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Encoded Therapeutics Presents Preclinical Data Across its Gene Therapy Portfolio at the 27th Annual Meeting of the American Society of Gene & Cell Therapy (ASGCT)

- *Four presentations highlight expansion of the company's CNS pipeline and vector engineering platform*
- *Preclinical data presented supports potential to advance programs in Angelman Syndrome and Lennox-Gastaut Syndrome*
- *Proof-of-concept data demonstrating knock-down of neuropathic pain (SCN9A) and Alzheimer's disease (MAPT) targets showcase advancements in the company's vector engineering platform*

SOUTH SAN FRANCISCO, Calif. – Encoded Therapeutics Inc., a biotechnology company developing genetic medicines for severe central nervous system (CNS) disorders, today highlights oral and poster presentations on the Company's preclinical gene therapy programs and vector engineering platform at the 27th ASGCT Annual Meeting being held May 7 – 11, 2024 in Baltimore, MD.

"We are thrilled to share multiple advancements across our portfolio of precision genetic medicines, showcasing substantial progress across various fronts. These data underscore our platform's potential to deliver precision therapies for a range of CNS diseases," said Stephanie Tagliatela, Chief Scientific Officer at Encoded. "Alongside clinical advancement of our lead program, ETX101 for SCN1A+ Dravet syndrome, we are poised to nominate multiple programs to development in 2025, marking yet another significant milestone."

Oral Presentation

Title: **GABA Selective AAV-mediated Gene Therapy Provides Durable Seizure Protection in Multiple Refractory Epilepsy Models** (Abstract #19)
Session: AAV Vectors – Preclinical and Proof-of-Concept: Therapy Focus
Date & Time: Tuesday, May 7, 1:45-2:00 p.m. ET
Location: Ballroom 2

Epilepsy affects approximately 1% of the population, with nearly one third of cases failing to respond to first- and second-line treatments. Encoded's vector engineering platform has enabled the development of GABA-selective AAV-mediated gene therapies designed to potentiate GABAergic neurotransmission and modulate the circuit dysfunction underlying refractory epilepsies. Our lead candidate reduced seizure incidence and severity in two biologically distinct seizure assays with no adverse impact on body weight, motor function or locomotion. Furthermore, the top candidate is well-tolerated in non-human primates (NHP) even at high doses. These data support further development of our candidate gene therapy for the treatment for refractory epilepsies.

Poster Presentations

Title: **Advancing Gene Therapy for STXBP1-related Disorders Through Targeted Vector Engineering: Efficacy and Safety Results in Mice and Non-Human Primates** (Abstract #508)

Date & Time: Wednesday, May 8, 5:30-7:00 p.m. ET
Location: Exhibit Hall

STXBP1-related disorders (STXBP1-RD) result from loss-of-function variants in *STXBP1*, causing severe developmental delay and treatment-resistant epilepsy. Encoded has engineered AAV9 vectors that drive potent expression within CNS tissue while reducing off-target expression in dorsal root ganglia (DRG) and non-neuronal tissues. These engineered AAV9-STXBP1 vectors achieved robust, dose-dependent improvements in seizure, cognitive, and motor phenotypes in *Stxbp1*$^{+/-}$ mice, with no observed dose-limiting toxicity. In NHPs, the engineered vectors showed strong CNS expression and were well-tolerated. Furthermore, the inclusion of a DRG de-targeting element reduced expression within the DRG and spinal cord by >10-fold, ameliorating microscopic DRG-related findings. These findings establish proof-of-concept for an AAV9-based gene therapy for STXBP1-RD and support the use of modular regulatory element engineering to drive desired expression profiles within the CNS.

Title: **A Vectorized miRNA-based Approach to Unsilence UBE3A in Angelman Syndrome** (Abstract #1125)
Date & Time: Thursday, May 9, 5:30-7:00 p.m. ET
Location: Exhibit Hall

Angelman syndrome (AS) is a severe neurodevelopmental disorder characterized by intellectual disability, ataxia, and seizures. AS is caused by loss-of-function of the maternally-inherited *UBE3A* gene. Unsilencing of the paternal copy of UBE3A has the potential address the underlying cause of the disease while mitigating the risk of UBE3A overexpression-related toxicity. We demonstrated that an AAV-based miRNA vector was capable of upregulating paternal UBE3A and correcting multiple phenotypes in the AS mouse model. Encoded's lead miRNA candidate was well-tolerated in NHPs and demonstrated potent unsilencing of paternal UBE3A in critical brain regions. Collectively, these data support further development an AAV-based miRNA treatment approach for Angelman Syndrome.

Title: **Identification of Potent and Selective AAV-miRNA Candidates to Knockdown Non-Monogenic Neurological Targets *SCN9A* (Pain) and *MAPT* (Tauopathies)** (Abstract #1601)
Date & Time: Friday, May 10, 5:30-7:00 p.m. ET
Location: Exhibit Hall

Encoded's innovative AAV-mediated miRNA platform offers a promising strategy for long-term knockdown of target genes in the central and peripheral nervous systems. We identified potent and target-specific miRNA candidates to effectively knock down two clinically relevant, non-monogenic neuronal targets: *SCN9A* and *MAPT*. *SCN9A* encodes the $Na_V1.7$ sodium channel, which is associated with pain sensation, while *MAPT* encodes the microtubule protein, Tau, which is implicated in Alzheimer's disease neuropathology. Encoded's miRNA candidates demonstrated potent, dose-dependent, and selective knockdown of *SCN9A* in human iPSC sensory neurons and in mouse dorsal root ganglion sensory neurons, establishing proof-of-concept for miRNA-based inhibition of $Na_V1.7$. Similarly, MAPT candidates significantly reduced Tau protein levels in vitro and in vivo. These findings support advancement of SCN9A and MAPT candidates to NHP studies and showcase the potential of vectorized miRNA knockdown as a promising treatment avenue for various neurological disorders.

About Encoded Therapeutics

Encoded Therapeutics is a clinical-stage genetic medicines company developing potentially disease-modifying therapies to improve the lives of people with severe CNS disorders. Our proprietary vector engineering approach combines novel regulatory elements and payloads with AAV vectors to unlock innovative solutions for debilitating, intractable CNS conditions. At the forefront is our flagship clinical program, ETX101 for Dravet syndrome, which targets the underlying cause of the disorder to enable highly selective upregulation of *SCN1A* for potentially long-lasting benefit. In parallel, we are advancing a pipeline of potentially best-in-class programs to address significant unmet needs across both monogenic and prevalent CNS conditions. For more information, please visit **www.encoded.com**.

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