Precision BioSciences Presents Preclinical Data Highlighting PBGENE-PMM as a Potential Therapy for Primary Mitochondrial Myopathy

March 19, 2024 at 7:00 AM EDT

- Data presented at Mitochondrial Medicine Therapeutic Development (MMTD) annual conference demonstrated ARCUS' ability to efficiently eliminate mutant mitochondrial DNA without nuclear off-target editing

- PBGENE-PMM shifted heteroplasmy by eliminating mutant m.3243 mitochondrial DNA (mtDNA) while repopulating wild type mtDNA, leading to improved mitochondrial function in cells

- Precision expects to submit a CTA and/or IND for PBGENE-PMM in 2025

DURHAM, N.C.--(BUSINESS WIRE)--Mar. 19, 2024-- Precision BioSciences, Inc. (Nasdaq: DTIL), an advanced gene editing company utilizing its novel proprietary ARCUS® platform to develop in vivo gene editing therapies for sophisticated gene edits, including gene elimination, insertion, and excision, today announced a poster presentation highlighting new data for the Company's PBGENE-PMM program, evaluating an ARCUS nuclease as a potential treatment for m.3243-associated primary mitochondrial myopathy (PMM). These data are being presented at the Mitochondrial Medicine – Therapeutic Development Annual Conference, being held from March 18-20, 2024 in Hinxton, UK.

"Today's data from our PBGENE-PMM program further validate our work with ARCUS and continue to demonstrate its ability to make precise edits while avoiding off-target activity," said Jeff Smith, PhD, Chief Research Officer of Precision BioSciences. "We believe ARCUS is uniquely suited for editing mitochondrial DNA due to its ability to discriminate a single nucleotide difference, making it ideal for editing point mutations such as m.3243. PBGENE-PMM is designed to eliminate mutant mitochondrial DNA leaving normal functioning wild-type mitochondrial DNA intact to repopulate the cell, resulting in a shift in heteroplasmy and improvement in mitochondrial function."

Smith continued, "Additionally, ARCUS can cross mitochondrial membranes in order to access the mitochondrial DNA. This is possible because ARCUS is a protein-only editor with both recognition and catalytic activity all in one single protein that does not require a guide-RNA. This is not possible for CRISPR-derived editors such as CRISPR-Cas, Base and Prime editors. We look forward to advancing PBGENE-PMM towards clinical readiness this year and anticipate filing a CTA and/or IND submission in 2025."

Details for the presentation are as follows:

Title: Shifting m.3243A>G heteroplasmy with PBGENE-PMM: Gene editing therapy for primary mitochondrial myopathy
Poster: P22
Presenter: Wendy Shoop, PhD, Research Lead, Precision Biosciences
Date and Time: Tuesday, March 19, 2024, 6:00-7:00 PM GMT
Location: Hinxton Hall Conference Centre, Wellcome Genome Campus, U.K.

In preclinical work presented today, ARCUS demonstrated highly selective elimination of mutant m.3423G mtDNA. PBGENE-PMM, which contains both a mitochondrial targeting sequence and a nuclear export signal, was found to localize exclusively to mitochondria and without any detectable off-target editing in the nuclear genome. As the m.3243A>G mutation only differs from the wild-type sequence by a single nucleotide, PBGENE-PMM was optimized to prevent cutting of wild-type mtDNA while maintaining activity against mutant mtDNA. When evaluated in cells that contain heteroplasmic m.3243A>G mtDNA, PBGENE-PMM-treated cells were found to contain 0.3% mutant mtDNA three days post-transfection, compared to control cells which contained 95% mutant mtDNA. This robust shift in heteroplasmy resulted in a nearly two-fold increase in both basal and maximal respiration. Together, these data support the development of PBGENE-PMM as a single-treatment, in vivo gene editing therapeutic for m.3243-associated primary mitochondrial myopathy.

About PBGENE-PMM

PBGENE-PMM is our wholly-owned, first of its kind treatment for m.3243 associated primary mitochondrial myopathy (PMM). Mitochondrial diseases are the most common hereditary metabolic disorder, affecting 1 in 4,300 people. PMM currently lacks a curative treatment and impacts approximately 50% of patients with mitochondrial disease. In the Company's 2023 publication in *Nature Metabolism*, Precision presented new data highlighting the high specificity and single component nature of the PBGENE-PMM and ability to specifically edit and eliminate mutant mitochondrial DNA while allowing wild-type (normal) mitochondrial DNA to repopulate in the mitochondria, thus restoring normal function. Precision expects to submit a CTA and/or IND for this program in 2025.

About ARCUS

ARCUS is a proprietary genome editing technology discovered and developed by scientists at Precision BioSciences. It uses sequence-specific DNA-cutting enzymes, or nucleases, that are designed to either insert (knock-in), excise (knock-out), eliminate, or repair DNA of living cells and organisms. ARCUS is based on a naturally occurring genome editing enzyme, I-CreI, that evolved in the algae *Chlamydomonas reinhardtii* to make highly specific cuts in cellular DNA and stimulate gene insertion at the cut site by homologous recombination. Precision's platform and products are protected by a comprehensive portfolio including more than 130 patents to date.

About Precision BioSciences, Inc.

Precision BioSciences, Inc. is an advanced gene editing company dedicated to improving life (DTIL) with its novel and proprietary ARCUS® genome editing platform that differs from other technologies in the way it cuts, its smaller size, and its simpler structure. ARCUS is a highly precise and versatile genome editing platform that was designed with therapeutic safety, delivery, and control in mind. Using ARCUS, the Company's pipeline is comprised of in vivo gene editing candidates designed to deliver lasting cures for the broadest range of genetic and infectious diseases where no adequate treatments exist. For more information about Precision BioSciences, please visit www.precisionbiosciences.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding the therapeutic potential of an ARCUS gene editing approach for the treatment of m.3243-associated PMM, including the ability of ARCUS to preferentially target and eliminate mutant m.3243G mtDNA with high specificity and without off-target activity, anticipated timing of a CTA and/or IND filing, the ability of mitoARCUS to shift heteroplasmy, and expected safety, efficacy, and benefit of our gene editing approaches.. In some cases, you can identify forward-looking statements by terms such as "aim," "anticipate," "approach," "believe," "contemplate," "could," "designed", "estimate," "expect," "goal," "intend," "look," "may," "mission," "plan," "possible," "potential," "predict," "project," "pursue," "should," "target," "will," "would," or the negative thereof and similar words and expressions.

Forward-looking statements are based on management's current expectations, beliefs and assumptions and on information currently available to us. These statements are neither promises nor guarantees, and involve a number of known and unknown risks, uncertainties and assumptions, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various important factors, including, but not limited to, our ability to become profitable; our ability to procure sufficient funding to advance our programs; risks associated with our capital requirements, anticipated cash runway, requirements under our current debt instruments and effects of restrictions thereunder, including our ability to raise additional capital due to market conditions and/or our market capitalization; our operating expenses and our ability to predict what those expenses will be; our limited operating history; the progression and success of our programs and product candidates in which we expend our resources; our limited ability or inability to assess the safety and efficacy of our product candidates; the risk that other genome-editing technologies may provide significant advantages over our ARCUS technology; our dependence on our ARCUS technology; the initiation, cost, timing, progress, achievement of milestones and results of research and development activities and preclinical and clinical studies, including clinical trial and investigational new drug applications; public perception about genome editing technology and its applications; competition in the genome editing, biopharmaceutical, and biotechnology fields; our or our collaborators' or other licensees' ability to identify, develop and commercialize product candidates; pending and potential product liability lawsuits and penalties against us or our collaborators or other licensees related to our technology and our product candidates; the U.S. and foreign regulatory landscape applicable to our and our collaborators' or other licensees' development of product candidates; our or our collaborators' or other licensees' ability to advance product candidates into, and successfully design, implement and complete, clinical or field trials; potential manufacturing problems associated with the development or commercialization of any of our product candidates; delays or difficulties in our and our collaborators' and other licensees' ability to enroll patients; changes in interim "top-line" and initial data that we announce or publish; if our product candidates do not work as intended or cause undesirable side effects; risks associated with applicable healthcare, data protection, privacy and security regulations and our compliance therewith; our or our licensees' ability to obtain orphan drug designation or fast track designation for our product candidates or to realize the expected benefits of these designations; our or our collaborators' or other licensees' ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations and/or warnings in the label of an approved product candidate; the rate and degree of market acceptance of any of our product candidates; our ability to effectively manage the growth of our operations; our ability to attract, retain, and motivate executives and personnel; effects of system failures and security breaches; insurance expenses and exposure to uninsured liabilities; effects of tax rules; effects of the COVID-19 pandemic and variants thereof, or any pandemic, epidemic, or outbreak of an infectious disease; the success of our existing collaboration agreements, and our ability to enter into new collaboration arrangements; our current and future relationships with and reliance on third parties including suppliers and manufacturers; our ability to obtain and maintain intellectual property protection for our technology and any of our product candidates; potential litigation relating to infringement or misappropriation of intellectual property rights; effects of natural and manmade disasters, public health emergencies and other natural catastrophic events; effects of sustained inflation, supply chain disruptions and major central bank policy actions; market and economic conditions; risks related to ownership of our common stock, including fluctuations in our stock price; our ability to meet the requirements of and maintain listing of our common stock on Nasdaq or other public stock exchanges; and other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2023, as any such factors may be updated from time to time in our other filings with the SEC, which are accessible on the SEC's website at https://www.sec.gov/ and the Investors page of our website under SEC Filings at investor.precisionbiosciences.com.

All forward-looking statements speak only as of the date of this press release and, except as required by applicable law, we have no obligation to update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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