Prime Medicine Unveils Program for the Treatment of Alpha-1 Antitrypsin Deficiency (AATD)

March 18, 2025

-- Prime Editing has potential to be best-in-class approach for AATD --

-- Previously undisclosed program now emerging from within liver platform; leverages proprietary, universal liver LNP --

-- High levels of editing at the target site in preclinical studies with full restoration of circulating wild-type AAT protein (M-AAT) to normal human range --

-- Expects to file IND and/or CTA in mid-2026 --

CAMBRIDGE, Mass., March 18, 2025 (GLOBE NEWSWIRE) -- Prime Medicine, Inc. (Nasdaq: PRME), a biotechnology company committed to delivering a new class of differentiated one-time curative genetic therapies, today unveiled a preclinical program for the treatment of alpha-1 antitrypsin deficiency (AATD), the next program within its liver franchise. Prime Medicine expects to file an investigational new drug (IND) and/or clinical trial application (CTA) in mid-2026.

"We are excited to announce our AATD program, the second high-value program to emerge from our liver franchise, and the second liver program that we expect to advance into the clinic next year," said Keith Gottesdiener, M.D., President and Chief Executive Officer of Prime Medicine. "This program exemplifies our strategy of using our proprietary, modular liver LNP to accelerate the development of new Prime Editors, as well as our ability to leverage learnings, regulatory frameworks and manufacturing synergies to efficiently advance our efforts. We look forward to progressing our AATD and Wilson's Disease programs toward clinical data in 2027, where we hope to demonstrate Prime Editing's best-in-class potential across two of the largest genetic liver diseases."

Dr. Gottesdiener continued, "We are also pleased to share the first *in vivo* preclinical data for our AATD program. These data reinforce the potential of Prime Editing to restore the disease-causing mutation back to wild-type and address the underlying pathology of both lung and liver manifestations of AATD, without the risk of bystander edits or detectable off-target edits."

Prime Medicine's Approach to AATD

Prime Medicine's program leverages the Company's universal liver lipid nanoparticle (LNP) to edit the E342K (Pi*Z) mutation in the SERPINA1 gene, the prevalent disease-causing mutation in AATD, restoring the mutated protein sequence back to wild-type M protein, with the potential to treat both lung- and liver-associated disease.

In Prime Medicine's initial *in vivo* data, LNP delivery of Prime Editors targeting the Pi*Z (E342K) mutation demonstrated up to 72% precise correction of the SERPINA1 gene in the hepatocytes of fully humanized mice. Importantly, this restored over 95% of serum AAT to the corrected isoform, with healthy AAT (M-AAT) protein in the serum at levels well above 20μM, indicating restoration of M-AAT to normal levels in a humanized mouse model.

Prime Medicine's universal LNP contains a GalNAc-targeting ligand (GalNAc-LNP), a validated component 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 using unoptimized surrogate Prime Editors for genetic diseases in non-human primate (NHP) models showed greater than 50% editing, with an excellent safety profile, and no detectable off-target edits or unintended edits at the target site. Based on these data, Prime Medicine believes Prime Editing has the ability to correct disease-causing mutations with high efficiency, without introducing off-target or bystander edits.

Prime Medicine is advancing its AATD program through the final stages of lead optimization and expects to file an IND and/or CTA filing in mid-2026.

About AATD

AATD is a progressive, genetic disorder caused by mutations in the SERPINA1 gene; these mutations lead to decreased levels of circulating AAT protein in the blood, as well as the build-up of toxic mutant AAT protein in the liver. Because the primary function of AAT is to protect lungs from inflammation caused by infection and inhaled irritants, low levels of circulating AAT can result in lung-related symptoms, including shortness of breath, wheezing, chronic cough and frequent chest colds. Additionally, the build-up of abnormal AAT in the liver can cause jaundice, ascites, and cirrhosis. There are currently no disease-modifying or curative treatments approved for the approximately 200,000 people in the United States and European Union with AATD, and many patients ultimately progress to liver failure or severe lung disease, eventually resulting in premature death.

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.

© 2025 Prime Medicine, Inc. All rights reserved. PRIME MEDICINE, the Prime Medicine logos, and PASSIGE are trademarks of Prime Medicine, Inc. All other trademarks referred to herein are the property of their respective owners.

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 continued development and advancement of its AATD and Wilson's Disease programs, including the timing for release of clinical data in 2027; the timing for completion of lead optimization of the AATD program and filing of IND and/or CTA applications in mid-2026; the potential of Prime Editing to correct the causative mutation of AATD and Wilson's Disease; 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: 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.

Investor Contacts

Gregory Dearborn
Prime Medicine
713-503-3364
gdearborn@primemedicine.com

Hannah Deresiewicz
Precision AQ
212-362-1200
hannah.deresiewicz@precisionaq.com

Media Contact

Dan Budwick, 1AB
dan@1ABmedia.com