

Encoded Therapeutics Presents Updated Data from POLARIS Phase 1/2 Trials of ETX101 Gene Therapy in Dravet Syndrome at the 16th European Epilepsy Congress

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- Substantial seizure frequency reductions sustained through 52 weeks following ETX101 administration –*
- Cognitive trajectories of children treated before two years of age continue to diverge from Dravet natural history with up to 76 weeks of observation –*
- Progressive gains in adaptive behavior observed through 52 weeks across the full age range, including substantial gains in communication and motor function –*
- Favorable safety profile demonstrated across all dose levels, with no treatment-related serious adverse events with up to 117 weeks of follow-up –*

SOUTH SAN FRANCISCO, Calif. – Encoded Therapeutics, Inc. (“Encoded”), a clinical-stage biotechnology company developing precision genetic medicines for severe neurological disorders, today announced that new Phase 1/2 POLARIS data for ETX101, its investigational AAV9-based gene regulation therapy designed as a one-time, disease-modifying treatment for SCN1A+ Dravet syndrome, were presented in an oral session at the 16th European Epilepsy Congress (EEC) in Athens, Greece by Professor Ingrid Scheffer, Pediatric Neurologist and Laureate Professor of Pediatric Neurology at The University of Melbourne.

Substantial Seizure Reduction Sustained Through 52 Weeks

ETX101 continues to demonstrate substantial and durable reductions in monthly countable seizure frequency (MCSF) following a single administration. In the cumulative analysis from Week 5 through Week 52 or each participant’s latest study visit, dose level 3 (DL3; n=5) and DL4 participants (n=9) achieved a median MCSF reduction of approximately 76% and 60%, respectively. Among participants who completed 52 weeks of observation, the median MCSF reduction at Month 12 (Weeks 49-52) was approximately 79% for DL3 (n=3) and 89% for DL4 (n=5).

“With longer follow-up and additional data available, we are encouraged by the magnitude and durability of seizure reduction following a single administration of ETX101,” said Sal Rico, M.D., Ph.D., Chief Medical Officer of Encoded. “Importantly, the emerging clinical profile extends beyond seizure control, with continued improvements across cognitive and adaptive behavior measures supporting the potential to address the broader manifestations of Dravet syndrome.”

Evidence of Neurodevelopmental Benefit

Presented data demonstrate progressive gains in cognition and adaptive behavior. Among participants treated before two years of age, Bayley Scales of Infant and Toddler Development, Fourth Edition (Bayley-4) cognitive growth scale values (GSVs) showed substantial gains over time, with developmental trajectories approaching the range expected for neurotypical children. With up to 76 weeks of follow-up, participants showed continued and progressive divergence from the stagnation observed in the ENVISION natural history study.

Additionally, the Vineland Adaptive Behavior Scales, Third Edition (VABS-3) showed clinically meaningful improvements across all evaluated domains, including communication, motor skills, socialization, and daily living skills across the full age range. Particularly notable were gains in receptive communication, expressive communication and motor function, substantially narrowing the gap with neurotypical peers.

Finally, the EEC presentation highlighted outcomes in the oldest participant dosed at DL4. Treated at 3 years and 9 months of age, the participant experienced substantial seizure frequency reduction, an extended period of seizure freedom, and meaningful developmental gains over 52 weeks of observation.

“Dravet syndrome places a heavy and constant burden on families,” said Dr. Scheffer. “In clinic, we see how persistent seizures and developmental challenges shape daily life for these children and their families. That’s why these results stand out. When a single treatment of ETX101 has shown gains in seizure control and neurodevelopment, as observed in POLARIS, it suggests we may be able to fundamentally change the trajectory of this disease-giving us genuine reason for hope.”

Safety and Tolerability

To date, ETX101 has shown a favorable safety profile and has been well-tolerated across all four dose levels with up to 117 weeks of follow-up, with no treatment- or procedure-related serious adverse events. Treatment-related adverse events included transaminase elevations (n=7/21) and thrombocytopenia (n=3/21), both of which were clinically asymptomatic and resolved in all participants. All efficacy and safety analyses reflect data through the August 3, 2026, data cutoff.

About the POLARIS Clinical Development Program

The POLARIS program is a comprehensive clinical investigation of ETX101 in children and adolescents with *SCN1A*+ Dravet syndrome, comprising multiple Phase 1-3 clinical trials. The first phase of POLARIS includes three ongoing open-label, Phase 1/2 dose-escalation, multicenter trials (ENDEAVOR Part 1 (US), EXPEDITION (UK), and WAYFINDER (Australia)) in infants and young children aged 6 months to 7 years. ENDEAVOR Part 1B, an expansion study in the US, is actively enrolling children and adolescents aged 4 to 18 years. These studies are evaluating the safety and preliminary efficacy of ETX101 in children and adolescents with Dravet syndrome due to variants in the *SCN1A* gene. The pivotal ENDEAVOR Part 2 study is also ongoing, evaluating seizure and neurodevelopmental outcomes in young children aged 6 months to 4 years.

About ETX101

ETX101 is an investigational AAV9-based gene regulation therapy designed to increase the expression of the *SCN1A* gene to restore sodium channel function in inhibitory interneurons. By

targeting the root mechanism, ETX101 has the potential to treat the full spectrum of Dravet syndrome symptoms, including seizures, communication and cognitive impairment, behavioral issues, and motor dysfunction. The therapy is administered via a single intracerebroventricular (ICV) injection and is designed for long-term benefit. ETX101 has received Breakthrough Therapy, Regenerative Medicine Advanced Therapy, Fast Track, Rare Pediatric Disease, and Orphan Drug designations from the FDA. It also was selected for the FDA's CMC Development and Readiness Pilot (CDRP) program and received Orphan designation from the European Medicines Agency (EMA).

About Encoded Therapeutics

Encoded Therapeutics is a clinical-stage biotechnology company developing one-time precision genetic medicines for severe monogenic and common neurological disorders. The company's vector engineering platform enables highly targeted and cell-type-selective control of gene expression in the brain and peripheral nervous system, allowing potent and precise modulation of disease-relevant genes to address underlying disease biology. Encoded's end-to-end innovation engine-spanning discovery, development, and in-house GMP manufacturing-creates a streamlined path to advance a diversified pipeline of one-time treatments across a broad range of neurological conditions. Encoded is driven by a mission to meaningfully improve the lives of patients and families affected by devastating neurological disorders. For more information, please visit www.encoded.com.

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