iECURE Announces FDA Clearance of Investigational New Drug Application for ECUR-506 to Initiate OTC-HOPE Trial for Treatment of Neonatal Onset Ornithine Transcarbamylase Deficiency in the U.S.

Clinical trial sites in the United States, United Kingdom, and Australia will evaluate ECUR-506, an investigational gene editing-based therapy, in newborn males with neonatal onset Ornithine Transcarbamylase (OTC) deficiency

ECUR-506 is the first in vivo *gene insertion program authorized for clinical investigation in infants in the U.S.*

PHILADELPHIA— April 4, 2024 – **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 clearance of its Investigational New Drug (IND) application from the U.S. Food and Drug Administration (FDA) for ECUR-506 in Ornithine Transcarbamylase (OTC) deficiency. ECUR-506 will be evaluated in the OTC-HOPE study in newborn males with genetically confirmed neonatal onset OTC deficiency. The OTC-HOPE study was previously cleared to begin in the United Kingdom by the Medicines & Healthcare Products Regulatory Agency (MHRA) and Australia by the Therapeutic Goods Administration (TGA).

"With this IND clearance, we are now activating sites in three countries in distinct geographical areas – United States, United Kingdom and Australia – which will facilitate families' ability to access this landmark clinical trial," said Joe Truitt, Chief Executive Officer of iECURE. "We are working diligently to open sites so we can start enrolling patients for dosing. The trial will be accepting eligible baby boys with neonatal onset OTC deficiency from all over the world, and we hope to see positive safety data and indications of efficacy with this trial."

The OTC-HOPE study is a Phase 1/2 first-in-human study in newborn males with genetically confirmed neonatal onset OTC deficiency. It is designed primarily to assess the safety and tolerability of ECUR-506 following intravenous administration of a single dose. Secondary objectives are to assess the pharmacokinetics and efficacy of ECUR-506. In addition, exploratory endpoints will assess disease-specific biologic markers, developmental milestones and quality of life. The ECUR-506 program is the first *in vivo* gene insertion program to be cleared in the U.S. for study in infants, and it represents the first time that the ARCUS® nuclease has been used to provide an *in vivo* insertion point for a functional gene in the clinic.

"There is a significant need for clinical research and treatment options for newborns with severe, neonatal onset OTC deficiency," said Gabriel M. Cohn, MD, Chief Medical Officer of iECURE. "For many families whose children are diagnosed with neonatal onset OTC deficiency, liver transplant is the only curative option, but carries with it serious risks and requires considerable immunosuppressant therapy to prevent transplant rejection. ECUR-506 represents hope for potentially enabling children to produce functional OTC enzyme in the long term without the need for transplantation."

"This milestone is the culmination of over 8 years of pre-clinical research in my laboratory addressing gene editing strategies for severe rare liver metabolic diseases," 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 hope that treatment with this investigational therapeutic will show promise for clinically meaningful improvements for infants with neonatal onset OTC deficiency and their families.”

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.[1] 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. ECUR-506 is being studied in the OTC-HOPE study, the first clinical meganuclease-based *in vivo* gene insertion program.

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 neonatal onset OTC deficiency and will test differing dose levels of ECUR-506. The study is enrolling baby boys up 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 preclinical and 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 is designed to differ 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. For more information about Precision BioSciences, 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 iECURE, 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.

Contacts
Investors:
David Garrett
dgarrett@iecure.com

Media:
Janine Bogris
Inizio Evoke Comms
janine.bogris@inizioevoke.com

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