Precision BioSciences Outlines Clinical Development Strategy for In Vivo Gene Editing Pipeline

September 9, 2021

- Accelerated Clinical Development Expected to Enable Three Investigational New Drug/Clinical Trial Applications Within Next Three Years, Including for Familial Hypercholesterolemia as early as 2022, Primary Hyperoxaluria Type 1 in 2023, and Chronic Hepatitis B in 2024

- Announced Licensing and Collaboration Agreement with iECURE to Advance PCSK9 Knockout Program for Familial Hypercholesterolemia Through Phase 1; iECURE Also Receives License to Develop Four ARCUS-Based Gene Insertion Programs

- Featured Preclinical Data Demonstrating Precision and Versatility of ARCUS Editing Platform, Including First Presentation of ARCUS-Mediated Gene Insertion in Non-Human Primates

- Gene Editing Event Broadcast at 8:00 am ET Includes Presentation by James M. Wilson, M.D., Ph.D., Professor in the Departments of Medicine and Pediatrics, Perelman School of Medicine, University of Pennsylvania and Chief Scientific Advisor of iECURE

DURHAM, N.C.--(BUSINESS WIRE)--Sep. 9, 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 provided strategic business updates on its *in vivo* gene editing pipeline during the Company's first gene editing R&D event.

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20210909005318/en/

"Gene editing promises to fundamentally reshape the treatment landscape across numerous therapeutic categories. Today's *in vivo* gene editing R&D event showcases the power of our ARCUS genome editing platform – including key demonstrations of capabilities, such as gene insertion and mitochondrial DNA gene editing – which offers distinct advantages in this emerging field," commented Matt Kane, CEO and co-founder of Precision BioSciences. "We are excited to announce a new collaboration with iECURE which we expect to help us expedite clinical validation of the ARCUS platform for both gene knockout and gene insertion."

"Today, we are excited to share additional data highlighting the precision and versatility of our ARCUS platform, which is designed to enable safe, specific and efficient gene editing. Since ARCUS can be delivered via AAV or LNP, it has potential utility in treating diseases in the liver as well as many genetic diseases that affect tissues beyond the liver. In addition, the unique enzymology of ARCUS enables it to make complex gene insertion and gene repair edits more efficiently than other editing platforms," said Derek Jantz, Ph.D., Chief Scientific Officer and co-founder of Precision. "We believe these unique attributes of ARCUS support its differentiation for *in vivo* use and its potential to treat a broader range of genetic diseases than other editing technologies. We are very excited about our near-term pipeline and expect ARCUS to deliver on its full promise as we take on more challenging programs."

Precision expects that three of its preclinical programs will advance to investigational new drug (IND)/clinical trial application (CTA) in the next three years:

- As part of an agreement to expedite development, iECURE expects to advance Precision's **PBGENE-PCSK9** candidate for familial hypercholesterolemia (FH) through Phase 1 clinical studies with CTA filing expected as early as 2022.
- Precision has initiated IND-enabling activities and expects to submit an IND application for **PBGENE-PH1** for primary hyperoxaluria type 1 (PH1) in 2023.
- Precision will pursue clinical development of its **PBGENE-HBV** candidate for chronic hepatitis B virus (HBV) and expects to submit an IND/CTA in 2024.

Announced today in a separate release, Precision BioSciences has signed a license and collaboration agreement with iECURE, a mutation-agnostic *in vivo* gene editing company striving to cure devastating diseases with high unmet need, co-founded by James M. Wilson, M.D., Ph.D. Using Precision's PCSK9-directed ARCUS nuclease, iECURE plans to advance Precision's PBGENE-PCSK9 candidate into a Phase 1 study in FH and gain access to Precision's PCSK9-directed ARCUS nuclease to develop four other pre-specified gene insertion therapies for genetic diseases, focusing initially on liver diseases. Precision will retain rights to PBGENE-PCSK9, including for FH and all products developed for genetic indications except those licensed to iECURE. In return for its license grant, Precision will receive an equity stake in iECURE and is eligible to receive milestone and royalty payments on sales of iECURE products developed with ARCUS.

Presentations from Precision's *in vivo* Gene Editing R&D event will highlight the Company's clinical development strategy and updates on the following wholly-owned and partnered preclinical programs using ARCUS-mediated editing:

Featured Preclinical Data

- **ARCUS for Gene Insertion into the PCSK9 locus:** Due to the unique type of cut made by ARCUS nucleases, we believe ARCUS may be better suited for gene insertion than CRISPR-based gene editing tools. In non-human primates (NHPs), ARCUS was observed to be more efficient than CRISPR at inserting a Factor IX transgene into the PCSK9 locus. The

Factor IX transgene is responsible for making the coagulation Factor IX protein associated with hemophilia B bleeding disorder.

"Research conducted by the Gene Therapy Program has shown ARCUS is capable of precise edits that can be applied broadly across genetic diseases in a mutation-dependent manner," said Dr. James M. Wilson. "Additionally, as reported today, ARCUS has demonstrated highly efficient gene insertion with a PCSK9-directed nuclease that will be foundational to iECURE in addressing rare genetic diseases, as well as long-term durability reflecting its curative potential with a single administration. Taken together, these findings continue to support what we have learned over years of collaborating with Precision: that the unique properties of ARCUS are differentiated versus other tools in this field."

- **ARCUS for Chronic HBV (PBGENE-HBV):** Current standard-of-care treatments for HBV suppress viral replication, but often do not clear the virus, leaving covalently closed circular DNA (cccDNA) and integrated HBV genomes that enable viral persistence. Precision's gene editing program for HBV applies ARCUS to knockout this persistent cccDNA and potentially further reduce viral persistence.

New preclinical data to be presented today, and data previously presented at the American Society of Gene & Cell Therapy Annual Meeting, show that ARCUS efficiently targeted and degraded HBV cccDNA in HBV-infected primary human hepatocytes and reduced expression of HBV S-antigen (HBsAg) by as much as 95%. Similar levels of HBsAg reduction were observed in a newly developed mouse model of HBV infection following administration of ARCUS mRNA using lipid nanoparticle (LNP) delivery. Precision will pursue clinical development of its PBGENE-HBV candidate using LNP delivery and expects to submit an IND in 2024.

- **ARCUS for Mitochondrial Genome Editing**: Mitochondrial diseases frequently are caused by pathogenic mutations in the mitochondrial genome that reduce the ability of mitochondria to convert food and oxygen into energy to sustain life and support organ function. Mitochondrial diseases affect approximately 1 in 5,000 individuals.

Recent preclinical studies used mitochondrial-targeted ARCUS (mitoARCUS) to selectively eliminate mutant mitochondrial genomes that cause disease in cell and animal models. In work conducted by Precision BioSciences, a hybrid cell model with a mixture of wild-type (healthy) and mutant mitochondrial genomes, a single treatment with mitoARCUS mRNA converted the cells to >99% wild-type. Work led by Carlos T. Moraes, Ph.D., Esther Lichtenstein Professor in Neurology at the University of Miami Miller School of Medicine and in a mouse model of mitochondrial disease and published online in *Nature Communications* on May 28, 2021, found that mitoARCUS delivered by AAV effectively targeted and depleted mutant mitochondrial genomes in multiple tissues. No editing of potential nuclear off-target sites could be detected, and liver and skeletal muscle showed robust elimination of mutant mtDNA with concomitant restoration of markers of mitochondrial function.

- **ARCUS for FH (PBGENE-PCSK9):** Precision's gene editing program for FH seeks to knockout expression of the PCSK9 gene. As published by Wang et al. in *Molecular Therapy* in June 2021, "Long-term Stable Reduction of Low-density Lipoprotein in Nonhuman Primates Following *In Vivo* Genome Editing," PBGENE-PCSK9 is supported by extensive NHP data over a three-year period, which demonstrates a long-term, stable edit accompanied by up to an 82% reduction from baseline in PCSK9 levels and up to a 62% reduction in LDL levels.

Data will be presented on the clinical nuclease which is expected to be delivered by AAVrh79 in a Phase 1 clinical study to be conducted by iECURE.

- **ARCUS for PH1 (PBGENE-PH1):** Precision's gene editing program for PH1 applies ARCUS to knockout the well-characterized HAO1 gene to prevent the production of a toxic metabolite called oxalate that causes extremely severe and potentially fatal kidney stone accumulation in patients.

NHP data supporting this approach has shown, on average, a 98.0% reduction in HAO1 mRNA and a 97.9% reduction in the encoded protein after a single administration of an AAV vector encoding ARCUS. Compared to published results with siRNAs targeting HAO1, Precision's approach appeared to provide an improved metabolic profile with the potential for long-term benefit from a single dose. Precision has initiated IND-enabling activities and expects to submit an IND application for this program in 2023 using LNP delivery.

- **ARCUS for Duchenne Muscular Dystrophy (DMD) (PBGENE-DMD):** ARCUS genome editing has previously been shown to increase expression of a shortened version of dystrophin in cultured myoblasts from a DMD patient. The approach uses two ARCUS nucleases delivered by a single AAV to simultaneously cut and delete a large segment of the dystrophin gene that encodes exons 45 through 55 of dystrophin – a region of the gene that accounts for more than 50% of DMD-causing mutations.

In November 2020, Precision and Lilly announced an exclusive license agreement to utilize ARCUS genome editing for the research and development of up to six potential *in vivo* targets for genetic disorders. The collaboration initially included three gene targets, with the lead program targeting the dystrophin gene responsible for DMD (**PBGENE-DMD**). In addition, Precision will use ARCUS for one liver-directed target (**PBGENE-LLY2**) and one CNS-directed target (**PBGENE-LLY3**).

Dr. Jantz continued, "The versatility of our platform offers us the optionality to pursue numerous therapeutic applications through strategic partnerships, enabling us to capture more of the value of the ARCUS technology and accelerate key programs. For example, in addition to rapidly advancing PBGENE-PCSK9 to the clinic, iECURE will provide critical validation of ARCUS' gene-insertion capabilities. Lilly will help us research ARCUS-mediated editing in muscle and CNS. Even as we aggressively invest in wholly-owned programs, we will continue to leverage collaborations that enable us to explore novel applications of ARCUS and reach patients quicker."

The Company's balance of cash and cash equivalents is approximately $167 million as of August 31, 2021. The Company continues to expect that existing cash and cash equivalents will be sufficient to fund planned operations into 2023.

Call and Webcast Information

Precision's gene editing R&D event is being held today, September 9, 2021, at 8:00 a.m. ET. The dial-in conference call numbers for domestic and international callers are (866) 970-2058 and (873) 415-0216, respectively. The conference ID number for the call is 6376435. Participants may also access the live webcast, including slides, available in the Investors and Media section under Events and Presentations. An archived replay of the webcast will be available on Precision's website for one year following the presentation.

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 (knockout), 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 80 patents to date.

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 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 further development and potential of our ARCUS platform, the clinical development and timeline of PBGENE-PCSK9, PBGENE-PH1 and PBGENEHBV, our agreement with iECURE and the potential clinical development and benefits thereunder, our agreement with Lilly and the potential clinical development and benefits thereunder, and our expected use of cash and cash equivalents. 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," 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 June 30, 2021, 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 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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Investor Contact:
Alex Kelly
Chief Financial Officer
Alex.Kelly@precisionbiosciences.com

Media Contact:
Maurissa Messier
Senior Director, Corporate Communications
Maurissa.Messier@precisionbiosciences.com

Source: Precision BioSciences, Inc.