Precision BioSciences Announces MHRA Approval for Partner iECURE to Expand Phase 1/2 Clinical Trial of ARCUS Gene Editing Program in OTC Deficiency

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- Insertion of a functional OTC gene through ARCUS in vivo gene editing may provide lasting clinical benefit for children with OTC deficiency who are in dire need for effective treatments

- CTA approval for ECUR-506 in the United Kingdom provides further regulatory support for Precision BioSciences' ARCUS in vivo gene editing platform

DURHAM, N.C.--(BUSINESS WIRE)--Mar. 6, 2024-- Precision BioSciences, Inc. (Nasdaq: DTIL), an advanced gene editing company utilizing its novel proprietary ARCUS® platform to develop *in vivo* gene editing therapies for sophisticated gene edits, including gene insertion, excision, and elimination, today announced that its partner iECURE has received approval from the U.K. Medicines & Healthcare products Regulatory Agency (MHRA) for the company's Clinical Trial Authorization (CTA) application to expand the Phase 1/2 OTC-HOPE study evaluating ECUR-506 into the U.K. The OTC-HOPE study is investigating ECUR-506, incorporating an ARCUS nuclease, for the treatment of Ornithine Transcarbamylase (OTC) deficiency in infants. The CTA approval by the MHRA follows the previous approval to begin the OTC-HOPE study by the Australian Therapeutic Goods Administration (TGA). In 2021, Precision licensed to iECURE an ARCUS nuclease that inserts a functional copy of the OTC gene for treatment of OTC deficiency.

"Congratulations to iECURE for bringing the first gene editing approach into clinical investigation for patients with OTC deficiency. Approval from the MHRA to expand iECURE's OTC-HOPE Phase 1/2 study represents yet another milestone, which both advances our partner's work to potentially revolutionize the treatment of OTC deficiency in infants while validating the differentiated ability of ARCUS to efficiently insert genes and restore function," said Michael Amoroso, Chief Executive Officer of Precision BioSciences. "To that end, we view progression through multiple regulatory agencies around the world as important proof-points for ARCUS that reflects our broader strategy to leverage ARCUS with select development partners as we continue to advance our wholly owned hepatitis B program toward an investigational new drug (IND) application and/or CTA filing in 2024."

OTC deficiency, the most common urea cycle disorder, is an inherited metabolic disorder caused by a genetic defect in a liver enzyme responsible for the detoxification of ammonia. Individuals with OTC deficiency can build up excessive levels of ammonia in their blood potentially resulting in devastating consequences, including irreversible neurological damage, coma, and death. The severe form of the condition emerges shortly after birth and is more common in boys than girls. The only corrective treatment for early onset severe OTC deficiency is a liver transplant. Currently available medical therapies do not correct the disease and do not eliminate the risk of life-threatening symptoms or crises.

About Precision BioSciences, Inc.

Precision BioSciences, Inc. is an advanced 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, Precision'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.

About ECUR-506

iECURE's approach to gene editing for its initial programs, including OTC deficiency, relies on the delivery of two adeno-associated virus (AAV) capsids, each carrying different payloads. ECUR-506 comprises two vectors, an ARCUS® nuclease vector targeting gene editing in the well-characterized PCSK9 gene locus and a donor vector that inserts the desired functional OTC gene. iECURE has licensed the ARCUS nuclease for ECUR-506 from Precision BioSciences. The cut in the PCSK9 site serves as the insertion site for the OTC gene, providing a potential path to permanent expression of a healthy gene.

About the OTC-HOPE Study

The OTC-HOPE study is a Phase 1/2 first-in-human clinical trial of ECUR-506 in baby boys with genetically confirmed OTC deficiency and will test up to two dose levels of ECUR-506. The study is enrolling baby boys aged 24 hours to seven months who are diagnosed with severe neonatal onset OTC deficiency and meet certain other criteria. The primary objective is to assess the safety and tolerability of intravenous administration of a single dose of ECUR-506. It will also assess the pharmacokinetics and efficacy of ECUR-506 administration and the potential effects of ECUR-506 on disease-specific biologic markers, developmental milestones and quality of life.

About iECURE

iECURE is a clinical-stage gene editing company focused on developing therapies that utilize mutation-agnostic *in vivo* gene insertion, or knock-in, editing for the treatment of liver disorders with significant unmet need. We believe our approach has the potential to replace and restore the function of a dysfunctional gene, regardless of mutation, by knocking-in a healthy copy of that gene to offer durable gene expression and long-term, potentially

curative, therapeutic benefit. Our management team has extensive experience in executing global orphan drug and gene therapy clinical trials and successfully commercializing multiple products. We intend to leverage our team's core strength in research and development strategy to identify what we believe to be the most suitable target and modality for our product candidates to address particular liver diseases. We are collaborating with the University of Pennsylvania's Gene Therapy Program (GTP) led by James M. Wilson, M.D., Ph.D., to utilize GTP's world-class translational expertise and infrastructure, which has helped generate our initial pipeline of potential product candidates. For more information, visit *https://iecure.com* and follow on LinkedIn.

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 and our partners' product candidates and gene editing approaches including editing efficiency; the suitability of ARCUS nucleases for gene insertion and other gene editing approaches; the expected timing of regulatory processes; expectations about our and our partners' operational initiatives and strategy; and anticipated timing of clinical data. 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," "possible," "potential," "predict," "project," "pursue," "should," "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 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; 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 the COVID-19 pandemic and variants thereof, or any pandemic, epidemic, or outbreak of an infectious disease; 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; 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, 2023, 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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