Prime Medicine Announces U.S. FDA Clearance of Investigational New Drug Application for PM647 in Alpha-1 Antitrypsin Deficiency

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-- Clearance highlights continued execution, modularity and momentum across Prime Medicine's liver franchise, building on recent regulatory clearances for PM577a --

-- Initial clinical data expected in 2027 --

CAMBRIDGE, Mass., Sept. 24, 2026 (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 that the U.S. Food and Drug Administration (FDA) has cleared the Company's Investigational New Drug (IND) application for PM647, an investigational *in vivo* Prime Editor for Alpha-1 Antitrypsin Deficiency (AATD). The clearance enables PM647 to proceed to clinical study initially in the United States, where approximately 100,000 people carry the PiZZ genotype that PM647 is designed to correct.

"FDA clearance of the PM647 IND is an important milestone for Prime Medicine, marking continued momentum across our liver franchise," said Allan Reine, M.D., Chief Executive Officer of Prime Medicine. "PM647 has the potential to change how AATD is treated, offering a Prime Editing-based approach that moves beyond protein replacement and targets the root cause of disease. By correcting the underlying mutation and restoring production of fully functional AAT, PM647 may simultaneously address both lung and liver manifestations of AATD and provide a differentiated, one-time treatment approach for patients. Beyond its therapeutic potential, PM647 demonstrates the repeatability and productivity of Prime Medicine's platform. Just months after regulatory clearances for PM577a, the advancement of PM647 into clinical development also reinforces how Prime Medicine's modular platform and universal liver LNP can support the rapid progression of multiple programs."

Phase 1/2 Clinical Trial

The Phase 1/2 clinical trial will be a global, single-arm, open-label, first-in-human study designed to evaluate the safety, tolerability and preliminary clinical efficacy of ascending doses of a one-time intravenous infusion of PM647 in adults with AATD. The study will initially enroll adult participants with lung-only manifestations of AATD. Upon demonstration of tolerability in lung-only participants, the study will expand to include a separate cohort enrolling adults with significant liver disease, with or without concurrent lung manifestations of AATD.

About PM647

PM647 is an investigational, one-time *in vivo* Prime Editor designed to correct the E342K (Pi*Z) mutation in the SERPINA1 gene, the most common cause of AATD. By correcting the mutation at its source, PM647 is designed to restore production of functional M-AAT and address both the liver and lung manifestations of the disease. In fully humanized mouse models, PM647 achieved high editing efficiency and restored corrected M-AAT protein into the healthy human range at clinically relevant doses with a single infusion. PM647 uses the same liver-directed lipid nanoparticle (LNP) as PM577a, Prime Medicine's investigational program for Wilson disease.

About Alpha-1 Antitrypsin Deficiency

Alpha-1 Antitrypsin Deficiency is an inherited genetic disorder caused by variants in the *SERPINA1* gene. In people with severe disease, insufficient functional alpha-1 antitrypsin can lead to progressive lung damage, while accumulation of mutant protein in the liver can cause progressive liver disease. Patients have no approved curative treatment that addresses the underlying genetic cause of both manifestations of the disease. Approximately 200,000 people are estimated to carry the PiZZ genotype across United States and Europe.

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 its 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 potential of PM647 to

correct the causative mutations of, and to treat, AATD; the Phase 1/2 clinical trial of PM647, including the trial design, global reach of the trial and the anticipated timing of initial clinical data in 2027; the continued development and advancement of the Company's AATD and Wilson disease programs; the modularity of the Prime Editing platform and universal liver LNP and the benefits thereof; and the potential of Prime Editing to unlock opportunities across thousands of potential indications.

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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