Precision BioSciences Announces New Study Published in Nature Communications Using Engineered ARCUS Nuclease to Target Mutant Mitochondrial DNA In Vivo

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Learnings to be Presented by Carlos Moraes, Ph.D., from University of Miami at UMDF's Mitochondrial Medicine Symposium on June 4, 2021

DURHAM, N.C.--(BUSINESS WIRE)--Jun. 1, 2021-- Precision BioSciences, Inc. (Nasdaq: DTIL), a clinical stage biotechnology company developing allogeneic CAR T and *in vivo* gene correction therapies with its ARCUS® genome editing platform, today announced a new paper published online in *Nature Communications* that reports preclinical results using an ARCUS nuclease to target mitochondrial DNA (mtDNA) and reduce levels of mutant mtDNA *in vivo*.

The study, "Mitochondrial targeted meganuclease as a platform to eliminate mutant mtDNA in vivo" was led by Carlos T. Moraes, Ph.D., Esther Lichtenstein Professor in Neurology at the University of Miami Miller School of Medicine, with Ugne Zekonyte as first author.

Mitochondrial disorders impair the function of mitochondria, the organelles that produce the energy needed by cells. Organs and tissues that require more energy, such as the heart, muscles and brain, are more often affected. Additionally, both mutant and wild-type mtDNA can co-exist within the mitochondria of a cell, a phenomenon called mtDNA heteroplasmy. When specific threshold levels of mutant mtDNA are reached, cell function can be compromised, and disease can manifest[1]. It is believed that a shift in mtDNA heteroplasmy toward wild-type may provide therapeutic benefit for patients, and not all mutant mtDNA must be eliminated to achieve improvements in symptoms; mutant mtDNA levels just need to be reduced below the disease threshold level.

"In the past, mitochondrial-targeted nucleases have been successful in shifting mtDNA heteroplasmy but have come with unwanted drawbacks, most notably large size, heterodimeric nature, inability to distinguish single base changes, or low flexibility and effectiveness," said Dr. Moraes. "In this study, a mitochondrial-targeted ARCUS nuclease (mitoARCUS) used to edit mutant mtDNA was particularly effective, in part because of the nuclease's small size and single protein nature. We are very excited with this early research and the great promise we believe it suggests for using ARCUS editing in patients with mtDNA diseases in the future."

Researchers involved with the study reported mitoARCUS-induced heteroplasmic shifts of up to 60% *in vitro*, with changes persisting for up to three weeks. When tested in a heteroplasmic mouse model, mitoARCUS delivered by AAV effectively shifted heteroplasmy towards wild-type in several of the analyzed tissues of juvenile mice, with no depletion in total mtDNA levels at 6, 12, or 24 weeks. In adult mice treated with AAV-mitoARCUS, there was no editing at any of the potential nuclear off-target sites, and liver and skeletal muscle showed robust elimination of mutant mtDNA with concomitant restoration of mitochondrial transfer RNA levels.

"This is the first time ARCUS has been used to edit outside the nuclear genome and has done so with encouraging safety and efficacy in this mouse model," said Derek Jantz, Ph.D., co-author of the paper and Chief Scientific Officer at Precision BioSciences. "We continue to see promising results in preclinical studies suggesting that ARCUS could potentially effectively edit mutant mtDNA *in vivo* in human clinical trials. I congratulate Carlos and his team on this research and look forward to further work on this program."

Dr. Moraes will discuss this paper during the United Mitochondrial Disease Foundation's Mitochondrial Medicine 2021 Virtual " Meet the Scientific Program Faculty" on Friday, June 4, 2021 at 12:00 PM EDT.

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), remove (knock-out), 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. Precision's platform and products are protected by a comprehensive portfolio including more than 75 patents to date.

About Precision BioSciences, Inc.

Precision BioSciences, Inc. is a clinical stage biotechnology company dedicated to improving life (DTIL) with its wholly proprietary ARCUS® genome editing platform. ARCUS is a highly specific and versatile genome editing platform that was designed with therapeutic safety, delivery, and control in mind. Using ARCUS, the Company's pipeline consists of multiple "off-the-shelf" CAR T immunotherapy clinical candidates and several *in vivo* gene correction therapy candidates to cure 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 potential results, uses and advancement of our in vivo gene editing programs and ARCUS-based gene editing technology, including, without limitation, its differentiating attributes and effects in shifting mtDNA heteroplasmy and upon mtDNA diseases. In some

cases, you can identify forward-looking statements by terms such as “aim,” “anticipate,” “believe,” “could,” “expect,” “should,” “plan,” “intend,” “estimate,” “target,” “mission,” “goal,” “may,” “will,” “would,” “should,” “could,” “target,” “potential,” “project,” “predict,” “contemplate,” “potential,” “suggests”, 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. Such statements are subject to 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 and requirements under our current debt instruments and effects of restrictions thereunder; risks associated with raising additional capital; our operating expenses and our ability to predict what those expenses will be; our limited operating history; the 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; our dependence on our ARCUS technology; the initiation, cost, timing, progress, achievement of milestones and results of research and development activities, preclinical or greenhouse studies and clinical or field trials; public perception about genome editing technology and its applications; competition in the genome editing, biopharmaceutical, biotechnology and agricultural biotechnology fields; our or our collaborators’ ability to identify, develop and commercialize product candidates; pending and potential liability lawsuits and penalties against us or our collaborators related to our technology and our product candidates; the U.S. and foreign regulatory landscape applicable to our and our collaborators’ development of product candidates; our or our collaborators’ 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; our or our collaborators’ 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; our ability to obtain an adequate supply of T cells from qualified donors; our ability to achieve our anticipated operating efficiencies at our manufacturing facility; delays or difficulties in our and our collaborators’ 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; the rate and degree of market acceptance of any of our product candidates; 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; our ability to effectively manage the growth of our operations; our ability to attract, retain, and motivate key executives and personnel; market and economic conditions; effects of system failures and security breaches; effects of natural and manmade disasters, public health emergencies and other natural catastrophic events effects of the outbreak of COVID-19, or any pandemic, epidemic or outbreak of an infectious disease; insurance expenses and exposure to uninsured liabilities; effects of tax rules; risks related to ownership of our common stock and other important factors discussed under the caption “Risk Factors” in our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2021, as any such factors may be updated from time to time in our other filings with the SEC. These filings are accessible on the SEC’s website at www.sec.gov and the Investors & Media page of our website 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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[1] Craven, L., et al., *Recent Advances in Mitochondrial Disease.* Annu Rev Genomics Hum Genet, 2017. 18: p. 257-275.

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