**iECURE Reports Complete Clinical Response in First Infant Dosed with its *In Vivo* Gene Editing Candidate ECUR-506 in an Ongoing Phase 1/2 Clinical Trial in Ornithine Transcarbamylase (OTC) Deficiency**

- *First* in vivo *gene insertion clinical trial dosing infants reports complete clinical response in the first participant at the lowest dose level (1.3 x $10^{13}$ GC/kg) of ECUR-506 from three months post exposure to the end of study (six months post exposure) as demonstrated by the removal of standard of care ammonia scavenging medicines, followed by absence of hyperammonemic crises and normalization of protein intake*
- *The OTC-HOPE Phase 1/2 trial has regulatory authorization in four geographies (US, UK, Spain and Australia) and is currently enrolling with the complete data readout anticipated in 1H 2026*
- *ECUR-506 for neonatal onset OTC deficiency represents a meaningful potential clinical and commercial opportunity, affecting over 1,000 births per year globally*

**PHILADELPHIA**— January 9, 2025 – **iECURE, Inc.,** a gene editing company focused on the development of mutation-agnostic *in vivo* gene insertion therapies for the treatment of liver disorders with significant unmet need, today reported preliminary findings from the first infant dosed in the ongoing OTC-HOPE Phase 1/2 study of ECUR-506, the company's clinical candidate designed to treat neonatal onset ornithine transcarbamylase (OTC) deficiency. Treatment with ECUR-506 was generally well tolerated in this infant with no significant clinical safety concerns apart from asymptomatic transaminitis at four weeks. The asymptomatic transaminitis was managed with immunosuppressive therapy and resolved within four weeks. Twelve weeks after a single dose of ECUR-506, ammonia scavenger medication was discontinued and mean daily protein intake was increased to age-appropriate levels. Protein liberalization was well tolerated, and the subsequent mean ammonia level remained within normal limits and was reduced compared to the mean pretreatment level.

iECURE's approach to gene editing for its initial programs, including OTC deficiency, relies on the delivery of two adeno-associated virus (AAV) vectors comprised of the same capsid, but 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 (Nasdaq: DTIL).[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 functional gene.

"Our team is highly encouraged to see this baby, who after having experienced two spikes in blood ammonia levels before three and a half months of age, reach a point where he no longer needs ammonia scavengers and is eating age-appropriate levels of protein for a baby of his age," said Julien Baruteau, M.D., Ph.D., MRC Clinical Scientist Fellow and Group Leader at University College London Great Ormond Street Institute of Child Health and Consultant in Metabolic Medicine at Great Ormond Street Hospital for Children in London, and principal investigator in the study. "Standard of care for babies with neonatal OTC deficiency relies on liver transplantation in infancy, a procedure with significant risks of complications. This novel gene therapy approach might enable bypassing the need for liver transplantation. While this is very early data, I am hopeful that this baby will continue along this encouraging trajectory and that other babies who enroll in this study will have similar experiences. This

novel gene therapy technology may herald new avenues to treat babies with severe liver genetic diseases."

OTC deficiency is a serious rare genetic disease wherein ammonia, a waste product that is generated when the body breaks down proteins, builds up in the blood (hyperammonemia). Ammonia is toxic to the brain when it accumulates at high levels. Newborns with neonatal onset OTC deficiency experience symptoms of hyperammonemia shortly after birth, including lethargy, poor suck and vomiting, that if left untreated can quickly escalate to seizures, brain damage, coma and eventual death.

Rescuing newborns from their first hyperammonemic crisis (HAC) often requires dialysis and intravenously delivered ammonia scavenger medicines. Once the infant is stabilized, ongoing medical management, including ammonia scavenger dosing and use of a protein-restricted diet, is conducted to protect the brain against further ammonia buildup. Despite medical management, additional HACs can occur leading clinicians to recommend a liver transplantation in the first year of life. While curative, liver transplantation includes risks such as graft failure and an increased risk of malignancy and infection due to prolonged use of immunosuppressive drugs.

"To our knowledge, this is the very first infant to have ever received an *in vivo*, liver-directed, gene insertion investigational product. While still early days and follow up is limited to the first six months post exposure, the elimination of this baby's need for the current standard of care observed after a few months of receiving ECUR-506 may represent a historic milestone for children with neonatal OTC deficiency, their families and their care teams. *In vivo* gene insertion may foretell the future treatment approach for a host of severe, early-onset, genetic conditions and may mark the beginning of a new chapter in the evolution of gene therapy," said Gabriel Cohn, M.D., MBA, Chief Medical Officer of iECURE. "It is important to note that elevations in liver enzymes, particularly ALT, are not uncommon in AAV-mediated gene therapy trials. We have updated the clinical trial protocol to more promptly detect and more aggressively manage this type of event, if needed, in future clinical trial participants."

Summary of Findings in the First Participant:

- The first infant dosed with ECUR-506 was initially diagnosed with neonatal onset OTC deficiency following a HAC during the first week of life, and he was stabilized with hemodialysis and managed with standard of care ammonia scavenger medication and protein restriction. Molecular genetic testing confirmed the diagnosis.
- At 3.5 months of age, while on a protein restricted diet and on scavenger medicine, the participant experienced a breakthrough HAC.
- At 6.5 months of age, the participant received a single infusion of the lowest dose ($1.3 \times 10^{13}$ GC/kg) of ECUR-506, which was generally well tolerated.
- Asymptomatic transaminitis was noted during routine lab testing at four weeks post-ECUR-506 exposure. A liver biopsy was subsequently performed at six-weeks post dosing which confirmed an acute T-cell inflammatory response. By eight weeks post-ECUR 506 exposure, following immunosuppressive therapy management, the grade 3 transaminitis resolved.
- On the basis of reduced serum glutamine levels, ammonia scavenger medication weaning was initiated with complete discontinuation achieved at 12 weeks post-ECUR-506 dosing.
- Protein allowance was subsequently increased to the age-appropriate level for infants without OTC deficiency.

- The participant's mean ammonia and serum glutamine levels have remained within normal limits, and the participant has not experienced any HAC as of 6 months post treatment.
- The participant transitioned to the long term follow up study (ECUR-LTFU) for further monitoring.
- Dosing of cohort 1 (Low Dose) continues and the complete six-month data readout for all patients is anticipated in the first half of 2026.
- Full study data of the first participant will be presented at the 2025 American College of Medical Genetics and Genomics (ACMG) Annual Clinical Genetics Meeting in Los Angeles, California on March 18-22, 2025.

"The current standard of care for infants affected by neonatal onset OTC deficiency leaves significant room for improvement, and should these results hold true for additional participants, we believe there is tremendous potential for our gene editing approach to treat this devastating disease," said Joe Truitt, Chief Executive Officer of iECURE. "These initial findings are encouraging, and in 2025 we look forward to engaging with regulatory agencies on potential accelerated approval pathways, expand the trial locations across the globe and complete the enrollment of the OTC-HOPE trial."

In addition to reporting these data from the first participant, iECURE also announced updates around clinical trial locations. UCLA Mattel Children's Hospital and Children's Hospital of Colorado are the first two clinical trial sites in the United States open for enrollment. Also, iECURE has secured Clinical Trial Authorization from the European Union (EU) and the European Economic Area (EEA) under the EU Clinical Trial Regulation by the Spanish Agency of Medicines and Medical Devices (AEMPS) and will be working to open additional sites in Spain.

**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 has been cleared to evaluate ascending dose levels of ECUR-506, if necessary. The study is enrolling newborn males up to seven months of age at screening 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. The main study will occur in a series of stages over a 10-month period, including screening, stabilization, dosing eligibility, study drug administration, and six-month follow-up. Upon completion of the OTC-HOPE study, participants transition to the 14.5 year long term follow up study (ECUR-LTFU). For more information, visit ***https://OTC-HOPE.com***.

**About iECURE**
iECURE is a clinical-stage gene editing company focused on developing therapies that utilize mutation-agnostic *in vivo* gene insertion for the treatment of liver disorders with significant unmet need. We believe our approach has the potential to restore the function of a dysfunctional gene, regardless of mutation, by knocking-in a functional 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. For more information, visit ***https://iecure.com*** and follow on ***LinkedIn***.

**About Precision BioSciences & ARCUS®**

Precision BioSciences, Inc. is a clinical stage 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 such as chronic hepatitis B where no adequate treatments exist. For more information about Precision BioSciences, visit ***www.precisionbiosciences.com***.

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