Prime Medicine Presents First-ever Prime Editing Data in Non-human Primates Demonstrating Highly Efficient Ability of Prime Editors to Precisely Correct Disease-causing Mutation of GSD1b

October 27, 2023

Up to 83% of Hepatocytes (up to 50% whole liver) Precisely Edited for p.L348fs Mutation Following IV Infusion of Prime Editor in NHPs with No Safety Concerns Observed; Editing Well Above Anticipated Threshold Necessary to Reverse Disease Manifestations

Up to 56% Whole Liver Editing Observed in Humanized GSD1b Mouse Model

No Detectable Off-target Edits Observed Following Comprehensive in vitro Analysis

Data Presented Today in an Oral Presentation at ESGCT 2023

CAMBRIDGE, Mass., Oct. 27, 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 reported new preclinical data demonstrating the ability of liver-targeted Prime Editors to efficiently and precisely correct one of the most prevalent disease-causing mutations of glycogen storage disease 1b (GSD1b) in non-human primates (NHP) and mouse models. The data were presented today at the European Society of Gene and Cell Therapy (ESGCT) 2023 Congress in Brussels, Belgium.

"The data presented today are highly encouraging, both for patients and caregivers impacted by GSD1b, as well as for Prime Medicine and the field of gene editing," said Jeremy Duffield, M.D., Ph.D., Chief Scientific Officer of Prime Medicine. "These data are the first Prime Editing data in NHPs and provide further proof-of-concept for our Prime Editing approach to potentially address a wide range of diseases, in this case, by targeting a specific gene with a liver-directed LNP. We have designed our Prime Editors for GSD1b to correct the two most prevalent disease-causing mutations of the disease – p.L348fs and p.G339C – and are highly encouraged by the efficient and precise corrections we have observed across in vitro evaluations, in vivo rodent studies and now, NHP studies. Importantly, we continue to observe minimal to no detectable off-target edits with our Prime Editors, providing further confidence in the precision of this technology."

GSD1b is a rare, serious progressive disease that causes impaired glycogen metabolism and affects approximately 1,500 patients. It results from mutations in the glucose-6-phosphate transporter (G6PT), which is encoded by the gene SLC37A4. Deficiencies in this transporter result in hypoglycemia, or low blood glucose levels, which can be fatal if patients do not adhere to a strict dietary regimen, including consuming slow-release glucose and overnight feeding. P.L348fs and p.G339C mutations are known to be the most prevalent disease-causing mutations and are found in approximately 46-52% of the GSD1b patient population. According to scientific literature and Prime Medicine research, correcting SLC37A4 gene mutations in fewer than 10% of liver cells may be sufficient to reverse many manifestations of this disease.

To address the underlying genetic cause of GSD1b, Prime Medicine is advancing Prime Editors that are delivered to the liver by single intravenous infusion and designed to enable a precise correction of the disease-causing mutations, restoring G6PT protein expression and glucose homeostasis. The Prime Editors are composed of a Prime Editor guide RNA (pegRNA) targeting the respective mutations, a nick-guide RNA (ngRNA) and a messenger RNA (mRNA) packaged in Prime's universal lipid nanoparticle (LNP) formulation that includes a ligand targeting the LNP to hepatocytes. Through high-throughput screening and subsequent optimization, Prime researchers identified pegRNAs that precisely corrected the p.L348fs and p.G339C mutations in liver cells, which were then evaluated in vitro, demonstrating average editing of 77% and 37%, respectively.

In today's presentation at ESGCT, Prime Medicine highlighted data from in vivo rodent and NHP studies with its Prime Editor targeting the p.L348fs mutation. Key findings from the studies showed:

- Up to 50% whole liver precise editing of p.L348 in NHPs at day 14 without significant on-target unintended edits. Up to 83% of the key target cells, liver hepatocytes, were estimated to have both alleles precisely edited by this single LNP administration.
- Up to 56% whole liver precise correction of the p.L348fs mutation in a GSD1b humanized mouse model with on-target unintended editing of less than 0.2% across dose levels evaluated.
- Prime Editing of up to 44% led to restored levels of G6PT protein expression of up to 46%, with the extent of correction directly correlating with the extent of G6PT protein restoration in the humanized mouse model.
- Redosing of the universal LNP in non-naïve animals was tolerated similarly to naïve animals with no infusion reactions, no body weight changes, and transient, modest liver function changes that resolved by day 7; minimal transient cytokine abnormalities were observed.
- No detectable off-target edits were observed in patient-derived induced pluripotent stem cells (iPSCs) following a comprehensive off-target screening analysis, consistent with what has been observed to date across Prime Medicine's extensive off-target analyses for each of its programs.

These findings provide important proof-of-concept for Prime Medicine's LNP liver-targeted delivery approach, and support the further advancement of the Company's Prime Editors targeting the p.L348fs and p.G339C mutations in GSD1b, as well as its additional liver-targeted programs.

Presentation Details

- **Title:** OR79. Prime Editing Precisely Corrects Prevalent Pathogenic Mutations Observed in Glycogen Storage Disease

Type 1b (GSD1b) Patients
- **Date & Time:** October 27, 2023
- **Session:** Gene Editing: Towards Clinical Trials
- **Location:** Brussels, Belgium

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.

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, our ability to demonstrate additional preclinical data in NHPs that provide further proof-of-concept for our Prime Editing approach to address a range of diseases, the potential of Prime Editors to reproducibly correct disease-causing genetic mutations across different tissues, organs and cell types, the continued development and optimization of our universal liver-targeted LNP delivery approach, the further advancement of Prime Editors to maximize their versatility, precision and efficiency, and the potential of Prime Editing to 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 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.

Investor Contact
Hannah Deresiewicz
Stern Investor Relations, Inc.
212-362-1200
hannah.deresiewicz@sternir.com

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