Prime Medicine to Present New Preclinical Data Highlighting Broad Potential of Prime Editing Technology at ASGCT 26th Annual Meeting

May 17, 2023

Data demonstrated Prime Editors efficiently, reproducibly and durably corrected the causative mutation of CGD, supporting advancement of development candidate PM359

New preclinical data highlighted ability of PASSIGE™ platform to generate multiplex-edited CAR-T cells without using viruses

CAMBRIDGE, Mass., May 17, 2023 (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 the presentation of new preclinical data that further demonstrated the potential of Prime Editing to correct the causative mutation of chronic granulomatous disease (CGD) and preclinical data that showcased the potential application of the Prime Editing Assisted Site-Specific Integrase Gene Editing (PASSIGE™) platform to generate multiplex-edited CAR-T cells for the treatment of certain cancers and immune diseases. The data are being presented today during the American Society of Gene and Cell Therapy (ASGCT) 26th Annual Meeting, being held May 16-20, 2023, in Los Angeles, California.

"We are very pleased to present these new data for our CGD program and PASSIGE platform today at ASGCT, which underscore our belief in the breadth and potential of Prime Editing to offer curative treatments for many diseases," said Jeremy Duffield, M.D., Ph.D., Chief Scientific Officer of Prime Medicine. "Our CGD program is progressing well, and with today's data demonstrating the reproducibility of PM359 to correct the disease-causing mutation in CD34$^+$ cells *ex vivo* with no off-target editing detected in the comprehensive set of studies done to date, we look forward to the PM359 program's advancement through Investigational New Drug-enabling studies. Further, while the benefits of autologous CAR-T therapies are well established, their full potential is often hindered by manufacturing and delivery challenges. With our PASSIGE platform, we believe we can create allogeneic products that may overcome these challenges with a one-step, non-viral approach that could expand the applicability of T cell therapies for the potential treatment of tumors and immune diseases."

CGD Presentation Highlights
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 NADPH oxidase, an enzyme that kills bacteria and fungi to control infection. Prime Medicine is advancing an *ex vivo* Prime Editing program that aims to correct the disease-causing mutation in *NCF1* in CGD patient CD34$^+$ hematopoietic stem cells (HSCs) and restore NADPH oxidase function. Prime Medicine has previously shared data from the CGD program that demonstrated the ability of Prime Editing to correct a CGD causative mutation in CD34$^+$ cells *ex vivo*. The Prime Edited CD34$^+$ cells engrafted long-term *in vivo* with editing levels greater than 92%. Today's findings added to that, showing:

- Prime Editing was highly reproducible, demonstrating greater than 90% Prime Editing in CD34$^+$ cells from each of four donors
- 16-week engrafted Prime Edited CD34$^+$ cells repopulated the bone marrow, reconstituted production of human blood cells, and biodistributed to the spleen and peripheral blood
- Comprehensive off-target analyses demonstrated no detected off-target activity, large deletions or translocations in Prime Edited CD34$^+$ cells
- These findings provide further support for the advancement of the company's first development candidate, PM359, as a potential treatment for CGD

PASSIGE Presentation Highlights
Prime Medicine is advancing a platform technology known as PASSIGE, which combines Prime Editing with an integrase or site-specific recombinase enzyme to enable the introduction of large-sized cargo into the genome as a potential one-time therapy. This approach is designed to expand the versatility of Prime Editing with the intent to broaden the range of permanent genomic edits that Prime Editing can make to potentially treat disease, including the ability to insert, delete or invert gene-sized pieces of DNA. In today's presentation, Prime Medicine highlighted expanded work using PASSIGE technology and a non-viral approach to generate CD19 CAR-T cells, as well as robust disruption of relevant target genes (*TRAC* and *B2M*) using Prime Editing in primary human T cells. Results showed:

- Single-step PASSIGE-mediated insertion of a CD19-CAR at the *TRAC* genetic locus in primary human T cells led to greater than 90% loss of T cell receptor expression and 60% targeted integration of a 3.5 kb CD19 CAR transgene, with no observed impact on T cell viability or T cell expansion
- PASSIGE-generated CD19 CAR-T cells exhibited potent anti-tumor activity *in vitro* and *in vivo*
- Prime Editing of the *B2M* gene in primary human T cells led to greater than 90% knock-out of B2M protein expression
- Efficient multiplex Prime Editing at three genomic target sites in primary human T cells
- These results support the potential of PASSIGE and Prime Editing to provide a modular, one-step system to create best-in-class, potent and targeted, allogeneic CAR-T cell therapies

Presentation Details
Abstract Title: (101) Prime Editing of Human CD34+ Long-Term Hematopoietic Stem Cells Precisely Corrects the Causative Mutation of p47phox Chronic Granulomatous Disease and Restores NADPH Oxidase Activity in Myeloid Progeny

Date & Time: Wednesday, May 17, 2023, 5:15 – 5:30 p.m. PT
Room: Room 515 AB
Session Title: Genome Editing Therapies & Safety I
Presenter: Jennifer Gori

Abstract Title: (602) An All-Prime Editing One-Step Approach for Non-Viral Generation of a Multiplex-Edited Allogeneic CAR-T Cell Product
Date & Time: Wednesday, May 17, 2023, 12:00 p.m. PT
Session Title: Wednesday Poster Session
Presenter: Emily Pomeroy

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 leveraging its proprietary Prime Editing platform, a versatile, precise and efficient gene editing technology, to develop a new class of differentiated, one-time, potentially 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.

Prime Medicine is currently progressing a diversified portfolio of eighteen programs initially focused on genetic diseases with a fast, direct path to treating patients or with a high unmet need because they cannot be treated using other gene-editing approaches. Over time, the Company intends to maximize Prime Editing's therapeutic potential and advance potentially curative therapeutic options to patients for a broad spectrum of diseases. For more information, please visit www.primemedicine.com.

Cautionary Note Regarding 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 initiation, timing, progress, and results of its research and development programs, preclinical studies and future clinical trials, and the release of data related thereto, including the initiation of IND-enabling studies for PM359, the potential of PM359 to correct the causative mutation of CGD, the capacity of its PASSIGE technology to edit CAR-T cells for the treatment of certain cancers and immune diseases, and the potential for Prime Editors to repair genetic mutations. 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 the authorization, initiation, and conduct of preclinical and other development requirements for potential product candidates, including uncertainties related to 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 Quarterly Report on Form 10-Q, 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
Stern Investor Relations, Inc.
212-362-1200
hannah.deresiewicz@sternir.com

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