Prime Medicine Presents Preclinical Data Demonstrating Ability of PM359 to Efficiently, Reproducibly and Durably Correct Causative Mutation of Chronic Granulomatous Disease (CGD)

May 8, 2024

Findings demonstrate ability of PM359 to correct disease-causing mutation in CGD patient blood stem cells, leading to restored immune function in vivo with no off-target edits detected

IND for PM359 recently cleared by U.S. FDA; data support advancement into Phase 1/2 clinical trial

CAMBRIDGE, Mass., May 08, 2024 (GLOBE NEWSWIRE) -- Prime Medicine, Inc. (Nasdaq: PRME), a biotechnology company committed to delivering a new class of differentiated, one-time curative genetic therapies, today reported new preclinical data demonstrating the ability of its *ex vivo* Prime Editing program, PM359, to correct a common disease-causing mutation of chronic granulomatous disease (CGD). The data will be presented today at an oral presentation during the American Society of Cell & Gene Therapy 27th Annual Meeting in Baltimore. Prime Medicine recently announced that the U.S. Food and Drug Administration (FDA) has cleared its investigational new drug (IND) application for PM359 for the treatment of CGD.

“These data are incredibly exciting—showing for the first time that Prime Editing can not only correct the disease-causing mutation of CGD in human blood stem cells, but that those cells can produce neutrophils with restored immune function and healthy activity following engraftment in rodents with no off-target edits observed,” said Jennifer Gori, Ph.D., Vice President, Head of Hematology and Immunology at Prime Medicine. “Further, we were able to demonstrate clinical-scale production of Prime Edited blood stem cells, supporting our planned advancement into the clinic with PM359.”

CGD is a rare inherited disease that leads to recurrent, debilitating and often life-threatening infections. CGD is caused by mutations in any one of the subunits comprising the NADPH oxidase complex, an enzyme that kills bacteria and fungi to control infection. CGD causative mutations are estimated to occur in between one in 100,000 and one in 200,000 births in the U.S., and most children are diagnosed within the first three years of life. The second most common form of CGD, which represents approximately 25% of cases, is caused by loss-of-function mutations in both copies of the NCF1 gene encoding the p47phox protein.

Prime Medicine is advancing an ex vivo Prime Editing program, PM359, that aims to correct the predominant mutation in NCF1 in CGD patient CD34+ hematopoietic stem cells (HSCs) and restore NADPH oxidase function.

In today’s presentation at ASGCT, Prime Medicine highlighted data from a series of in vivo non-clinical studies using human CGD patient CD34+ HSCs. Notably, findings demonstrated restoration of neutrophil function after stem cell engraftment in mice, as well as the ability to scale up production of Prime Edited cells to clinical scale. Detailed findings are as follows:

- Prime Editing precisely corrected the CGD causative mutation in greater than 75% of CGD patient CD34+ cells
- The CGD causative mutation is corrected in ≧80% Prime Edited CGD patient CD34+ cells that engraft the bone marrow in a mouse model
- NADPH oxidase activity was restored in bone marrow neutrophils in the mice engrafted with Prime Edited CGD patient CD34+ cells
- Interferon-regulated gene expression in Prime Edited CGD patient cells was reduced compared to unedited CGD patient cells and similar to healthy donor cells, suggesting Prime Editing restored cells to healthy state
- No unintended or off-target edits were detected in engrafted Prime Edited CGD patient CD34+ cells
- Process development supported reproducible and efficient manufacturing of clinical-scale healthy donor drug products (HDDP) with high purity, viability, potency and Prime Editing efficiency
    - Long-term engraftment of HDDP was achieved with human multilineage blood production and biodistribution maintained

“We are very pleased to report these data from our PM359 program in CGD, which supported the basis of our IND application package to the U.S. FDA,” said Jeremy Duffield, M.D., Ph.D., Chief Scientific Officer of Prime Medicine. “With our recent IND clearance, we are working efficiently to move forward with our Phase 1/2 clinical trial of PM359, from which we expect to report first-in-human data in 2025. This is a significant moment for Prime Medicine and the gene editing field, and I am grateful for the unwavering commitment of my colleagues to advance this program. I look forward to the planned evaluation of PM359 in the clinic so that we can truly realize the impact this novel technology may have on patients in need of new treatments.”

Presentation Details:

- **Presentation Name:** Development of a Prime Edited CD34+ cell Drug Product for the Treatment of P47phox Chronic Granulomatous Disease
    - **Date & Time:** Wednesday, May 8, 2024, 5:15 p.m. ET
    - **Presenter:** Jennifer Gori, Ph.D.

About PM359
PM359, Prime Medicine’s first product candidate within its hematology and immunology area of focus, targets the p47phox variant of chronic

granulomatous disease (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 core areas of focus: hematology and immunology, liver, lung, ocular and neuromuscular. Across each core area, Prime Medicine's initial focus is on genetic diseases with a fast, direct path to treating patients, and those with high unmet need not currently addressable using other gene editing approaches. Over time, the Company intends to maximize Prime Editing's broad and versatile therapeutic potential to expand beyond the genetic diseases in its initial pipeline, potentially including 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 a causative mutation of CGD; its expectations regarding the breadth and potential of Prime Editing technology; the anticipated maturation into a clinical-stage company by bringing PM359 into clinical development in 2024 with initial data expected in 2025; and the potential for Prime Editors to repair genetic mutations and offer curative genetic therapies for a wide spectrum of diseases. The words "may," "might," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "expect," "estimate," "seek," "predict," "future," "project," "potential," "continue," "target" and similar words or expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks associated with: uncertainties related to Prime Medicine's product candidates entering clinical trials; the authorization, initiation, and conduct of preclinical and IND-enabling studies and other development requirements for potential product candidates, including uncertainties related to opening INDs and obtaining regulatory approvals; risks related to the development and optimization of new technologies, the results of preclinical studies, or clinical studies not being predictive of future results in connection with future studies; the scope of protection Prime Medicine is able to establish and maintain for intellectual property rights covering its Prime Editing technology; Prime Medicine's ability to identify and enter into future license agreements and collaborations; and general economic, industry and market conditions, including rising interest rates, inflation, and adverse developments affecting the financial services industry. 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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