Precision BioSciences Announces Preclinical Data Showcasing Premier In Vivo Gene Editing Capabilities at American Society of Gene & Cell Therapy Annual Meeting

May 16, 2022

Multiple Oral Presentations and Posters to Demonstrate Differentiated Attributes of ARCUS® Genome Editing Platform for Efficient Gene Insertion and Gene Knockout

New Primary Hyperoxaluria Type 1 (PH1) Preclinical Data Demonstrate a Robust ARCUS Nuclease Optimization Process Leading to 98% Knockdown of HAO1 Protein in Non-human Primates (NHP)

DURHAM, N.C.--(BUSINESS WIRE)--May 16, 2022-- Precision BioSciences, Inc. (Nasdaq: DTIL), a clinical stage gene editing company developing ARCUS-based *ex vivo* allogeneic CAR T and *in vivo* gene editing therapies, today announced preclinical data will be presented this week on ARCUS genome editing including two oral presentations and two posters at the American Society of Gene & Cell Therapy (ASGCT), May 16-19, 2022 at the Walter E. Washington Convention Center in Washington, D.C.

"The preclinical findings presented this week at the ASGCT conference are very encouraging and further support our novel gene editing approach with ARCUS and our plans to advance three wholly owned product candidates, PBGENE-PH1, PBGENE-HBV and PBGENE-PCSK9, to the clinic over the next three years," said Derek Jantz, Ph.D., Chief Scientific Officer and Co-founder of Precision BioSciences. "Translating these preclinical results to the clinic will further validate ARCUS as a premier gene editing platform with the precision and versatility needed to develop novel therapeutics that aim to deliver functional cures for conditions including PH1 and chronic hepatitis B."

Oral Presentations:

Abstract #447: *Targeting the Hepatitis B cccDNA with a Sequence-Specific ARCUS Nuclease to Eliminate Hepatitis B Virus In Vivo*

Data from this preclinical study demonstrate Precision's gene editing approach designed to eliminate hepatitis B virus (HBV). ARCUS efficiently targeted and degraded HBV covalently closed circular (cccDNA) by 85% and reduced expression of Hepatitis B Surface Antigen (HBsAg) by 77% in HBV-infected primary human hepatocytes (PHH). Similar levels of editing were achieved in novel mouse and NHP models following lipid nanoparticle (LNP) delivery of ARCUS mRNA, resulting in a 96% reduction in HBsAg in mice. These data suggest that LNP-delivered ARCUS mRNA is a promising approach and potential functional cure for chronic hepatitis B. Precision will continue developing its PBGENE-HBV product candidate using LNP delivery and expects to submit an IND/CTA in 2024.

Abstract #811, Presidential Symposium and Presentation of Top Abstracts: *AAV-Meganuclease-Mediated Gene Targeting Achieves Efficient and Sustained Transduction in Newborn and Infant Macaque Liver*[1]

Preclinical data will be presented during the Presidential Symposium and highlight an ARCUS-based gene insertion approach for the treatment of ornithine transcarbamylase (OTC) deficiency. This strategy was informed by previous work in adult NHPs, which showed safe, efficient and stable reductions of PCSK9 following adeno associated virus (AAV) delivery of an ARCUS nuclease. In this study, therapeutically meaningful and stable levels of OTC expression were observed in NHPs. Treatment was well-tolerated in all animals, showing no evidence of transaminase elevations or liver histopathology in any ARCUS-treated animals. Preliminary data suggests that the level of editing is stable over one year. Together, these data demonstrate preclinical feasibility of using an ARCUS-mediated gene insertion approach for the treatment of OTC deficiency.

Poster Presentations:

Abstract #239: *Optimization of Hydroxyacid Oxidase 1 (HAO1) Targeting ARCUS Nucleases for the Treatment of Primary Hyperoxaluria Type 1 (PH1)*

Preclinical data presented in this poster demonstrate HAO1-targeting and optimization of ARCUS nucleases delivered via AAV in NHPs. A single infusion of AAVs carrying first generation HAO1-targeting nucleases resulted in >95% knockdown of HAO1 protein in NHP liver and increases in serum glycolate up to 80μM. ARCUS nuclease optimization through iterative rounds of protein engineering resulted in improvements in both potency and specificity of HAO nucleases. These data demonstrate the ability to optimize ARCUS nucleases to specifically target the HAO1 gene to control the glyoxylate metabolic pathway responsible for PH1. Precision has initiated a NHP study for PBGENE-PH1 delivered by LNP and expects to submit an IND or CTA in 2023.

Abstract # 561: *ARCUS Gene Editing to Eliminate MELAS-associated m.3243A>G Mutant Mitochondrial DNA*[2]

Preclinical data presented in this poster demonstrate Precision's gene editing approach to shift mitochondrial DNA (mtDNA) heteroplasmy for the m.3243A>G mtDNA mutation. This mutation resides in mitochondrial tRNA and is responsible for >80% of cases of mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS). This study found that mitoARCUS was successfully trafficked to the mitochondria and, once there, specifically cleaved and eliminated m.3243G mutant mtDNA without impacting wild-type (WT) mtDNA. This resulted in preferential replication of WT mtDNA, and, consequently, improvements in mitochondrial function. Precision BioSciences' protein engineering and optimization platform allowed for the generation of highly specific nucleases that accurately discriminated between WT and mutant mtDNA despite only a single nucleotide difference.

Together, these data showcase the promise of ARCUS as a potential *in vivo* gene editing approach for the treatment of disease-causing heteroplasmic mtDNA mutations.

About Precision BioSciences, Inc.

Precision BioSciences, Inc. is a clinical stage biotechnology company dedicated to improving life (DTIL) with its novel and proprietary ARCUS genome editing platform. 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 consists of multiple *ex vivo* "off-the-shelf" CAR T immunotherapy clinical candidates and several *in vivo* gene editing candidates designed 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 our preclinical studies, including targeting hepatitis B cccDNA with ARCUS nucleases in novel animal models, ARCUS-based gene insertion approach for the treatment of OTC deficiency, HAO1-targeting and optimization of ARCUS nucleases, the expected timing of future IND and CTA filings, and expected IND updates and advancement of preclinical programs to IND or CTA. In some cases, you can identify forward-looking statements by terms such as "aim," "anticipate," "approach," "believe," "contemplate," "could," "estimate," "expect," "goal," "intend," "look," "may," "mission," "plan," "potential," "predict," "project," "promising," "should," "suggest," "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. 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 studies and clinical trials; public perception about genome editing technology and its applications; competition in the genome editing, biopharmaceutical, and 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 COVID-19 pandemic and variants thereof, 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 Annual Report on Form 10-K for the fiscal year ended December 31 2021, as any such factors may be updated from time to time in our other filings with the SEC, including, but not limited to, our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2022, to be filed with the SEC, which are accessible on the SEC's website at 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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[1] University of Pennsylvania's Gene Therapy Program oral presentation sponsored by iECURE

[2] Research conducted in collaboration with the University of Miami Miller School of Medicine

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