iECURE Secures Clearance from Australian Therapeutic Goods Administration for its Clinical Trial Application for the OTC-HOPE Phase 1/2 Study of ECUR-506

ECUR-506 is a gene editing-based investigational therapy for the treatment of Ornithine Transcarbamylase (OTC) deficiency

PHILADELPHIA— Dec. 13, 2023 – **iECURE, Inc.,** a gene editing company focused on the development of mutation-agnostic *in vivo* gene insertion, or knock-in, editing therapies for the treatment of liver disorders with significant unmet need, announced today that the Australian Therapeutic Goods Administration (TGA) has approved the Company's Clinical Trial Notification (CTN) for ECUR-506 (formerly GTP-506), an investigational therapy in development for the treatment of Ornithine Transcarbamylase (OTC) deficiency in pediatric (or neonatal) patients. The CTN approval represents the first of such regulatory approvals to begin clinical trials, with additional approvals expected in 2024. iECURE is in the process of preparing sites for the global, first-in-human Phase 1/2 clinical study and anticipates initiation of such clinical trial in the first half of 2024.

"The TGA's clearance to begin clinical trials for the OTC-HOPE study represents major milestones for the OTC deficiency community and for the iECURE team," said Joe Truitt, Chief Executive Officer of iECURE. "ECUR-506 has the potential to restore the function of the OTC enzyme in infants who lack this critical component of the urea cycle. The current standard of care relies on low protein diets, kidney dialysis, the use of ammonia scavengers and eventual liver transplant for babies with severe OTC. We are hopeful that our approach will be a better option for these children."

The OTC-HOPE study is a Phase 1/2 first-in-human study in baby boys with genetically confirmed neonatal-onset OTC deficiency. It is designed primarily to assess the safety and tolerability of ECUR-506 delivered as a single dose intravenously. Secondary objectives are to assess the pharmacokinetics and efficacy of ECUR-506. In addition, exploratory endpoints will assess disease-specific markers, developmental milestones and quality of life.

"For too long, families managing a child with severe OTC deficiency have had no choice other than liver transplant, which carries significant risks including life-long immunosuppression caused by medicines needed to prevent organ rejection," said George Diaz, M.D., Ph.D., Vice President and Therapeutic Area Lead for Urea Cycle Disorders at iECURE and a recently practicing metabolic genetics physician at The Mount Sinai Hospital in New York treating patients with OTC deficiency. "If ECUR-506 lives up to its potential of permanently enabling these children to create healthy OTC enzyme, it could enable them to avoid significant future nervous system and liver damage that high ammonia levels cause or the need for liver transplants."

In preclinical studies, administration of ECUR-506 resulted in a durable response in nonhuman primates, with up to 28.2% of liver cells demonstrating expression of the human OTC gene at the 1-year time point. A 5% threshold of enzymatic activity has the potential for clinical benefit as previously identified by research published in **Annals of Clinical and Translational Neurology.** Separately, in a mouse model of OTC-deficiency, the injection of ECUR-506 in newborn mice efficiently inserted a healthy copy of the

OTC gene. Mice with the inserted gene were challenged with a high protein diet but were protected from a lethal buildup of ammonia compared to the control group.

“For years, the development of an effective genetic-based therapy for severe OTC deficiency was precluded by the rapid division of liver cells,” said James M. Wilson, M.D., Ph.D., Rose H. Weiss professor and director, Orphan Disease Center; professor in the Departments of Medicine and Pediatrics, Perelman School of Medicine; and director of the Gene Therapy Program (GTP) at the University of Pennsylvania, whose laboratory developed ECUR-506 as a novel gene editing approach to treat OTC deficiency. “We are excited about the potential for ECUR-506 to provide lasting clinical benefit for these children, and the acceptance of the clinical study by regulatory authorities in Australia is a significant step towards this goal.”

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 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 therapeutic donor vector that inserts the OTC gene to provide the desired functional gene. iECURE has licensed the ARCUS nuclease for ECUR-506 from Precision BioSciences.[1] The cut in the PCSK9 site serves as the insertion site for the therapeutic gene, providing a potential path to permanent expression of a healthy gene.

About the OTC-HOPE Trial
The OTC-HOPE Trial is a Phase 1/2 first-in-human clinical trial of ECUR-506 in baby boys with genetically confirmed Ornithine Transcarbamylase deficiency. The study is enrolling baby boys aged 24 hours to seven months who are diagnosed with severe neonatal-onset OTC deficiency and will test up to two dose levels of ECUR-506. 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 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***.

About Precision BioSciences & ARCUS®

Precision BioSciences, Inc. is an advanced gene editing company dedicated to improving life (Nasdaq: 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**.

Penn's Financial Disclosure

The University of Pennsylvania (Penn) and Dr. Wilson each hold equity interests in iECURE. Penn also receives significant sponsored research support from the Company, and both Penn and Dr. Wilson stand to benefit from licensing revenues received from iECURE based on successful technology development and commercialization of the technologies licensed from Penn. Dr. Wilson serves as Chief Scientific Advisor for iECURE.

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[1] iECURE has licensed the ARCUS® nuclease from Precision BioSciences for four gene insertion programs including OTC, CTLN1 and PKU.