Encoded Therapeutics Announces US IND Clearance and Australian CTA Approval for Dravet Syndrome Gene Therapy Candidate ETX101

- Initial studies will focus on infants and young children; company plans to begin clinical trials in the United States and Australia in the first half of 2024
- There are currently no approved disease-modifying treatments for Dravet syndrome

SOUTH SAN FRANCISCO, CA – February 6, 2024 – Encoded Therapeutics Inc., a biotechnology company focused on developing genetic medicines for severe central nervous system (CNS) disorders, today outlined the global development strategy for its lead gene therapy candidate, ETX101, for the treatment of SCN1A+ Dravet syndrome. Individuals with Dravet syndrome, the most common developmental and epileptic encephalopathy, experience a spectrum of clinical symptoms, including treatment-resistant seizures and neurodevelopmental stagnation. Dravet syndrome is primarily caused by loss-of-function variants in the SCN1A gene, accounting for over 85% of cases. ETX101 is an AAV9-mediated candidate gene regulation therapy designed to selectively upregulate expression of the SCN1A gene in GABAergic inhibitory interneurons and potentially address the underlying cause of the disease.

ETX101 Global Clinical Development

Encoded has received clearance for its Investigational New Drug (IND) application from the US Food and Drug Administration and approval under the Clinical Trial Approval (CTA) scheme from the Australia Therapeutic Goods Administration to initiate clinical trials of its gene therapy candidate, ETX101. The company plans to initiate ENDEAVOR, a two-part, Phase 1/2 clinical trial in US patients 6 months to <3 years of age with SCN1A+ Dravet syndrome in the first half of 2024. WAYFINDER, a Phase 1/2 trial in patients 3 to <7 years of age in Australia, will be conducted concurrently with ENDEAVOR.

“Dravet syndrome is a devastating disorder that necessitates a paradigm shift from conventional symptomatic management towards precise and targeted interventions at the genetic level. I’m hopeful that gene therapy will not just alleviate symptoms but address the root cause of Dravet syndrome, marking a potentially transformative approach in our quest to address the ongoing medical burden of families living with Dravet syndrome,” said Joseph Sullivan, M.D., Murphy Parker Endowed Professor in Pediatric Epilepsy, Professor of Neurology & Pediatrics at UCSF Pediatric Epilepsy Center of Excellence and Principal Investigator on the ENDEAVOR study.

The ENDEAVOR and WAYFINDER clinical trials are part of Encoded’s global clinical development program, POLARIS, which aims to assess safety and efficacy of ascending doses of ETX101 in infants and young children. Importantly, POLARIS will evaluate the initial effects of ETX101 on seizure burden, as well as potential long-term improvements in neurodevelopment. Furthermore, Encoded has aligned with FDA on the design of ENDEAVOR as a two-part study, which creates an opportunity to seamlessly transition to a potentially confirmatory trial following demonstration of initial safety and efficacy.

The POLARIS program is based on preceding patient-focused drug development initiatives (Dravet ENGAGE), a multipronged biomarker discovery project (ELUCIDATE) and a recently completed natural history study (ENVISION), the largest longitudinal natural history study in Dravet syndrome to date. These initiatives have informed the optimal clinical design for POLARIS and emphasize the urgent unmet need for disease-modifying therapies.

“ETX101 represents a groundbreaking advancement in the therapeutic landscape for Dravet syndrome, with potential not only for seizure management but also for addressing the broader spectrum of non-seizure manifestations. ENDEAVOR and WAYFINDER are the first step in bringing a potentially one-time, disease-modifying gene therapy to the Dravet community, and we are excited to be partnering with leading experts in the care of patients with Dravet syndrome to begin clinical trials in the US and Australia in the coming months,” said Sal Rico, M.D., Ph.D., Chief Medical Officer.

Encoded will be providing additional updates on its research pipeline, which is focused on both rare genetic and common disease programs, in addition to clinical progress with ETX101 for Dravet syndrome later in 2024.

“Encoded is committed to creating innovative genetic medicines that bring renewed hope and possibilities to patients living with severe CNS disorders. The initiation of clinical trials in Dravet syndrome and the advancement of our CNS pipeline strategically positions Encoded to achieve pivotal program milestones in 2024. We look forward to sharing additional company updates in the coming months,” said Kartik Ramamoorthi, Ph.D., Co-Founder and Chief Executive Officer.

About ETX101

Encoded is developing ETX101 as a potential one-time, disease-modifying gene regulation therapy targeting the underlying cause of SCN1A+ Dravet syndrome. In ETX101, a transgene encoding an engineered transcription factor under the control of a cell-selective regulatory element is delivered within a clinically-validated capsid (AAV9) to upregulate, or increase, the expression of the endogenous SCN1A gene. This approach is expected to increase production of NaV1.1 protein sodium channels in target neurons in the brain, leading to restored function. By targeting the underlying mechanism, ETX101 has the potential to address the full range of symptoms associated with Dravet syndrome. ETX101 has been granted Orphan Drug Designation and Rare Pediatric Disease Designation by the US Food and Drug Administration and Orphan Designation by the European Medicines Agency.

About Encoded’s ETX101 Clinical Development Program POLARIS

POLARIS is built upon Encoded’s comprehensive preclinical research, and incorporates a multipronged biomarker discovery program (ELUCIDATE), patient-focused drug development initiatives (Dravet ENGAGE), and the recently completed natural history study (ENVISION), the largest prospective, longitudinal natural history study of Dravet patients to date. This foundational work has enabled optimization of POLARIS’ rigorous clinical design, beginning with ENDEAVOR and

WAYFINDER, to assess the safety and efficacy of ETX101 in infants and young children with SCN1A+ Dravet syndrome.

ENDEAVOR Clinical Study (United States)

ENDEAVOR is a two-part Phase 1/2 dose escalation study of ETX101 in infants and young children aged 6 months to <3 years. In Part 1, up to two doses of ETX101 will be evaluated in 4 participants. The primary aims of the study are to evaluate the safety and tolerability of ETX101, to assess preliminary efficacy, and to contribute to therapeutic dose selection. ETX101 has received IND clearance, and ENDEAVOR Part 1 is expected to begin in the first half of 2024. Part 2 is planned following demonstration of safety and efficacy in ENDEAVOR Part 1.

WAYFINDER Clinical Study (Australia)

WAYFINDER is a Phase 1/2 dose escalation study of ETX101 in young children aged 3 to <7 years with SCN1A+ Dravet syndrome. Up to two doses of ETX101 will be evaluated in 4 participants. The primary aims of the study are to evaluate the safety and tolerability of ETX101, to assess preliminary efficacy, and to contribute to therapeutic dose selection. WAYFINDER has received TGA approval and is expected to begin in the first half of 2024.

About Dravet Syndrome

Dravet syndrome is a severe, lifelong disorder of the central nervous system that occurs in approximately 1 in 16,000 births worldwide, with the majority of cases resulting from loss-of-function variants in the SCN1A gene. This developmental and epileptic encephalopathy equally affects people of both sexes and all races, manifesting in a wide array of symptoms. Frequent, prolonged, and treatment-resistant seizures primarily begin in the first year of life of a typically developing infant. Severe cognitive and developmental stagnation, sleep abnormalities, motor impairment and behavioral difficulties usually manifest by the second or third year of a child's life. More information about Dravet syndrome can be found at www.dravetfoundation.org.

About Encoded Therapeutics

Encoded Therapeutics is creating one-time, potentially disease-modifying gene therapies to improve the lives of people with severe CNS disorders. Our cell-selective targeting and regulation platform offers potentially unprecedented gene specificity and cell selectivity to unlock novel opportunities by targeting a range of disease mechanisms. We are overcoming key limitations of current gene therapies by incorporating platform innovations into therapeutic development and advancing potentially best-in-class programs in Dravet syndrome and additional CNS disorders. For more information, please visit www.encoded.com.

Contact

Jennifer Gorzelany, communications@encoded.com, 650-515-9695