Prime Medicine Announces Breakthrough Clinical Data Showing Rapid Restoration of DHR Positivity After Single Infusion of PM359, an Investigational Prime Editor for Chronic Granulomatous Disease

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-- First ever clinical data supporting safety and efficacy of Prime Editing in humans --

-- Initial data from first patient dosed in Phase 1/2 trial finds single dose of PM359 led to 58% DHR positivity by Day 15 and 66% by Day 30, well above levels believed to be potentially curative --

-- Rapid engraftment observed in both neutrophils and platelets --

-- Encouraging safety profile; no serious adverse events related to PM359 --

-- Initiating efforts to explore continued clinical development opportunities for PM359 external to Prime Medicine --

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 positive initial data from the first patient dosed in its ongoing Phase 1/2 clinical study of PM359 in Chronic Granulomatous Disease (CGD). Preliminary results from the first patient demonstrated that PM359 was well-tolerated, showed rapid engraftment and restored NADPH oxidase activity to well above the threshold for clinical benefit, as measured by the dihydrorhodamine (DHR) assay.

CGD is a rare inherited disease that leads to recurrent, debilitating and often life-threatening infections. It is caused by mutations in genes, including *NCF1*, that encode proteins that form the NADPH oxidase complex, an enzyme that kills bacteria and fungi to control infection. PM359, an ex vivo Prime Edited autologous hematopoietic stem cell (HSC) product for the treatment of $p47^{phox}$ CGD and the first Prime Editor generated therapy to be administered in humans, is designed to correct the delGT mutation in *NCF1*, the most prevalent disease-causing mutation in the $p47^{phox}$ variant of CGD, thereby addressing its underlying pathophysiology. Prime Medicine estimates that CGD causative mutations occur in between one in 100,000 and one in 200,000 births in the United States, with approximately 25 percent of patients presenting with the $p47^{phox}$ form of the disease.

“We created prime editing five and a half years ago as a versatile, precise genome editing technology that in principle could correct almost all mutations known to cause genetic diseases,” said David Liu, Ph.D., Co-Founder of Prime Medicine and Richard Merkin Professor and Director of the Merkin Institute of Transformative Technologies in Healthcare at the Broad Institute of MIT and Harvard. “Today’s data represent a milestone in medicine, establishing that prime editing in a patient's cells can correct a pathogenic mutation and can change the course of a life-limiting disease. I am thrilled by the implication of these results for the CGD patient community, and more generally for people living with genetic diseases.”

PM359 is being evaluated in a Phase 1/2, multinational, first-in-human trial designed to assess safety, biological activity and preliminary efficacy in adult and pediatric study participants. Initial safety and efficacy data reported today are from the first adult patient treated in the trial.

This patient was treated with a single dose of PM359, administered by intravenous infusion. NADPH oxidase activity was measured by the dihydrorhodamine (DHR) assay at baseline, Day 15 and Day 30. Treatment with PM359 led to complete restoration of NADPH oxidase activity in 58% of neutrophils by Day 15 and 66% of neutrophils by Day 30, significantly exceeding the anticipated minimum threshold for clinical benefit of 20%.

Additionally, this patient experienced rapid engraftment of his autologous transplant following myeloablative conditioning. Engraftment was confirmed in neutrophils on Day 14 and in platelets on Day 19. Of note, this is nearly two-times faster than approved gene editing technologies, where median engraftment has been reported to occur on Days 27 and 35 across these same measures.

Treatment with PM359 was generally well-tolerated, with an acceptable safety profile. Adverse events (AEs) were generally consistent with AEs otherwise observed during myeloablative conditioning with busulfan. No serious AEs related to PM359 were reported as of the data cutoff.

“The data reported today are important for two reasons. First, for people living with CGD, these results suggest Prime Editing may offer a reprieve from their disease, restoring NADPH oxidase function and, therefore, reducing the risk of acquiring a deadly infection or suffering from inflammation of the lung, liver or bowel,” said Mohammed Asmal, M.D., Ph.D., Chief Medical Officer of Prime Medicine. “We are grateful to our first patient and to his family and caretakers for their trust and participation in our trial.”

Dr. Asmal continued, “Second, these data answer key questions about Prime Editors, confirming their potential to be delivered safely and restore normal gene function. This reaffirms our conviction that Prime Editing will be the foundation of a new class of differentiated, one-time genetic therapies, and we look forward to advancing our broader pipeline of investigational programs, directed towards large genetic diseases that impact the liver and lung.”

Prime Medicine does not plan to independently advance its efforts in CGD. 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.

Going forward, Prime Medicine will focus its resources on advancing its in vivo liver franchise, where the Company is advancing programs to cure two of the largest genetic liver diseases, Wilson’s Disease and Alpha-1 Antitrypsin Deficiency (AATD). 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.

About PM359

PM359, Prime Medicine's first product candidate within its hematology and immunology area of focus, targets the p47 ^{phox} variant of CGD, a serious, life-threatening disease that presents in childhood. PM359 comprises autologous hematopoietic stem cells (HSCs) modified ex vivo using Prime Editors that have been designed to correct a high percentage of cells containing the disease-causing mutation. PM359 has received rare pediatric drug designation and orphan drug designation from the U.S. Food and Drug Administration.

About Chronic Granulomatous Disease (CGD)

Chronic granulomatous disease (CGD) is a rare inherited hematologic disorder characterized by susceptibility to severe, difficult-to-treat infections, and inflammatory/autoimmune complications. CGD is caused by mutations in any one of the subunits comprising the NADPH oxidase complex, which is required for phagocytic cells, in particular neutrophils, to destroy many invasive microorganisms. CGD causative mutations are estimated to occur between one in 100,000 and one in 200,000 births in the United States, and most children are diagnosed within the first three years of life. Beginning in childhood, patients with CGD develop infections from a range of both typical and unusual bacteria, fungi and mycobacteria. These infections may present in various organ systems, and protracted infections can lead to long-term organ damage and failure. In addition, patients have non-infectious inflammatory disease, most commonly presenting as inflammatory bowel disease, soft tissue granulomas, and strictures of the urinary or digestive tract. Undiagnosed or untreated, the infectious manifestations of CGD are rapidly fatal, with refractory or antimicrobial resistant infection the leading cause of mortality.

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.

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; 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; and its ability to identify an external partner to deliver PM359 therapy in X-linked CGD to patients.

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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