Prime Medicine Presents In Vivo Proof-of-Concept Data Highlighting Interim Preclinical Advances in its Wilson's Disease Program and the Broad Potential of its Universal Liver-Targeted LNP at ESGCT 31st Annual Congress

October 24, 2024

Delivery of Prime Editors with a proprietary, universal liver-targeted LNP was well tolerated, with no safety concerns or detectable off-target edits observed across multiple preclinical studies

On track to initiate IND-enabling activities for Wilson's Disease program in 4Q 2024, with IND and/or CTA filing expected in 1H 2026

CAMBRIDGE, Mass., Oct. 24, 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 presented data from multiple studies showcasing the potential of its proprietary, universal lipid nanoparticle (LNP) platform to precisely deliver Prime Editors to correct disease-causing mutations in the liver. The *in vivo* proof-of-concept data shared at the European Society of Gene and Cell Therapy (ESGCT) 31st Annual Congress demonstrated successful correction of disease-causing mutations in Wilson's Disease in both mouse and non-human primate (NHP) models. Additionally, the Company highlighted the ability of its universal liver-targeted LNP platform to deliver Prime Editors to correct the underlying mutational cause of Glycogen Storage Disease Type 1b (GSD1b) in humanized mice and NHPs, reinforcing the potential for its modular LNP to support future programs in rare and non-rare liver indications.

"Our liver-targeted LNP platform represents a significant step forward in gene editing, providing a novel framework that can be used repeatedly to generate candidates that we believe can safely and precisely correct pathogenic mutations across a range of liver diseases," said Jeremy Duffield, M.D., Ph.D., Chief Scientific Officer of Prime Medicine. "We believe the modularity of our LNP platform allows us to seamlessly introduce alternative guide RNAs that address different genetic targets, while the shared components of the LNP platform enable increased potency, as well as an improved safety profile and biodistribution compared to other commonly used LNPs in development. The preclinical data from our GSD1b program played a critical role in validating our universal LNP approach, and findings from this work laid the groundwork for our current efforts in Wilson's Disease, where we believe we can efficiently advance our program into the clinic with the potential to deliver benefit to thousands of patients."

Dr. Duffield continued, "At ESGCT, we will present the first *in vivo* data from our Wilson's Disease program. We are very encouraged by these interim results, which show that LNP delivery of our Prime Editors results in efficient editing, well above the threshold anticipated to be necessary to reverse disease manifestations. As we continue to optimize toward our final drug candidate, we expect to share updated data and initiate IND-enabling activities by year end. We remain confident in the potential for our universal LNP to deliver transformative treatments not only for Wilson's Disease and GSD1b, but also for other rare and non-rare liver indications."

Prime Medicine's universal LNP contains a GalNAc-targeting ligand (GalNAc-LNP), a validated mechanism for liver-specific delivery of gene editors. In preclinical studies, delivery of Prime Editors using a GalNAc-LNP has demonstrated increased potency and both an improved safety profile and biodistribution when benchmarked against other LNPs that have gone into the clinic. Preclinical studies in GSD1b animal models, including new data presented at ESGCT, demonstrated that delivery of GalNAc-LNP Prime Editors restored glycogen metabolism in a humanized mouse model and achieved up to 85% precise liver cell editing of the L348 mutation in NHPs at a dose that was well tolerated and durable up to 44 weeks, with an excellent safety profile, and no detectable off-target edits or unintended edits at the target site. The Company believes these findings validate Prime Medicine's LNP platform and support its continued evaluation in other liver-related diseases, including 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 without liver transplant can be fatal. Research suggests that correcting a Wilson's Disease mutation in 20-30% of hepatocytes could be potentially curative. To address Wilson's Disease, Prime Medicine is advancing its GalNAc-LNP Prime Editor program that targets two prevalent mutations in the *ATP7B* gene – H1069Q and R778L – which combined account for up to 50% of Wilson's Disease patients.

In the data presented today, GalNAc-LNP delivery of Prime Editors targeting the H1069Q mutation in Wilson's Disease demonstrated up to 80% precise correction of the H1069Q mutation and restoration of ATP7B mRNA to wild-type levels in a humanized mouse model, as well as precise editing of liver cells in NHPs, with up to 51% precise editing with a surrogate H1069Q Prime Editor. In preclinical studies completed to-date, Prime Medicine observed significant reductions in copper accumulation in the livers of humanized mice. In both mouse and NHP studies, no detectable off-target edits or unintended edits at the target site were observed. Prime Medicine is completing the final stages of lead optimization and expects to initiate IND-enabling activities of its Wilson's Disease program by year-end, with an IND and/or CTA filing expected in the first half of 2026.

Details of the presentations are as follows:

- **Presentation Title:** LNP delivered Prime Editors restore glycemic control in humanized rodent models of Glycogen Storage Disease Type 1b (GSD1b)
  Date & Time: October 24, 2024, 5:00 p.m. CEST
- **Poster Title:** Prime Editing advancements enable *in vivo* therapeutic correction of *ATP7B* p.H1069Q and p.R778L mutations in Wilson's Disease
  Date & Time: October 24, 2024, 6:00 – 7:30 p.m. CEST

About Wilson's Disease
Wilson's Disease is a devastating rare disease of the liver, with manifestations throughout the body, that is caused by copper accumulation. Most

people are diagnosed between ages five and 35 years. With reported prevalence rates ranging between 1 in 10,000 and 1 in 30,000, Wilson's Disease is believed to affect upwards of 35,000 to 100,000 patients in the United States and Europe. Normally, excessive copper is excreted through the liver in bile. For patients with Wilson's Disease, copper is not eliminated correctly and accumulates to toxic levels. While the key site of pathology is the liver, and many patients present with liver disease, patients often show persistent neurological problems including involuntary movements, tremor, and gait disturbance, as well as kidney, hematological or psychiatric problems. Wilson's Disease is caused by mutations, including H1069Q and R778L, in both genomic copies of the *ATP7B* gene, which encodes a copper transporter that removes excess copper. Prime Medicine is advancing a liver-directed Prime Editor program that aims to correct mutations in *ATP7B* to restore copper metabolism.

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: hematology, immunology and oncology, liver and lung. 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 timing, progress, and results of its Wilson's Disease program, including the timing of the release of updated data, IND-enabling activities, and the opening of an IND and/or CTA application; the potential for its modular universal LNP platform to precisely deliver Prime Editors, correct disease-causing mutations in the liver, and deliver transformative treatments for Wilson's Disease, GSD1b, and other rare and non-rare liver indications; the modular universal LNP platform's ability to be used repeatedly to generate candidates that offer an improved safety profile and biodistribution compared to other LNPs in development; the potential for the treatment of Wilson's Disease with Prime Editors to result in efficient editing well above the threshold anticipated to be necessary to reverse disease manifestations; the safety profile, tolerability, and durability of its universal LNP; the initiation, timing, progress, and results of its research and development programs, preclinical studies and future clinical trials; the modularity of the Prime Editing platform and the benefits thereof; the potential for Prime Editors to more precisely and effectively achieve genetic modification; the potential for Prime Editors to repair genetic mutations and offer curative genetic therapies for a wide spectrum of diseases; the potential of Prime Editors to reproducibly correct disease-causing genetic mutations across different tissues, organs and cell types; its expectations regarding the breadth of Prime Editing technology and the implementation of its strategic plans for its business, programs, and technology; and the potential of Prime Editing to unlock opportunities across thousands of potential indications. 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: 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; and the effect of unfavorable macroeconomic conditions or market volatility resulting from 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 and Quarterly Report on Form 10-Q for the quarter ended June 30, 2024, 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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