Precision BioSciences Announces Phase 1 Safety and Efficacy for Cohort 1, Lowest Dose Level in ELIMINATE-B, a First-In-Human Trial of PBGENE-HBV for Chronic Hepatitis B

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- Proof-of-activity now established for PBGENE-HBV, the first and only clinical modality designed to eliminate covalently closed circular DNA (cccDNA) and inactivate integrated DNA, with the goal of complete cure

- Cohort 1, the lowest dose cohort (0.2 mg/kg) of ELIMINATE-B, established a safe and well-tolerated profile across multiple dose administrations for all patients

- PBGENE-HBV demonstrated substantial antiviral activity in all three patients in Cohort 1, with best responses achieving a 47-69% Hepatitis B surface antigen (HBsAg) reduction

- Durable HBsAg reduction of approximately 50% in patient 1 is observed 7 months after initial dose administration

- Dr. Mark Sulkowski, M.D., Professor of Medicine at the Johns Hopkins University School of Medicine and world-renowned expert in hepatitis B, expands role to Head Clinical Development Advisor

- Extended expected cash runway to the second half of 2027 providing more than two years of operating cash

DURHAM, N.C.--(BUSINESS WIRE)--Aug. 6, 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, announced ELIMINATE-B results as of the data cutoff of July 28, 2025. Data include completed Cohort 1 (dosed at 0.2 mg/kg), the lowest dose level of the ELIMINATE-B trial, and initial safety data from Cohort 2 (dosed at 0.4 mg/kg). The ELIMINATE-B trial is designed to investigate PBGENE-HBV at multiple ascending dose levels with three dose administrations per level in patients afflicted with chronic hepatitis B who are Hepatitis B e-Antigen (HBeAg)-negative, treated daily with nucleos(t)ide analog therapies, and have ≥200 IU/mL HBsAg without an upper limit.

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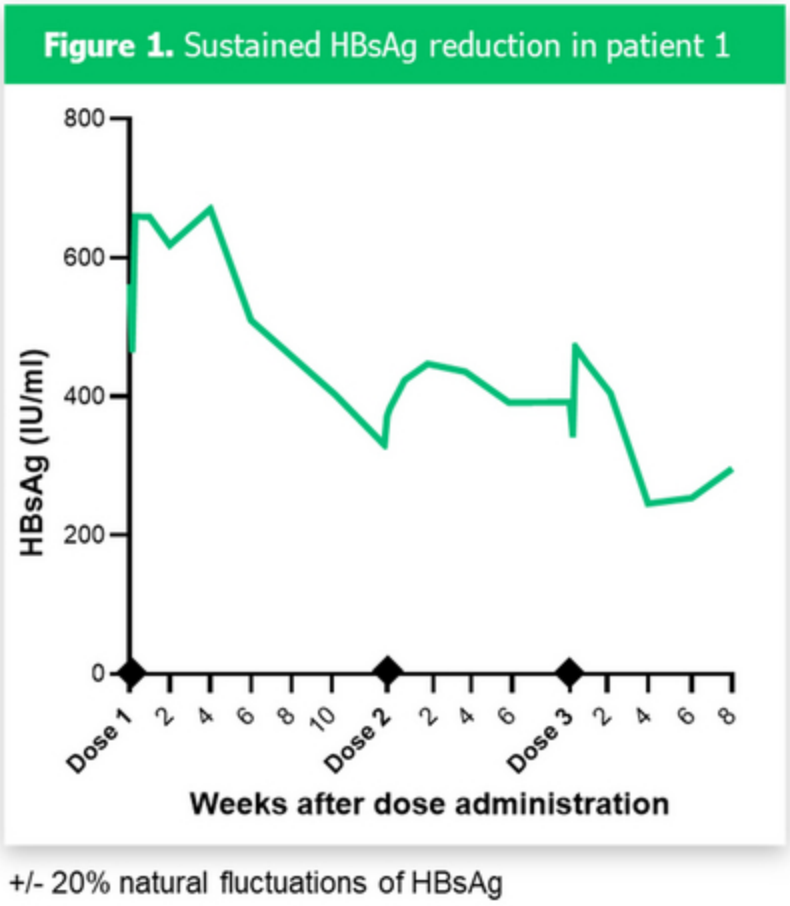


Figure 1 - Sustained HBsAg Reduction in Patient 1

“For decades investments in potential new treatments aimed to cure chronic hepatitis B have focused on modalities that cannot alter cccDNA, the genetic source of the disease. As a result, clinicians around the world have lacked the tools necessary to cure hepatitis B or prevent hepatitis B-related liver cancer, which affects over 500,000 patients globally on an annual basis,” said Jordan Feld, M.D., M.P.H., Professor of Medicine at the University of Toronto and Precision Hepatitis Scientific Advisory Board Member. “Now, for the first time, the hepatitis B community is investigating a gene editing modality, PBGENE-HBV, that is specifically designed to deliver a complete cure for hepatitis B by eliminating cccDNA, the genetic source of viral replication. We are hopeful that this approach will offer a safe drug that will raise the achievable functional cure rate from the current 1-3% to the global goal of 30%.”

Cohort 1 of the Phase 1 ELIMINATE-B study consisted of three patients, each of whom received three planned administrations of 0.2 mg/kg of PBGENE-HBV dosed approximately eight weeks apart. The patients treated in Cohort 1 possessed different baseline characteristics: age of infection, duration of infection, and baseline level of HBsAg with no upper limit (HBsAg range of 562-11,813 IU/mL). The primary objective of the study is to characterize the safety of PBGENE-HBV. The low dose in Cohort 1 was selected with endorsement of global regulators to maximize the safety margin for first-in-human investigation. This starting dose in humans is significantly less (60%) than the dose administered in the non-human primate proof of efficacy study where viral DNA editing was observed.

Safety in Cohort 1 – Well-Tolerated in All Patients:

PBGENE-HBV was well-tolerated and active in all three patients in Cohort 1. Across Cohort 1, no patient experienced above a Grade 2 treatment-related adverse event, a serious adverse event, or a dose-limiting toxicity. Additionally, no clinically significant lab abnormalities were observed, including liver enzymes and platelets.

Efficacy in Cohort 1 – Sustained Response in Patient 1:

At 0.2mg/kg, PBGENE-HBV demonstrated a substantial HBsAg reduction in all three patients with best response reductions of 56% (0.36 log), 69% (0.51 log) and 47% (0.28 log) compared to baseline levels in patients one, two and three, respectively. One of three patients (33%) in Cohort 1 achieved a durable HBsAg reduction of approximately 50% (0.3 log) from baseline that was maintained as of the data cutoff-date, which was seven months after the initial dose of PBGENE-HBV (Figure 1). These results are evidence of the ability of PBGENE-HBV to drive a durable antiviral response by editing the viral DNA at the source of chronic hepatitis B infection and give further reason to believe in the ELIMINATE-B trial objective of achieving durable undetectable levels of HBsAg in some patients. The other two patients in Cohort 1 demonstrated antiviral response after each dose administration and eventually returned to baseline levels of HBsAg. Transcriptional upregulation from unedited viral DNA remaining after administration at the lowest dose is likely responsible for the HBsAg increase in these patients.

“This exciting dataset provides the first clinical evidence of substantial HBsAg reductions as a result of direct cccDNA elimination and/or inactivation of integrated HBV DNA in all patients, even at this lowest dose level. PBGENE-HBV was both well-tolerated and highly active in all chronic hepatitis B

patients after three dose administrations. The data from the first cohort supports the tolerability of multiple administrations of PBGENE-HBV and gives me reason to believe that we can safely escalate the dose and increase drug exposure of this novel technology to potentially drive a complete cure by not leaving any viral DNA behind," said Man-Fung Yuen, MBBS, M.D., PhD, DSc ELIMINATE-B Investigator and Chair Professor of The University of Hong Kong and the Chief of the Division of Gastroenterology and Hepatology at Queen Mary Hospital.

Progress in Cohort 2:

Cohort 2 in the ELIMINATE-B study is evaluating PBGENE-HBV at 0.4 mg/kg. As of the data cut off, 1 patient received three dose administrations with two weeks of follow-up, and two patients received one dose administration with four weeks of follow-up. In these patients, no adverse events above Grade 2, no serious adverse events, nor dose-limiting toxicities were observed. There were no clinically significant liver transaminase elevations noted. One additional patient did not complete their dose due to a transient infusion-related serious adverse event that led to dose interruption at minute two. This event quickly resolved within minutes of ceasing the infusion, and the patient is doing well. The Data Monitoring Committee (DMC) deemed the event not dose-related or dose-limiting.

"We are pleased to continue to observe an impressive clinical safety profile, with transient changes in liver transaminases remaining less than three times the upper limit of normal with no clinical symptoms for both dose levels," said Cassie Gorsuch, PhD, Chief Scientific Officer. "Given the low starting dose of 0.2 mg/kg and dosing every eight weeks, we did not expect to eliminate 100% of the virus in Cohort 1 and based on dose-dependency observed in nonclinical models we anticipate deeper and more durable responses as we progress in the study. Given our mechanism, proof of sustained viral marker reduction as a result of viral editing in one patient was critical to reinforce the thesis behind PBGENE-HBV. The ELIMINATE-B trial was designed with two levers to optimize efficacy; the first is dose escalation. Given the favorable safety profile in Cohort 1 and 2, the DMC has endorsed enrolling Cohort 3 this month to test the next higher dose level. The second lever is to shorten the dosing interval, which we expect to prevent the opportunity for any remaining virus to upregulate transcriptional activity. The ELIMINATE-B protocol permits shortening the dosing interval, which is now supported by human safety data from Cohort 1 and Cohort 2 currently in progress."

"We have made significant progress advancing our lead asset PBGENE-HBV, and we believe the early Phase 1 data supports first signs of viral elimination of chronic hepatitis B," said Michael Amoroso, President and Chief Executive Officer of Precision BioSciences. "Our early data shows that we have a novel, safe and active drug in all patients treated, with a durable effect in one-third of patients, even at the lowest dose level. To deliver a complete cure and reduce long term liver disease and cancer risk, we must ensure we are eliminating the root cause of disease replication– the cccDNA. We are generating molecular data using liver biopsies to demonstrate PBGENE-HBV's mechanism of action to eliminate cccDNA and inactivate integrated HBV DNA."

In further support of advancing PBGENE-HBV through clinical development, the Company also announced that Mark Sulkowski, M.D., Professor of Medicine at the Johns Hopkins University School of Medicine and renowned expert in hepatic and infectious diseases has expanded his advisory role. In the newly created role, Head Clinical Development Advisor, Dr. Sulkowski will work closely with Precision's leadership and cross-functional teams to support clinical strategy across the development lifecycle for the Company's on-going PBGENE-HBV Phase 1 clinical trial as well as initiation of later stage trials. His advisory role will focus on optimizing clinical trials, including translational integration, and aligning scientific rationale with regulatory objectives.

"Dr. Sulkowski has already proven to be an invaluable member of our Hepatitis Scientific Advisory Board," said Michael Amoroso. "As we advance the clinical evaluation of PBGENE-HBV, his wealth of experience will be a critical resource to help guide our medical and clinical development organization. We are thrilled to expand his involvement at such an important time for the Company and look forward to benefitting from his hands-on strategic expertise to help us drive ELIMINATE-B towards later phase studies."

The Company is on track to complete dosing of all three patients with three planned dose administrations in Cohort 2 and commence dosing Cohort 3. The Company intends to evaluate PBGENE-HBV at increasing and more frequent doses until a maximum tolerated dose is reached, with the goal of establishing the right dose and administration schedule leading to a complete cure and optimal therapeutic index. The Company expects to provide a data update later in 2025.

Cash Runway Extension:

As Precision advances the ELIMINATE-B clinical trial into its expansion phase and prepares to file an IND and/or CTA for the PBGENE-DMD program, the Company is taking proactive steps to invest fully in these programs while extending our expected cash runway to the second half of 2027. This is expected to enable the commencement of a Phase 2 study for PBGENE-HBV and a pivotal study for PBGENE-DMD. The cash runway extension enables later stage clinical data readouts for both programs. Accordingly, in July 2025 the Company initiated an operating efficiency program, including employment-related and other operating expense reductions in early research which are designed to reduce the Company's annual operating expenses in both 2026 and 2027 by approximately $25 million compared to the 2025 annual cash operating expense level.

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 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. Lipid nanoparticle technology for PBGENE-HBV has been provided by Acuitas Therapeutics Inc.

About Hepatitis B:

Hepatitis B is a leading cause of morbidity in the US and death globally, with no curative options currently available for patients. Despite the availability of approved antiviral therapies, an estimated 300 million people globally and 1-2 million people in the US are estimated to have chronic hepatitis B infection. An estimated 15% to 40% of patients with HBV infections may develop complications, such as cirrhosis, liver failure, or liver cancer (hepatocellular carcinoma), which account for the majority of HBV-related deaths.

Chronic hepatitis B infection is primarily driven by persistence of HBV cccDNA, which enables continued viral replication, and integration of HBV DNA into the human genome in liver cells. Current treatments for patients with chronic hepatitis B include agents that result in long-term viral suppression as indicated by reduction of circulating HBV DNA, but these therapies do not eradicate HBV cccDNA, rarely lead to functional cure, and require lifelong administration.

About the ELIMINATE-B Trial:

The Phase 1 ELIMINATE-B study is currently enrolling HBeAg-negative chronic hepatitis B patients at world-class sites in Moldova, Hong Kong, and New Zealand, and imminently commencing in the U.S. The goal of the study is to define the optimal dose and number of dose administrations for safely eliminating cccDNA and inactivating integrated HBV DNA. With regulatory approval already granted, Precision expects to expand the study to clinical trial sites in the U.S. and U.K. and continue accelerating recruitment and evaluation of a genetically diverse patient population in the Phase 1 study.

About Dr. Mark Sulkowski:

Mark Sulkowski, M.D. is a Professor of Medicine at the Johns Hopkins University School of Medicine and the Director of the Division of Infectious Diseases at Johns Hopkins Bayview Medical Center. He also serves as the Medical Director of the Viral Hepatitis Center in the Divisions of Infectious Diseases and Gastroenterology/Hepatology in the Department of Medicine and is the Senior Associate Dean for Clinical Trials. Dr. Sulkowski has been the principal investigator for more than 120 clinical trials related to the management of viral hepatitis B and C and has published over 300 peer reviewed articles with works in Annals of Internal Medicine, New England Journal of Medicine, JAMA, Clinical Infectious Diseases, Journal of Hepatology, and Hepatology.

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. 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 such as in the Company's PBGENE-HBV program), and excision (removing a large portion of a defective gene by delivering two ARCUS nucleases in a single AAV such as in the Company's DMD program).

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 PBGENE-HBV and our gene editing approaches, the design of PBGENE-HBV to deliver a complete a cure of chronic hepatitis B by eliminating cccDNA, the source of viral replication, while also inactivating integrated HBV DNA resulting in reductions of downstream viral markers, including hepatitis B surface antigen (HBsAg); the data from the first cohort supporting the safety of multiple administrations of PBGENE-HBV and giving reason to believe that the dose of PBGENE-HBV can be safely escalated to potentially drive a complete cure; the design of the ELIMINATE-B trial with two levers to optimize efficacy, dose escalation and shortening of the dose interval; the expected timing of regulatory processes and clinical operations, including filings, studies, enrollment and clinical data for PBGENE-HBV; the anticipation of deeper and more durable responses as the ELIMINATE-B clinical trial progress; the intent to evaluate PBGENE-HBV at increasing and more frequent doses until a maximum tolerated dose is reached, with the goal of establishing the right dose and administration schedule leading to a complete cure and optimal therapeutic index.; the anticipated timing of clinical data, including that the company is on track to complete dosing all three patients with all three preplanned dose administrations in Cohort 2 and will provide a data update later in 2025 and that Cohort 3 is expected to begin dosing this month.; the use of liver biopsies to generate molecular data to demonstrate PBGENE-HBV's mechanism of action of eliminating the cccDNA and inactivating integrated HBV DNA; and the extension of the Company's cash runway into the second half of 2027 enabling potential commencement of Phase 2 study for PBGENE-HBV and pivotal study for PBGENE-DMD. In some cases, you can identify forward-looking statements by terms such as "aim," "anticipate," "appear," "approach," "believe," "contemplate," "could," "designed," "encouraged", "estimate," "expect," "goal,", "hopeful","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 March 31, 2025, 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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