iECURE Receives FDA Orphan Drug Designation for GTP-506, an Investigational Gene Editing Product Candidate for the Treatment of Ornithine Transcarbamylase (OTC) Deficiency

- *FDA recently granted Rare Pediatric Disease Designation to GTP-506 for the treatment of OTC deficiency in a pediatric population*
- *Designations reinforce unmet need for treatment options for patients with this rare urea cycle disorder*
- *Company continues to advance toward an Investigational New Drug (IND) submission in mid-2023*

PHILADELPHIA—September, 06 2022 – **iECURE**, 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 today announced that the U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation to its lead product candidate GTP-506, an investigational product, for the treatment of Ornithine Transcarbamylase (OTC) deficiency, a rare genetic condition that can lead to irreversible neurological impairment, seizures, coma and death in a pediatric population.

"FDA's decision to grant both Orphan Drug Designation and Rare Pediatric Disease Designation for our investigational gene editing therapy aligns with our mission to provide treatments for patients where few if any options exist and highlights the urgency of developing a treatment for pediatric patients with OTC deficiency, a serious and life-threatening liver disease," said Joe Truitt, Chief Executive Officer of iECURE. "We look forward to filing an IND application with the FDA for our first-in-human clinical trial next year."

The FDA grants Orphan Drug Designation to drugs and biologics intended for the safe and effective treatment, diagnosis or prevention of rare diseases or conditions affecting fewer than 200,000 people in the United States. Orphan Drug Designation provides benefits to drug developers designed to support the development of drugs and biologics for small patient populations with unmet medical needs. These benefits include assistance in the drug development process, seven years of market exclusivity following FDA approval, waiver or partial payment of FDA fees, and tax credits for clinical testing expenses conducted after orphan designation is received.

"OTC deficiency is a devastating genetic disease that presents as early as the first few days of life with loss of OTC enzyme activity. Current treatment options involve life-long dietary restrictions, nitrogen scavenger therapy, as well as liver transplant for patients who qualify," said George Diaz, M.D., Ph.D., VP of Urea Cycle Disorders at iECURE. "Targeted genome editing using GTP-506 has the potential to enable OTC-deficient patients to produce healthy, functional OTC enzyme in their own liver cells."

About GTP-506

iECURE's approach to gene editing for its initial programs, including OTC deficiency, relies on the delivery of twin adeno-associated virus (AAV) capsids carrying different payloads. GTP-506 comprises two vectors, an ARCUS® nuclease vector (GTP-506A) targeting gene editing in the well-characterized PCSK9 gene locus and a therapeutic donor vector (GTP-506D) that inserts the OTC gene to provide the

desired genetic correction.[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 OTC Deficiency
OTC deficiency, the most common urea cycle disorder, is an inherited metabolic disorder caused by a genetic defect in a liver enzyme responsible for detoxification of ammonia. Individuals with OTC deficiency can build-up excessive levels of ammonia in their blood, potentially resulting in devastating consequences, including cumulative and 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 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 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 by knocking-in a healthy copy, regardless of mutation, 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, or 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 ***www.iecure.com*** and follow on ***LinkedIn***.

Financial Disclosure
The University of Pennsylvania (Penn) and Dr. Wilson hold equity interests in iECURE. Penn also receives significant sponsored research support from the Company, and both Penn and Dr. Wilson 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.

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