD program: Targeted in vitro Analysis of 550 potential off-target sites of off-target editing. [2]Data from in vivo analysis from mouse bone marrow harvested 16 weeks after engraftment was complete. [3]Positive control generated by transfecting HEK293T with sgRNA 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

prime_ medicine

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

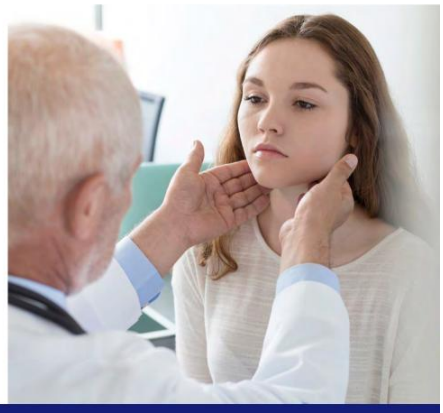

Hematology and Immunology

Advancing Prime Editors for Chronic Granulomatous Disease (CGD), A Disease of Significant Unmet Need

prime medicine

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, 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 X-CGD 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

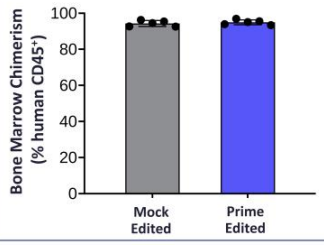
PM359: Preclinical Data Support Advancement for the Treatment of Chronic Granulomatous Disease

prime medicine

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

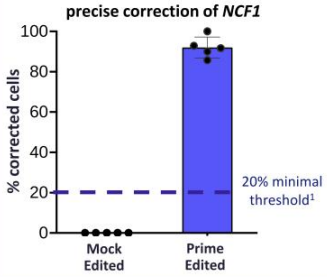
Engraftment

Prime Edited LT-HSCs showed complete engraftment in vivo



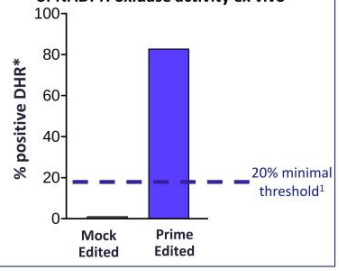
Editing Efficiency

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

prime medicine

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

Liver Disease

Advancing Prime Editors for Multiple Mutations Within Wilson's Disease

prime_ medicine

Large, genetically defined disease subsets well suited for Prime Editing

- **Disease severity and opportunity**
  - Common liver and systemic disease presenting in teens to 20's
  - 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

Prime Medicine utilizing its universal LNP for delivery of Prime Editors to correct mutations in ATP7B gene

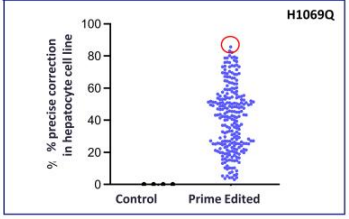
Wilson's Disease Program Utilizing Universal LNP Continues to Make Progress; IND Anticipated in H1 2026

prime medicine

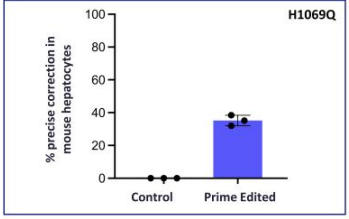
First effort targeting H1069Q mutation; follow-on targeting R778 mutation

In vitro data supporting Prime Editing hypothesis in Wilson's Disease

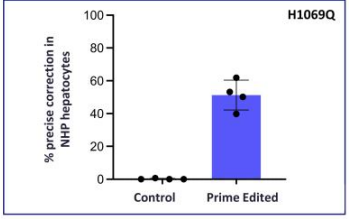
In vitro Prime Editor Screen in Human Hepatocyte Cell Line



In vitro Prime Editor in Primary Hepatocytes



In vitro NHP Surrogate Prime Editor in Primary NHP Hepatocytes



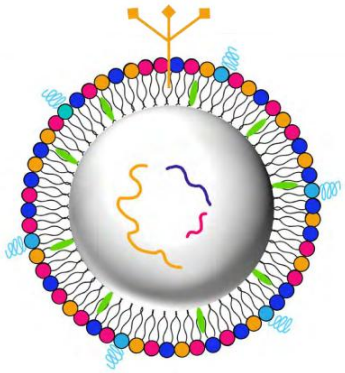
Prime Medicine to present initial *in vivo* data at ESGCT and AASLD in Q4 2024

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

prime medicine

LNP Modularity:

6 out of 8 components in the LNP are the same for all liver programs (only guide RNAs are not the same)



Ionizable Lipids	• Nucleic acid encapsulation and endosomal escape
Helper Lipids	• Stabilize and improve LNP pharmacokinetics • Facilitate membrane fusion and endosomal escape
PEG Lipids	• Control particle size and stability during manufacturing • Stealth coating reduces serum interactions and increasing half-life
Cholesterol	• Improve intracellular delivery • Increase LNP stability • Drive cellular uptake via ApoE binding and LDLR receptor
Targeting Ligand	• Improve biodistribution of LNPs to hepatocytes • Clinically validated for several siRNA delivery and liver indications
Prime Editor mRNA	• Prime editor enzyme
Two Guide RNAs	• pegRNA, +/- ngRNA • Guide RNAs are disease & mutation specific

Lung Disease

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

prime medicine

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

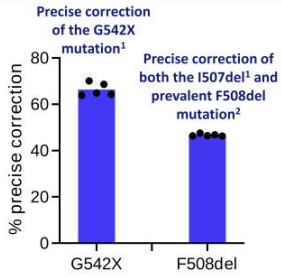
CF = Cystic Fibrosis

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

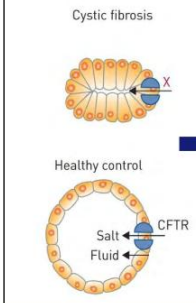
prime_ medicine

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

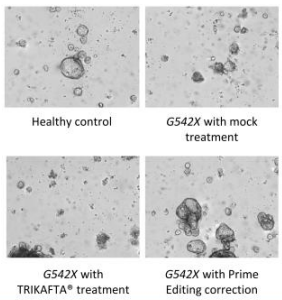
Prime Editors efficiently corrected the G542X mutation and mutations in the I507del/F508del "hotspot"



Intestinal organoids swelling assay for CFT function



Prime Editing of G542X patient intestinal organoids restored CFTR function



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

Corporate

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

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

Partnering Strategy

Enabled by scientific leadership in gene editing and program advancement

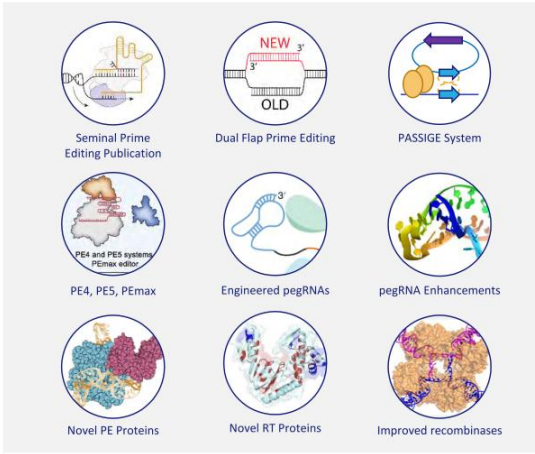
- Within Our Core
- Outside Our Core
- Access Enabling Innovation

Prime Medicine Holds Extensive Intellectual Property for Prime Editing Technologies

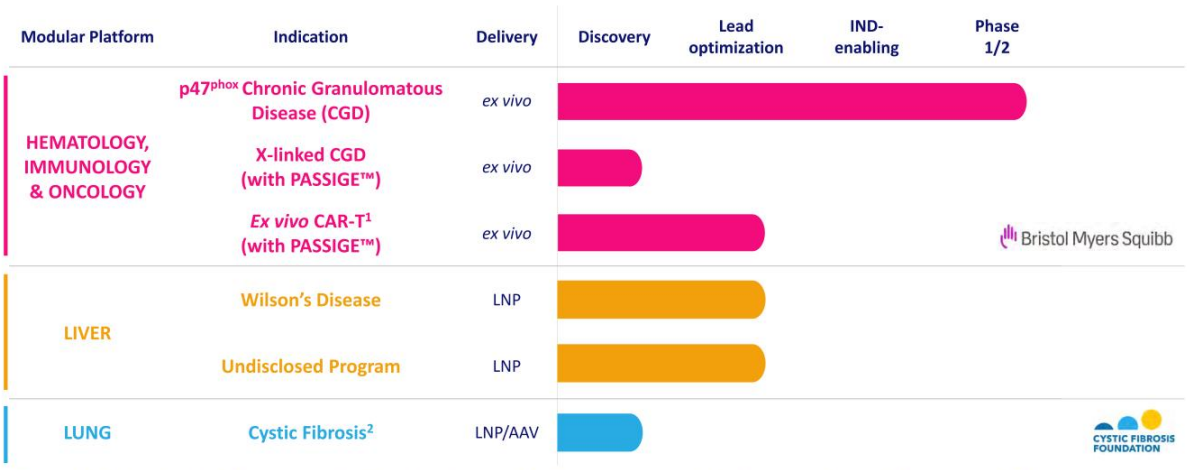
- ***Multiple configurations*** of RNA-templated gene editing
  - Prime Editor protein configurations: fusion, separate and split configurations
  - pegRNA configurations: fusion, split, separate and engineered configurations
  - Dual flap and dual guide RNA editing systems
- ***Broad diversity*** of 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



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



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.


prime medicine_
Delivering on the promise of Prime Editing
Appendix
primemedicine.com

Team with Significant Scientific and Drug Development Experience

prime medicine

Team

Keith Gottesdiener, M.D.
President and CEO
Rhythm · MERCK

Allan Reine, M.D.
Chief Financial Officer
FOGHORN THERAPEUTICS · pieris

Jeremy Duffield, M.D., Ph.D.
Chief Scientific Officer
VERTEX · Biogen

Ann L. Lee, Ph.D.
Chief Technical Officer
Bristol Myers Squibb · MERCK · Juno Therapeutics, A Celgene Company

Andrew Anzalone, M.D., Ph.D.
Co-Founder and Head of Prime Editing Platform
BROAD INSTITUTE

Meredith Goldwasser, Sc.D.
SVP, Head of Strategy and Corporate Ops
agios · Genentech · NOVARTIS

Richard Brudnick
Chief Business Officer
CODIAK · Bioverativ · Biogen

Niamh Alix
Chief Human Resources Officer
Orchard Therapeutics · Lonza · NOVARTIS

Fubao Wang, Ph.D
SVP, Head of Regulatory
SAREPTA THERAPEUTICS · MERCK · SANOFI

Mohammed Asmal, M.D., Ph.D.
Chief Medical Officer
bluebird bio · VERTEX

Karen Brown, Ph.D., JD
SVP, Intellectual Property and Legal Affairs
OBSIDIAN THERAPEUTICS · Ironwood · VERTEX

Carman Alenson, CPA
Chief Accounting Officer and SVP Finance
agios · amag

Board of Directors

Keith Gottesdiener, M.D.
President and CEO, Prime Medicine

David Schenkein, M.D.
General Partner, GV

Robert Nelsen
Managing Director, Arch Ventures

Jeff Marrazzo
Former CEO, Spark Therapeutics

Michael A. Kelly
Founder & President of Sentry Hill Partners, LLC

Wendy Chung, M.D., Ph.D.
Chair of Pediatrics, Boston Children's Hospital

Thomas Cahill, M.D., Ph.D.
Managing Partner, Newpath Partners

Kaye Foster
Senior Advisor, Boston Consulting Group

Scientific Advisory Board

David Liu, Ph.D.
(Co-Founder)

Yvonne Chen, Ph.D.

Agnieszka Czechowicz, M.D., Ph.D.

Guangping Gao, Ph.D.

Jim Haber, Ph.D.

Anastasia Khvorova, Ph.D.

Ben Kleinstiver, Ph.D.

Muthiah (Mano) Manoharan, Ph.D.

Eric Olson, Ph.D.

Gerald Schwank, Ph.D.

Jay Shendure, MD, Ph.D.

Samuel Sternberg, Ph.D.

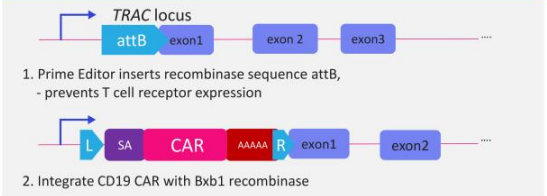
Shengdar Tsai, Ph.D.

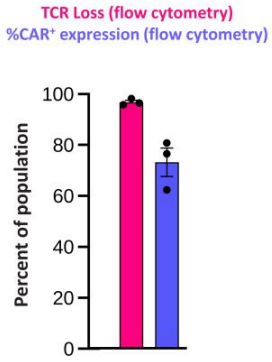
Non-Viral PASSIGE Delivery Supports Integration of CD19 CAR Under Endogenous Control of *TRAC* Locus in up to 80% of T Cells

prime_ medicine

Prime Editing at *TRAC* locus can lead to >95% loss of T cell receptor expression

Schematic for PASSIGE mediated CAR integration





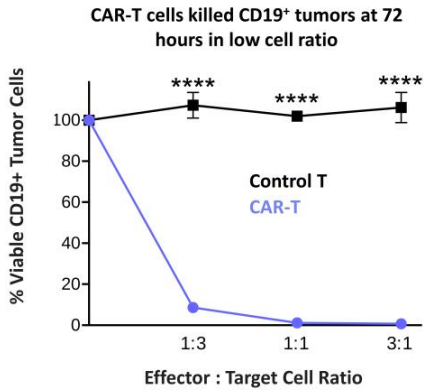
- ✓ Loss of endogenous TCR with attB insertion in *TRAC* exon 1
- ✓ Use of endogenous *TRAC* promoter allows for tuned regulation of CAR expression[1]
- ✓ Promoter-less cargo will not express if integrated elsewhere in genome
- ✓ Pilot studies – no integration elsewhere in genome
- ✓ Up to 8.9kB insertion with high efficiency may enable bi-cistronic CAR

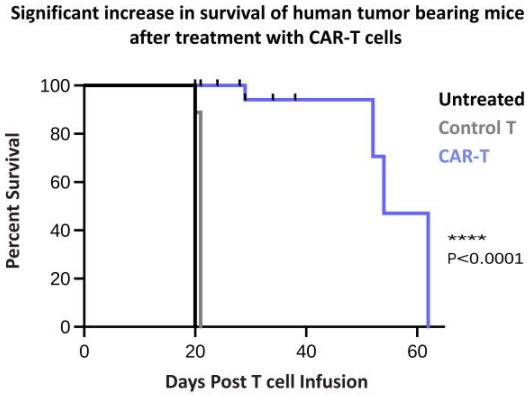
[1]Eyquem et al. (Sadelain) 2017. attB = recombinase attachment site; PASSIGE = prime assisted site-specific integrase gene editing; TCR = T cell receptor; CD19 = cluster of differentiation 19; CAR = chimeric antigen receptor; SA = splice acceptor; AAAAAA = polyA signal

Prime Medicine's Multiplexed CD19 CAR-T Cells are Functional *In Vitro* and *In Vivo*

prime medicine

In vitro and in vivo assays showed CD19 CAR-T functionality and specificity for target cell antigen





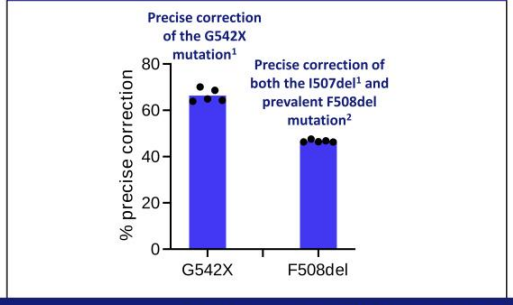
CAR = chimeric antigen receptor; PASSIGE = prime assisted site-specific integrase gene editing; CD19 = cluster of differentiation 19; Control T has GFP inserted in T cells instead of CD19 CAR; TRAC = T cell receptor alpha constant; in vitro data: statistical significance determine by one-way analysis of variance (ANOVA) with Bonferroni post-test; in vivo data: survival curve difference determined by log-rank test

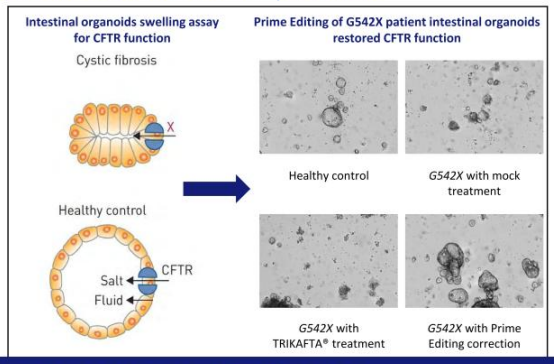
With Hotspot Editing, Prime Editors Corrected "High Unmet Need" CF Mutations, Including the Prevalent G542X (null) Mutation

prime_ medicine

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

- 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*

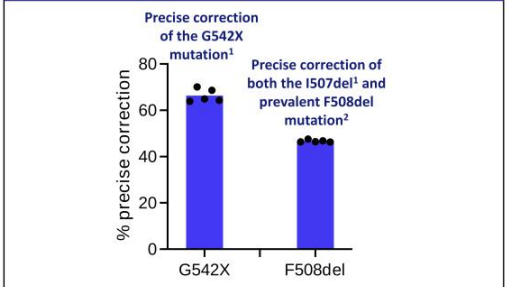
Van Mourik et al., 2019. Actual time course: 24 hours. TRIKAFTA® is a registered trademark of Vertex Pharmaceuticals, Incorporated.
¹G542X and I507del are "high unmet need" mutations; F508del is one of the most prevalent CF mutations; ²data show correction in patient induced pluripotent stem cells. Each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

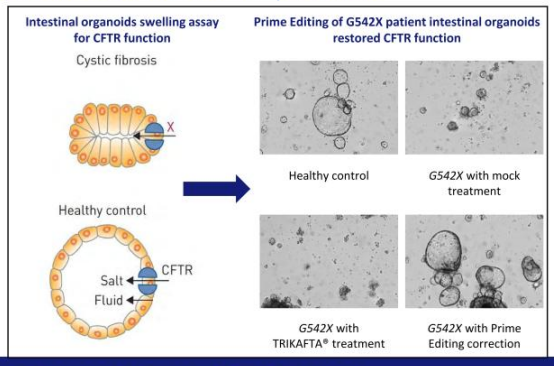
With Hotspot Editing, Prime Editors Corrected "High Unmet Need" CF Mutations, Including the Prevalent G542X (null) Mutation

prime_ medicine

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

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