Prime Medicine Announces Strategic Restructuring to Focus on Opportunities in Large Genetic Liver Diseases, Cystic Fibrosis, and Partnered Programs Alongside CEO Leadership Transition

May 19, 2025

-- Initial positive data from Phase 1/2 clinical trial of PM359 in CGD provide clinical proof-of-concept for Prime Editing as a transformative gene editing technology --

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

-- Allan Reine, M.D., CFO, to succeed Keith Gottesdiener, M.D., as CEO; Jeff Marrazzo, member of the Board of Directors, named Executive Chair --

-- Implementing cost cutting measures to significantly reduce cash needs in advance of key data inflection points --

CAMBRIDGE, Mass., May 19, 2025 (GLOBE NEWSWIRE) -- Prime Medicine, Inc. (Nasdaq: PRME), a biotechnology company committed to delivering a new class of differentiated one-time curative genetic therapies, today announced a strategic restructuring, including the deprioritization of its Chronic Granulomatous Disease (CGD) programs, as well as a cost and workforce reduction to focus on its liver franchise and programs funded through external partnerships.

Prime Medicine is currently advancing in vivo programs to cure two of the largest genetic liver diseases, Wilson's Disease and Alpha-1 Antitrypsin Deficiency (AATD), with initial clinical data from both programs expected in 2027. Prime Medicine will also continue its in vivo Cystic Fibrosis program with support from the Cystic Fibrosis Foundation, and its efforts to develop Prime Edited CAR-T products for hematology, immunology and oncology in partnership with Bristol Myers Squibb. In addition, Prime Medicine will continue to pursue additional business development opportunities to accelerate innovation, ensure the broadest application of Prime Editing, and further bolster its financial resources.

Also today, Prime Medicine announced that Keith Gottesdiener, M.D., has decided to step down as Chief Executive Officer (CEO) and a member of the Company's Board of Directors, effective immediately. Allan Reine, M.D., Prime Medicine's Chief Financial Officer (CFO), has been named CEO and member of the Board of Directors and Jeff Marrazzo, member of the Company's Board of Directors, has been named Executive Chair.

"The first-in-human data for PM359 announced today represent a landmark moment for the industry and for our company, demonstrating the unequivocal power of Prime Editing to change patients' lives, with a single dose of PM359 providing potentially curative benefit in a matter of weeks," said Allan Reine, M.D., Chief Executive Officer of Prime Medicine. "These data also reinforce the critical importance of ensuring Prime Medicine is positioned to withstand the challenges of the current environment, so that we can one day deliver the tremendous promise of Prime Editing to address a wide spectrum of genetic diseases. I am humbled by the opportunity to lead Prime Medicine through this next chapter, and committed to operating with excellence, efficiency and financial discipline as we focus our efforts internally on our Wilson's Disease and AATD programs, where, in the near-term, we have the potential to cure two of the largest genetic liver diseases."

Pipeline Prioritization:

Prime Medicine will focus its internal efforts on the development of in vivo programs for the treatment of Wilson's Disease and AATD, two of the largest genetic liver diseases. Prime Medicine expects to file an investigational new drug (IND) and/or clinical trial application (CTA) for its Wilson's Disease program in the first half of 2026 and for its AATD program in mid-2026; initial clinical data from both programs are expected in 2027.

- **Wilson's Disease:** Wilson's Disease is a rare and severe disorder caused by excess copper accumulation in the liver and brain that can lead to liver failure and neurocognitive decline and can be fatal without a liver transplant. There are currently no approved disease-modifying therapies for Wilson's Disease, which affects more than 20,000 people in the United States and European Union.
- **AATD:** AATD is a progressive, genetic disorder caused by mutations in the SERPINA1 gene, which can result in both lung- and liver-related symptoms, including shortness of breath, wheezing, chronic cough and frequent chest colds, as well as jaundice, ascites, and cirrhosis. There are currently no disease-modifying or curative treatments approved for the approximately 200,000 people in the United States and European Union with AATD, of which 20,000-30,000 people are currently diagnosed. Many patients with AATD ultimately progress to liver failure or severe lung disease, eventually resulting in premature death.

Prime Medicine will also continue its in vivo Cystic Fibrosis program with support from the Cystic Fibrosis Foundation, and its efforts to develop Prime Edited CAR-T products for hematology, immunology and oncology in partnership with Bristol Myers Squibb.

As announced in conjunction with initial data for PM359 this morning, Prime Medicine is exploring options for the continued clinical development of PM359 external to the company and ceasing further efforts in X-linked CGD. Prime Medicine believes PM359 has the potential to transform the care of $p47^{phox}$ CGD and is committed to working with urgency to identify an appropriate partner to help ensure this important therapy is delivered to patients.

Management and Corporate Update

Management Update:

The Board of Directors has appointed Dr. Reine, Prime Medicine's CFO, as CEO and member of the Board of Directors, effective immediately. Additionally, Jeff Marrazzo, member of the Board of Directors, has been named as Executive Chair.

- Dr. Reine is a seasoned executive with more than twenty years' experience in the biotechnology industry. Prior to joining Prime Medicine in 2024, Dr. Reine was CFO at Foghorn Therapeutics and, before that, at Pieris Pharmaceuticals. Previously, Dr. Reine spent fifteen years as a healthcare investor managing various healthcare portfolios primarily focused on biotechnology and pharmaceutical companies. In addition, Dr. Reine started his career in biotechnology investment banking and sell-side research. Dr. Reine also serves as Chairman of the Board of ONK Therapeutics.
- Mr. Marrazzo joined the Prime Medicine Board of Directors in 2023. Prior to that, he founded and built Spark Therapeutics into the world's first fully integrated, commercial gene therapy company, and successfully orchestrated its $4.8 billion sale to Roche in 2019. Under his leadership, Spark developed and launched LUXTURNA® for a rare blinding disorder, the first U.S. Food and Drug Administration (FDA)-approved gene therapy for a genetic disease in the U.S., developed BEQVEZ™, which was licensed to Pfizer and approved by the FDA for hemophilia B, and advanced multiple programs into Phase 3, including several which received Breakthrough Designation.

"The selection of Allan as Prime Medicine's next CEO is the result of thoughtful succession planning, designed to position the company for long-term success, while maintaining the culture of innovative thinking, scientific rigor and collaboration that has always defined the organization and that will continue to fuel its long-term growth," said Mr. Marrazzo. "As a seasoned CFO, former investor and physician, Allan brings a combination of financial and scientific acumen, which will enable him to champion and advance Prime Medicine's pipeline, while ensuring the company can successfully navigate the evolving market conditions. I look forward to working closely together as he assumes this new role."

Mr. Marrazzo continued, "Since its discovery in 2019, Keith has been an incredible advocate for Prime Editing. He was early to recognize the transformative power of this new technology and built Prime Medicine to enable its rapid development. With the announcement of positive initial data for PM359, and the changes in the company as part of the strategic prioritization, today marks a natural time to transition leadership of Prime Medicine. On behalf of the Board, I thank Keith for his visionary leadership and wish him the very best in his next professional endeavor."

Dr. Gottesdiener will continue to support Prime Medicine as a consultant for a period of one year.

Corporate Update:

Alongside the pipeline prioritization announced today, Prime Medicine is undertaking cost reduction measures and restructuring its team, including reducing its organizational headcount by approximately 25% percent. These initiatives are designed to significantly decrease Prime Medicine's operating expenses and cash burn, reducing anticipated cash needs by almost half through 2027.

Dr. Reine added, "I am deeply grateful to the employees who will be impacted as part of this restructuring. They all contributed mightily to advancing Prime Editing from concept to clinic, and their efforts across research and development and broader company-building will serve as the foundation for our success for many years to come. Importantly, while today's restructuring positions Prime Medicine to efficiently execute towards potentially transformative inflection points in Wilson's Diseases and AATD, we remain unwavering in our long-term ambition to realize the full promise of Prime Editing for a wide spectrum of diseases."

Also today, Prime Medicine announced that it recently engaged in binding arbitration proceedings with Beam Therapeutics, Inc. regarding the parties' 2019 Collaboration and License Agreement (the "Agreement") and specific to its AATD program. Prime Medicine is committed to honoring the terms of the Agreement, and confident that it has the rights to pursue AATD under the Agreement.

Based on its current plans, Prime Medicine continues to expect that its cash, cash equivalents and investments as of March 31, 2025 will be sufficient to fund its operations and capital expenditure requirements 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: liver, lung, and immunology and oncology. 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.

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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 its AATD and Wilson's 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 its research and development

programs, preclinical studies and future clinical trials, including the release of data related thereto; the potential of Prime Editing to correct the causative mutations of diseases, including of AATD, Wilson's Disease and CF; the breadth of Prime Editing technology and the implementation of its strategic plans for its business, programs, and technology; the potential of Prime Editing as a transformative gene editing technology and its ability to unlock opportunities across thousands of potential indications; its ability to identify an external partner to deliver PM359 therapy in X-linked CGD to patients; its rights to pursue AATD using its approach in connection with the arbitration proceedings with Beam Therapeutics, Inc.; and its expected cash runway.

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.

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