Precision BioSciences Highlights Preclinical Data and Outlines Design of First-in-Human Clinical Trial for PBGENE-HBV for Treatment of Chronic Hepatitis B

November 15, 2024 at 7:00 AM EST

– PBGENE-HBV preclinical data reinforce safety profile and potential to deliver a functional cure for chronic hepatitis B, supporting advancement into first-in-human clinical study –

– Phase 1 dose escalation and expansion trial, ELIMINATE-B, designed to assess safety and efficacy measured by durable reduction of key viral biomarkers –

– Global study recruiting patients following clearance of first clinical trial application (CTA), with additional CTAs pending approval; U.S. investigational new drug (IND) anticipated in 2025 –

– Investor event today, November 15, 10:00 a.m. EST / 7:00 a.m. PST, to feature presentations from company management and key opinion leader perspectives on PBGENE-HBV –

DURHAM, N.C.--(BUSINESS WIRE)--Nov. 15, 2024-- 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 sophisticated gene edits, today will present preclinical data supporting the advancement of PBGENE-HBV into clinical development. The Company will also outline the design of its first-in-human study, ELIMINATE-B, in patients with chronic hepatitis B. Company management will present these updates and host panel discussions on the unmet need in chronic hepatitis B and the approach to treatment with PBGENE-HBV during a virtual event being held today, November 15, 10:00 a.m. EST / 7:00 a.m. PST before commencement of the American Association for the Study of Liver Diseases (AASLD) Meeting.

“We are excited to share the preclinical data supporting PBGENE-HBV alongside the design of our Phase 1 trial, ELIMINATE-B, which will be the first clinical study of an *in vivo* gene editing program in chronic hepatitis B,” said Michael Amoroso, Chief Executive Officer, Precision BioSciences. “Chronic hepatitis B affects approximately 300 million people globally and represents a multi-billion-dollar market with chronic treatments currently serving more than 5 million patients worldwide. However, most available treatments for chronic hepatitis B target downstream aspects of the viral lifecycle, leaving the root of disease intact. Consequently, less than 3% of patients treated with existing approved treatments achieve a functional cure. This is unacceptable considering that up to 40% of patients with chronic hepatitis B will progress to develop life-threatening liver disease or liver cancer. PBGENE-HBV is uniquely designed to address this unmet need at the source of viral replication.”

“Our preclinical results reflect the robust data package submitted to regulators in support of our global Phase 1 trial and underscore our conviction in PBGENE-HBV, which has so far demonstrated compelling safety and selectivity, highly efficient editing, and confirmation of its mechanism to eliminate cccDNA and viral DNA integrated into hepatocytes,” said Murray Abramson, M.D., M.P.H., Head of Clinical Development, Precision BioSciences. “Importantly, the ELIMINATE-B study will evaluate patients who are controlled but not cured by nucleoside analogues. We believe ELIMINATE-B will highlight the differentiated mechanism of PBGENE-HBV. By simultaneously targeting the two distinct drivers of disease – cccDNA and viral DNA integrated into hepatocytes – PBGENE-HBV has the potential to deliver a much-needed functional cure for people living with chronic hepatitis B.”

Mr. Amoroso added, “With regulatory authorization in place and global sites coming online, we are excited to begin dosing patients with PBGENE-HBV and look forward to sharing clinical data as it matures in 2025.”

PBGENE-HBV Preclinical Data Highlights:

Today, Precision will present preclinical data generated to date, which support the progression of PBGENE-HBV into a first-in-human clinical trial. The Company will share robust safety, tolerability, and efficacy signals observed through an array of preclinical models. Key highlights are as follows:

Safety and Tolerability:

- Comprehensive off-target analysis demonstrated a high degree of specificity for PBGENE-HBV, with no increased risks of translocations or integrations in HBV-infected human liver cells;
- PBGENE-HBV was well tolerated over multiple administrations in mice and non-human primates (NHPs), with rapid clearance after each dose administration, transient transaminase elevations which resolved rapidly, and non-adverse changes in blood parameters;
- PBGENE-HBV does not distribute to germ cells, as evidenced by NHP studies; and
- PBGENE-HBV’s high-quality mRNA and optimized LNP formulation contributed to a compelling safety profile.

Efficacy:

- PBGENE-HBV effectively distributed to all hepatocytes in the liver;
- PBGENE-HBV demonstrated 99% viral DNA editing in NHPs;

- Confirmed PBGENE-HBV's dual mechanism with elimination of cccDNA observed in primary human hepatocyte, mouse, and NHP models and inactivation of integrated HBV DNA observed in transgenic mouse models and HBV cell lines; and
- Observed sustained declines in key viral biomarkers, HBV DNA and hepatitis B surface antigen (HBsAg), indicative of a functional cure in transgenic mouse models following administration of PBGENE-HBV and nucleoside analogue withdrawal.

Based on these data, Precision has submitted clinical trial applications to authorities in multiple geographies and has so far received clearance to initiate its Phase 1 study in Moldova. Additional regulatory applications are under review or planned for other jurisdictions, including a U.S. IND.

ELIMINATE-B Phase 1 Trial Design and Overview:

ELIMINATE-B is a global, multi-site, Phase 1 clinical trial, which will evaluate up to 45 HBV patients that are hepatitis B e antigen (HBeAg)-negative and virologically suppressed on nucleos(t)ide analogues (NUCs). Since greater than 80% of patients with chronic hepatitis B are HbeAg-negative, this represents the majority of patients with hepatitis B. The ELIMINATE-B trial is targeted for enrollment of 45 patients in up to five countries and will progress in two stages: (1) a staggered, multiple ascending dose cohort, deploying a standard 3+3 design with each patient receiving up to 3 dose administrations; and (2) a dose expansion cohort once the appropriate dose and schedule has been determined. The key safety endpoint of the trial will be frequency and severity of dose-limiting toxicities. Efficacy will be determined by antiviral activity throughout finite duration PBGENE-HBV treatment and follow-up, including reduction in HBsAg, sustained HBV DNA negativity, and discontinuation of standard-of-care nucleos(t)ide analogues.

ELIMINATE-B is open and currently screening and accruing patients, and Precision expects to report data from the study as it matures throughout 2025.

Further details on the trial can be found in the event slides posted on Precision's website in the Investors section under Events & Presentations at investor.precisionbiosciences.com and on clinicaltrials.gov identifier NCT06680232.

Investor Event Webcast Information:

Precision's investor event will include presentations by management on the preclinical data for PBGENE-HBV and the design of ELIMINATE-B. Panel discussions will feature leading hepatitis experts and Precision Scientific Advisory Board members on the market opportunity in HBV, and investigators on their clinical experience treating HBV and the potential for PBGENE-HBV to address this unmet need.

The event will be webcast live on Friday, November 15, 2024, at 10:00 a.m. EST / 7:00 a.m. PST. To access the presentation and webcast, please use the following link or go to Precision's website in the Investors section under Events & Presentations at investor.precisionbiosciences.com. An archived replay of the webcast will be available for approximately 30 days following the event.

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 the broadest range of genetic and infectious diseases where no adequate treatments exist. Precision BioSciences is currently enrolling patients in the ELIMINATE-B Phase 1 trial evaluating PBGENE-HBV in patients with chronic hepatitis B. For more information on the ELIMINATE-B trial, please visit clinicaltrials.gov identifier NCT06680232. 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 a 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 clinical development and expected safety, efficacy and benefit of our product candidates (including PBGENE-HBV); 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 robust 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; expectations about achievement of key milestones; and anticipated timing of patient dosing and clinical data. 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," "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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