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Encoded Therapeutics Reports Clinical Progress of ETX101 Gene Therapy for Dravet Syndrome, Recaps 2024 Corporate Achievements and Provides 2025 Outlook

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- *POLARIS program, launched in 2024 to evaluate ETX101 for SCN1A+ Dravet syndrome, is ongoing. Expect to complete dosing and share preliminary safety and efficacy data in 2H25.*
- *ETX201 gene therapy clinical candidate for Angelman syndrome advanced to IND-enabling studies. Encouraging safety and target engagement data observed in non-human primates (NHPs).*
- *Research programs in pain and neurodegeneration advancing, with potential for development candidates in 2H25.*
- *Internal GMP facility to support ETX101 and pipeline programs will be fully operational in 1Q25.*
- *Collaboration agreement signed with Prevail Therapeutics, a wholly owned subsidiary of Eli Lilly and Company, for Lilly Gene Therapy to use Encoded's novel regulatory elements.*
- *Workforce reduction of 29% implemented to support company operations to the end of 3Q26 and through key ETX101 and pipeline program milestones.*

SOUTH SAN FRANCISCO, Calif. – Encoded Therapeutics Inc., a clinical-stage biotechnology company developing genetic medicines for severe central nervous system (CNS) disorders, today announced continued progress in its lead clinical program, ETX101, and highlighted corporate achievements that advance its research pipeline and further develop infrastructure to fully integrate the Company's gene therapy capabilities.

"In 2024, we launched our ongoing POLARIS program evaluating ETX101 in SCN1A+ Dravet syndrome. With multiple dose levels administered, we expect to share preliminary efficacy data in the second half of the year," said Kartik Ramamoorthi, Ph.D., co-founder and Chief Executive Officer. *"This rapid progress, coupled with advancement of our Angelman syndrome program, ETX201, and our broader CNS pipeline, underscores the potential for our organization to discover and develop innovative CNS therapies. Given the significant potential of our portfolio, Encoded is focusing resources on ETX101 and our established programs where we have the greatest opportunity to create near-term value. In parallel, we have made the difficult decision to reduce the size of our technology and early-stage research and development functions. I am exceptionally grateful for the team's contributions and confident that 2025 will be a transformative year for Encoded."*

ETX101 for Dravet Syndrome, POLARIS Program

- ETX101 is an AAV9-based gene regulation therapy designed to upregulate expression of the *SCN1A* gene in inhibitory neurons and is the first potential one-time therapy to address the underlying genetic cause of Dravet syndrome.
- POLARIS, a global clinical program in the US, UK and Australia enrolling infants and children (6 months – 7 years of age) with SCN1A+ Dravet syndrome is ongoing; eight patients have been treated at multiple dose levels.

- As of February 12, ETX101 has been well-tolerated; no treatment-related serious adverse events have been reported at any dose level.
- Completion of additional dose levels and reporting of preliminary safety and efficacy data are planned for 2H25.
- Encoded has aligned with FDA and MHRA on the design of a sham-controlled, delayed-treatment, potentially confirmatory trial.
- ETX101 has Fast Track, Rare Pediatric, and Orphan Drug Designations from FDA and Orphan Designation from EMA.

ETX201 for Angelman Syndrome

- ETX201 is an AAV9-based vectorized microRNA (miRNA) designed to reduce the expression of the UBE3A antisense transcript (UBE3A-ATS) and unsilence paternal *UBE3A* expression.
- Encoded presented positive results of an NHP study at the Foundation for Angelman Syndrome Therapeutics (FAST) Global Science Summit in November. Data showed that ETX201 was well-tolerated and capable of widespread paternal *UBE3A* upregulation across critical, disease-relevant brain regions.
- Following guidance from FDA, IND-enabling studies have been initiated to support a potential ETX201 IND filing in 2026.
- ETX201 has the potential to be a one-time treatment approach to address the underlying cause of Angelman syndrome.

Research Pipeline

- Chronic pain candidate, an AAV9-based vectorized miRNA designed to knock down expression of *SCN9A* ($Na_V1.7$), demonstrated robust and durable correction of multiple pain phenotypes in an established rodent pain model. NHP studies are ongoing with the potential to nominate a development candidate in 2H25.
- Alzheimer's disease candidate, an AAV9-based vectorized miRNA, demonstrated robust and durable knockdown (up to 32%) of *MAPT* (tau) across disease relevant brain regions in an NHP study.
- Data for both the pain and Alzheimer's disease programs will be presented at scientific meetings in mid-2025.

Strategic Reorganization

- Encoded implemented a 29% reduction in workforce, extending cash runway through 3Q26.
- Impacted functions primarily include technology and early-stage research and development.
- Enhanced runway supports our goal of achieving key milestones, including preliminary clinical safety and efficacy for ETX101, IND/CTA for ETX201, and nomination of development candidates for our common CNS programs.

Additional Corporate Updates

- In 2024, Encoded initiated the build of a GMP facility to support the next stage of development for ETX101 and the broader portfolio; facility will be fully operational in 1Q25. Moving forward, all drug substance material for ETX101, ETX201 and pipeline programs will be manufactured in-house.

- Encoded and Prevail Therapeutics, a wholly owned subsidiary of Eli Lilly and Company, signed a collaboration agreement in May 2024 for Lilly Gene Therapy to use Encoded's novel regulatory elements. These regulatory elements are designed to enhance or reduce transgene expression in specific tissues and organs. Encoded received an upfront payment and is eligible to receive preclinical, development, regulatory and commercial milestone payments.

About Encoded Therapeutics

Encoded Therapeutics is a clinical-stage genetic medicines company developing potentially one-time, disease-modifying therapies for severe CNS disorders. Our proprietary vector engineering technology combines novel regulatory elements and payloads with AAV vectors, unlocking innovative solutions for intractable CNS conditions. Our lead clinical-stage program, ETX101 for Dravet syndrome, targets the underlying cause of the disorder through selective upregulation of *SCN1A* for potentially long-lasting benefit. Encoded's second program, ETX201, is a development-stage vectorized miRNA-based gene therapy designed to restore expression of *UBE3A* in individuals with Angelman syndrome. In parallel, we are advancing potentially best-in-class programs for common CNS conditions, including chronic pain and Alzheimer's disease. Harnessing our proprietary technology platform and expertise, we can efficiently advance programs from discovery through clinical development. Encoded is committed to pioneering breakthrough treatments for CNS disorders. For more information, please visit **www.encoded.com**.

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