Precision BioSciences Announces Initial Safety and Antiviral Activity of PBGENE-HBV in the ELIMINATE-B Clinical Trial

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- *ELIMINATE-B Phase 1 dose finding study for chronic Hepatitis B executing on schedule with completion of first dose administration for cohort 1 (n=3 patients)*
- *PBGENE-HBV, the first LNP gene editing technology studied for Hepatitis B, was safe and well tolerated*
- *PBGENE-HBV demonstrated substantial antiviral activity measured by reduction of Hepatitis B surface antigen (HBsAg) after one administration at the lowest dose level*
- *First clinical proof-of-concept in chronic Hepatitis B for a unique editing modality designed to directly eliminate and inactivate the root cause of Hepatitis B virus from covalently closed circular DNA (cccDNA) and integrated DNA*
- *These PBGENE-HBV data mark the second clinical validation for ARCUS in vivo gene editing in 2025*

DURHAM, N.C.--(BUSINESS WIRE)--Feb. 19, 2025-- Precision BioSciences, Inc. (Nasdaq: DTIL), a clinical stage gene editing company utilizing its novel proprietary ARCUS® platform to develop *in vivo* gene editing therapies for high unmet need diseases, today announced initial results from the first administration of PBGENE-HBV in cohort 1, the lowest dose level of the ELIMINATE-B trial. The ELIMINATE-B trial is designed to investigate PBGENE-HBV at multiple ascending dose levels with three dose administrations per dose level in patients afflicted with chronic Hepatitis B who are HBeAg-negative.

PBGENE-HBV, which comprises an ARCUS-encoding mRNA encapsulated in a lipid nanoparticle (LNP), was safe and well tolerated in all three participants in cohort 1 after the first administration of a 0.2 mg/kg dose. The planned dosing schedule in ELIMINATE-B allows for two additional administrations at this dose level while in parallel investigating the next higher dose level. The participants treated in cohort 1 possessed different baseline characteristics: age of infection, duration of infection and level of HBsAg. Across the three participants dosed, none experienced a Grade ≥2 treatment-related adverse event or serious adverse event.

“This exciting initial safety data set provides evidence that ARCUS encapsulated in a LNP was well tolerated in chronic Hepatitis B patients upon first dose administration at dose level 1. When studying novel technologies and drug mechanisms it is important to monitor safety closely, and we believe the extensive preclinical safety experiments Precision conducted along with several rounds of mRNA optimization were critical steps to ensure patient safety,” said Murray A. Abramson, MD, MPH, Head of Clinical Development. “We are proud to share this first in human proof-of-concept data with the Hepatitis B community as we plan additional administrations at this dose level and escalating dose levels.”

In addition to safety, PBGENE-HBV demonstrated a substantial reduction in Hepatitis B surface antigen (HBsAg) in two of the three participants following the first administration at dose level 1. The ELIMINATE-B protocol is designed for three dose administrations at each dose level, with the goal to maximize cumulative viral editing to achieve undetectable levels of HBsAg. With a well-tolerated safety profile and early antiviral activity established at pre-specified timepoints, Precision will complete subsequent administrations in all cohort 1 patients.

“The ELIMINATE-B global investigators are enthusiastic about the initial safety and activity profile of PBGENE-HBV and look forward to treating additional patients globally. Patient interest in this trial remains very high, and these data are re-assuring to me for my patients with chronic Hepatitis B,” said Alina Jucov, MD, PhD, Principal Investigator, Arensia Research Clinic, Moldova.

“These data excite the entire Precision team, and we hope it instills confidence among the patients who are courageously embarking in our clinical trial. Progress against this wide-spread and devastating disease would not be possible without their participation,” said Michael Amoroso, President and Chief Executive Officer of Precision BioSciences. “This marks an important step forward for Precision in a large patient population and the second clinical validation of ARCUS *in vivo* gene editing following the recent clinical data from the OTC-HOPE study being conducted by our partner iECURE in a dire rare disease.”

The ELIMINATE-B study is currently enrolling HBeAg-negative chronic Hepatitis B patients at world-class sites in Moldova, Hong Kong, and New Zealand. Investigators accrued the first cohort of patients within a month. The company is on schedule to provide additional administrations at this dose level and subsequently plans to escalate to higher dose levels to define the optimal dose and number of dose administrations for safely eliminating cccDNA and inactivating integrated HBV DNA. Precision expects to expand the study to the U.S. and U.K. and continue accelerating recruitment and evaluation of a genetically diverse patient population in the Phase 1 study. Precision plans to share detailed clinical data throughout 2025.

“Prior to commencing the ELIMINATE-B clinical trial, we conducted numerous preclinical studies with PBGENE-HBV to understand the pharmacokinetics, safety, and impact on viral markers at various dose levels and following multiple dose administrations. Importantly, the early data in the first cohort of patients is consistent with the safety and HBsAg reductions observed in our preclinical models,” said Cassie Gorsuch, PhD, Chief Scientific Officer. “The safety and early reduction of HBsAg suggests that PBGENE-HBV is doing what no previous treatment has been able to accomplish, eliminating the source of viral replication in cccDNA and inactivating integrated disease.”

About PBGENE-HBV (Viral Elimination Program)**:** PBGENE-HBV is Precision’s wholly owned *in vivo* gene editing program under investigation in a

global first-in-human clinical trial, which is designed to potentially cure chronic hepatitis B virus (HBV) infection. Currently, it is estimated that 300 million people worldwide are afflicted with chronic hepatitis B. PBGENE-HBV is the first and only potentially curative gene editing program to enter clinical investigation that is specifically designed to eliminate cccDNA and inactivate integrated HBV DNA.

About the OTC Program (Gene Insertion Program): Led by iECURE, ECUR-506 is an ARCUS-mediated in vivo gene editing program currently in a first-in-human phase 1/2 trial (OTC-HOPE) evaluating ECUR-506 as a potential treatment for neonatal onset ornithine transcarbamylase (OTC) deficiency. In January 2025, iECURE reported clinical efficacy and safety data in the first patient dosed showing a complete clinical response from three months post exposure to the end of study (six months post exposure). ECUR-506 was generally well tolerated with no significant clinical safety concerns.

About Precision BioSciences, Inc.
Precision BioSciences, Inc. is a clinical stage 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. Key capabilities and differentiating characteristics may enable ARCUS nucleases to drive more intended, defined therapeutic outcomes. Using ARCUS, the Company's pipeline is comprised of *in vivo* gene editing candidates designed to deliver lasting cures for genetic and infectious diseases where no adequate treatments exist. For more information about Precision BioSciences, please visit www.precisionbiosciences.com.

The ARCUS® platform is being used to develop *in vivo* gene editing therapies for sophisticated gene edits, including gene insertion (inserting DNA into gene to cause expression/add function), elimination (removing a genome e.g. viral DNA or mutant mitochondrial DNA), and excision (removing a large portion of a defective gene by delivering two ARCUS nucleases in a single AAV).

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 well-tolerated safety profile and substantial antiviral activity established after the first administration at dose level 1 of PBGENE-HBV; the clinical development and demonstrated, potential and expected safety, efficacy and benefit of PBGENE-HBV, our other product candidates and those being developed by partners including ECUR-506; the unique design of PBGENE-HBV to eliminate cccDNA and inactivate integrated HBV DNA with high specificity, potentially leading to functional cures; the expected timing of regulatory processes (including filings such as IND's and CTA's and studies for PBGENE-HBV and the acceptance of these filings by regulatory agencies); the suitability of PBGENE-HBV for the treatment of hepatitis and the targeting of the root cause of the disease; the safety, tolerability and efficacy signals observed through preclinical evaluation in non-human primates (NHPs), transgenic and episomal mouse models, human cell models of HBV and primary human hepatocytes; the translatability of preclinical models to human clinical trials; the key advantages of ARCUS and its key capabilities and differentiating characteristics ; expectations about operational initiatives, strategies, and further development of PBGENE-HBV; plans to provide additional administrations of PBGENE-HBV at the first dose level; plans to escalate to higher dose levels in the ELIMINATE-B clinical trial to define the optimal dose and number of dose administrations for safely eliminating cccDNA and inactivating integrated HBV DNA; expansion of the ELIMINATE-B clinical trial to the United States and United Kingdom; expectations around acceleration of recruitment of the ELIMINATE-B clinical trial and plans to evaluate a genetically diverse patient population in the Phase 1 study. Precision plans to share detailed clinical data throughout 2025; expectations about achievement of key milestones; and anticipated timing of patient dosing and clinical data for PBGENE-HBV and ECUR-506. In some cases, you can identify forward-looking statements by terms such as "aim," "anticipate," "approach," "believe," "contemplate," "could," "design," "designed," "estimate," "expect," "goal," "intend," "look," "may," "mission," "plan," "possible," "potential," "predict," "project," "pursue," "should," "strive," "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. 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 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 any pandemic, epidemic, or outbreak of an infectious disease; the success of our existing collaboration and other license 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, 2024, 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 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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