Prime Medicine Unveils Strategically Focused Pipeline

September 30, 2024

-- Prioritizing Set of High Value Programs in Core Areas of Focus; Modularity of Prime Editing Platform Expected to Allow Prime Medicine to Generate Follow-on Candidates Rapidly and Efficiently --

-- Initial Clinical Data from Phase 1/2 Trial in CGD Expected in 2025 While Advancing Wilson's Disease Program Toward Expected IND Application and/or CTA in 1H 2026 --

-- Today Announced Strategic Research Collaboration and License Agreement with Bristol Myers Squibb to Develop and Commercialize Multiple Prime Edited Ex Vivo T-cell Therapies --

-- Together with $110 Million Upfront Consideration Received Under Agreement with Bristol Myers Squibb, Anticipated Cost Savings are Expected to Extend Cash Runway into the First Half of 2026 --

CAMBRIDGE, Mass., Sept. 30, 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 announced that it is focusing its pipeline 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.

"We founded Prime Medicine with a singular vision: to apply our groundbreaking Prime Editing platform to address the genetic causes of debilitating diseases and provide patients with long-lasting cures," said Keith Gottesdiener, M.D., President and Chief Executive Officer of Prime Medicine. "Over the past four years, we have started to translate this vision into reality, advancing PM359 into the clinic and generating preclinical data that show we can reproducibly and durably correct disease causative mutations in multiple cell types and successfully deliver Prime Editors across target tissues. In addition, we are encouraged by recent commentary from the U.S. Food and Drug Administration, which is increasingly supportive of modular approaches to developing genetic therapies, for which we believe Prime Editing is uniquely suited. We believe that Prime Medicine has the potential to change the treatment paradigm for a wide range of diseases, which collectively impact millions of people."

Dr. Gottesdiener continued, "In order to maximize Prime Editing's reach, we believe now is the time to strategically focus our efforts on a set of high value programs. Importantly, each prioritized program is intended to serve as a beachhead, allowing us to advance our technological leadership across a number of target tissues and cell types, while providing insights into research and development, regulatory strategy, CMC and delivery that will potentially allow us to progress our follow-on programs more rapidly and efficiently. In parallel, we plan to continue to leverage strategic business development, such as the collaboration with Bristol Myers Squibb that we announced this morning, to further extend Prime Editing's reach. We expect to share first-in-human clinical data from our Phase 1/2 trial in CGD in 2025 and new preclinical data for our Wilson's Disease program in the fourth quarter of 2024, as we work to bring this paradigm-shifting technology to patients."

Prime Medicine's Focused Pipeline

Hematology, Immunology & Oncology

Prime Medicine will focus on the development of two programs for the treatment of chronic granulomatous disease (CGD), which together have the potential to address the vast majority of people living with CGD:

- **PM359, an *ex vivo* autologous hematopoietic stem cell (HSC) product for the treatment of p47^{phox} CGD**. Approximately one quarter of patients with CGD present with a mutation in p47^{phox}. In April 2024, the U.S. Food and Drug Administration (FDA) cleared Prime Medicine's investigational new drug (IND) application for PM359, less than one month after the IND filing. The Company has initiated a Phase 1/2 clinical trial to assess the safety, biological activity and preliminary efficacy of PM359 in adult and pediatric patients and continues to expect initial clinical data from the study in 2025. Once proof-of-concept is established, Prime Medicine expects to advance PM359 rapidly into a pivotal study. PM359 has received rare pediatric drug designation and orphan drug designation from the FDA.

- ***Ex vivo* HSC product for the treatment of X-linked CGD.** Prime Medicine today announced its first follow-on program in hematology and immunology. Building on its efforts in p47^{phox} CGD, Prime Medicine is advancing a program for X-linked CGD, which utilizes its Prime Assisted Site-Specific Integrate Gene Editing (PASSIGE™) technology, and is expected to address over 90 percent of known mutations in the *CYBB* gene with a single approach. Mutations in the *CYBB* gene occur in approximately two thirds of patients with CGD. Prime Medicine intends to leverage modular elements from across the PM359 program, including the IND filing, chemistry, manufacturing and controls (CMC) work and clinical trial, with the aim to accelerate advancement of its X-CGD program.

BMS Collaboration:

- ***Ex vivo* T-Cell Therapies**. As announced this morning, Prime Medicine entered into a strategic research collaboration and license agreement with Bristol Myers Squibb, a global leader in cell therapy for hematology, immunology, and oncology, to develop and commercialize multiple Prime Edited *ex vivo* T-cell therapies. Under the terms of the agreement, Prime

Medicine will design optimized Prime Editor and PASSIGE reagents for a select number of targets in immunological diseases and cancer; Bristol Myers Squibb will be responsible for development, manufacturing and commercialization of the next generation cell therapies, with support from Prime Medicine in gene editing strategy and reagent development. Under the terms of the agreement, Prime Medicine will receive a $55 million upfront payment and a $55 million equity investment from Bristol Myers Squibb. Prime Medicine is also eligible to receive more than $3.5 billion in milestones, including up to $1.4 billion in development milestones and more than $2.1 billion in commercialization milestones, along with royalties on net sales.

Liver

- **Lipid nanoparticle (LNP) Prime Editor for the treatment of Wilson's Disease** . Prime Medicine is focused on advancing its Wilson's Disease program, which targets prevalent mutations in the *ATP7B* gene. Prime Medicine expects to present new preclinical data and initiate IND-enabling activities for this program in the fourth quarter of 2024, and intends to file an IND and/or clinical trial application (CTA) in the first half of 2026. The program will use Prime Medicine's universal LNP, a multi-component and modular delivery system that the Company expects will be used across all liver disease programs, allowing more rapid and cost-efficient expansion into follow-on rare and non-rare liver indications.

Lung

- **LNP / adeno-associated virus (AAV) Prime Editors for the treatment of Cystic Fibrosis (CF).** With funding from the Cystic Fibrosis Foundation, Prime Medicine is continuing to advance two strategies to potentially cure CF: hotspot editing and PASSIGE. Using hotspot editing, the Company aims to address multiple mutations at mutational hotspots with a small number of Prime Editors; using PASSIGE, the Company aims to address nearly all people with CF with a single superexon insertion strategy. Through the Cystic Fibrosis Foundation, Prime Medicine has access to infrastructural support and foundational guidance, including established assays, animal models reagents and patient samples, which may accelerate advancement of the Company's Prime Editors for CF.

Additional Programs
In order to pursue its prioritized high value programs as rapidly as possible, the Company is identifying partnership opportunities to advance its other programs, including those for neurological diseases, cell therapy, ocular diseases and hearing loss. Prime Medicine expects that business development will continue to play a critical role in accelerating and funding its pipeline, allowing the Company to maximize the potential and reach of Prime Editing, including in areas outside its core focus. Prime Medicine may also choose to advance these programs through internal efforts in the future.

Updated Financial Guidance
As a result of this strategic pipeline prioritization, Prime Medicine will streamline its operating expenses and capital expenditures. Together with the $110 million upfront consideration received from Bristol Myers Squibb under the strategic research collaboration and license agreement announced this morning, Prime Medicine expects its cash runway to fund operations into the first half of 2026.

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.

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 PM359 to correct the causative mutation of CGD; the anticipated maturation into a clinical-stage company by bringing PM359 into clinical development in 2024 with initial clinical data from the ongoing Phase 1/2 clinical trial of PM359 expected in 2025; 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; the collaboration with Bristol Myers Squibb and the intended and potential benefits thereof, including the receipt of potential milestone and royalty payments from commercial product sales, if any; certain activities and next steps to support the Company's maturation into a clinical-stage company, including opening an IND and/or CTA application, clinical data expectations, establishing proof-of-concept, advancing programs into lead optimization, advancing preclinical studies and initiating IND-enabling activities, and establishing AAV delivery platform and route of administration for neuromuscular programs; 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, and the capacity of its Prime Editing and PASSIGE technology to edit CAR-T cells for the treatment of certain cancers and immune diseases; its ability to demonstrate superior off-target profiles for Prime Editing programs; exploring business development opportunities that could accelerate existing work and the benefits thereof; the modularity of the Prime Editing platform and the benefits thereof; its expectations regarding the breadth of Prime Editing technology and the implementation of its strategic plans for its business, programs, and technology; the potential of Prime Editing to unlock opportunities across thousands of potential indications; and its expected cash runway.. 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 development and optimization of new technologies; 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; 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; and Prime Medicine’s expectations regarding the anticipated timeline of its cash runway and future financial performance. 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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