Prime Medicine Presents First In Vivo Proof-of-Concept Prime Editing Data Demonstrating Ability of Prime Editors to Treat Ophthalmological Diseases

October 24, 2023

New In Vivo Data in Humanized Mouse Model Demonstrate that Prime Editing Can Correct Predominant Mutations Accounting for Approximately 60% of Patients with RHO adRP

Up to 70% Precise Correction at RHO p.P23H Mutation and up to 65% at RHO p.V345L and p.P347L, Well Above Threshold Required to Stop Disease Progression in Photoreceptors

No Detectable AAV Genome Integration and No Detectable Off-target Edits Observed

Data Presented Today in an Oral Presentation at RD2023

CAMBRIDGE, Mass., Oct. 24, 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 Prime Editors to efficiently and precisely correct the predominant mutations that cause rhodopsin associated autosomal dominant retinitis pigmentosa (RHO adRP). The data were presented today at the International Symposium on Retinal Degeneration 2023 Congress (RD2023) in Costa del Sol, Spain.

RHO adRP is a rare inherited retinal disease that causes progressive vision loss in early adolescence, leading to eventual blindness in adulthood due to photoreceptor degeneration. It results from mutations in the gene *RHO,* which encodes rhodopsin, the light-sensitive G protein-coupled receptor involved in phototransduction in rods, a type of photoreceptor, and leads to the progressive loss of rods and, subsequently, cones in the retina.

“The data presented today are the first proof-of-concept data for Prime Editing’s application in treating ophthalmological indications, and highlight the ability of Prime’s novel, dual AAV delivery platform to efficiently deliver Prime Editors to the eye,” said Jeremy Duffield, M.D., Ph.D., Chief Scientific Officer of Prime Medicine. “Specifically, today’s data highlight the ability of two Prime Editors to correct the predominant mutations causing RHO adRP – one to correct p.P23H, the most common disease-causing mutation in *RHO* in the U.S., and one to correct 18 different mutations at a mutational hotspot in *RHO*, including p.V345L and p.P347L, which are the most prevalent mutations in Europe. With no detected off-target edits in human photoreceptors and no AAV integrations observed in these studies, today’s results are a positive step forward for those living with RHO adRP, for whom there are currently no approved treatment options.”

To address the predominant mutations causing RHO adRP, Prime Medicine conducted comprehensive high-throughput screening of more than 1,000 Prime Editor guide RNAs (pegRNAs). Two potent Prime Editors were identified – one that precisely corrected *RHO* p.P23H located near the N-terminus of rhodopsin, and one that precisely corrected the mutational hotspot located near the C-terminus, which includes 18 pathogenic mutations including *RHO* p.V345L and p.P347L. The Company then developed and optimized a proprietary dual AAV system to deliver the Prime Editors via subretinal injection in humanized mouse models. Prime Editor performance was assessed in a suite of in vitro assays and demonstrated up to 45% correction at *RHO* p.P23H, and more than 70% correction at *RHO* p.V345L and p.P347L. According to scientific literature and Prime Medicine research, 25% correction at both *RHO* p.P23H and the C-terminal mutational hotspot may be sufficient to halt progression of RHO adRP, and correcting these mutations has the potential to benefit approximately 60% of patients living with this disease.

In today’s presentation at RD2023, Prime Medicine shared findings from in vivo studies in humanized mice with its Prime Editors targeting these prevalent RHO mutations. Key findings from these studies showed:

- Up to 70% precise correction in photoreceptors at *RHO* p.P23H and up to 65% at *RHO* p.V345L or p.P347L at a mutational hotspot using Prime Editors delivered by a dual AAV system via subretinal injection with less than 0.5% on-target unintended edits detected.
- Efficient delivery of Prime Editors by dual AAV to human (retinal explants) and murine (in vivo) photoreceptors.
- *RHO* correction well tolerated with no detectable changes in retinal thickness or glial fibrillary acidic protein (GFAP) gene expression.
- No measurable integration of the AAV vector at the edit site, as measured by one-sided polymerase chain reaction (PCR).
- No detectable off-target edits observed in human photoreceptors following a genome-wide off-target screening analysis.

These results demonstrated that Prime Medicine’s proprietary dual AAV system effectively delivered Prime Editors to the eye with high efficiency and precisely corrected pathogenic mutations causing RHO adRP at high efficiencies well above the levels believed to have the potential to halt disease progression.

Presentation Details

- **Title:** Prime Editors efficiently and precisely correct pathological mutations causing rhodopsin associated autosomal dominant retinitis pigmentosa (adRP)
- **Date:** October 24, 2023
- **Location:** Costa del Sol, Spain

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, the ability of Prime Editors to correct the causative mutation of RHO adRP, its ability to expand preclinical proof-of-concept in vivo data in humanized mouse models, its ability to demonstrate superior off-target profiles for Prime Editing programs for the treatment of ophthalmological diseases, and the potential for Prime Editors to repair genetic mutations. 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.

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