ENCODED THERAPEUTICS, INC.
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New Preclinical Data from Encoded Therapeutics Demonstrate Therapeutic Potential of its One-time, Non-opioid Gene Therapy Candidate for Chronic Pain

- Preclinical data show the vectorized miRNA candidate achieved durable knockdown of *SCN9A* ($Na_V1.7$), a genetically validated pain target historically difficult to modulate
- In non-human primates, low-dose AAV9 delivery achieved target engagement levels exceeding thresholds for pain relief established in rodent models
- Program advancing toward development in 2026
- Data will be presented today at the European Society of Gene & Cell Therapy 32nd Annual Congress and next week at the 19th Annual Pain Therapeutics Summit

SOUTH SAN FRANCISCO, Calif. – Encoded Therapeutics Inc., a clinical-stage biotechnology company developing genetic medicines for severe neurological disorders, today announced preclinical data demonstrating that its AAV9 microRNA (miRNA) gene therapy candidate achieved robust knockdown of *SCN9A* ($Na_V1.7$), a key mediator of pain signaling, in non-human primates (NHPs). The levels of target engagement in NHPs exceeded therapeutic thresholds observed in an established rodent pain model. Together, these findings support the potential of Encoded's candidate as a one-time, non-opioid gene therapy for intractable chronic pain.

The candidate, developed through Encoded's vector engineering platform, is designed to selectively and durably knock down *SCN9A* ($Na_V1.7$), a voltage-gated sodium channel that is well-established as a key mediator of pain sensitivity. Despite its validation, achieving both selective inhibition of $Na_V1.7$ and sufficient access to dorsal root ganglia (DRG) neurons remains a significant challenge. Encoded's program leverages intrathecal delivery of clinically-validated AAV9 to enable selective knockdown of *SCN9A* in DRG sensory neurons, while limiting systemic biodistribution and potential off-target safety effects in organs such as the brain, heart, and liver.

"Chronic pain remains a highly prevalent and underserved neurological condition globally, with current treatments often offering limited relief, significant side effects, and a risk of dependency," said Stephanie Tagliatela, Chief Scientific Officer of Encoded Therapeutics. "Our approach is uniquely designed to knock down a well-validated mediator of pain signaling, *SCN9A* ($Na_V1.7$), through intrathecal delivery of low-dose AAV9 to DRG neurons. By integrating validated biology, optimized delivery, and translational insights from our clinical-stage ETX101 program, we see the potential for our candidate to emerge as a one-time, non-opioid therapy capable of transforming care for people living with chronic pain."

Preclinical Results

- NHP studies demonstrated 69% knockdown of *SCN9A* expression in lumbar DRG following a single dose of 1.5E13 vector genomes (vg)/animal, with minimal biodistribution in the brain, heart, and liver.
- In rats, consistent analgesic effects were observed in a well-established spared nerve injury model of chronic pain through 8 weeks post-dosing, with as little as 40% Scn9a knockdown sufficient to induce a durable analgesic response.
- Treatment was well-tolerated with no dose-limiting or treatment-related adverse findings across species.

These results establish a strong translational foundation for selective $Na_V1.7$ knockdown delivered with a validated AAV capsid, supporting potential broad application of gene therapy to a highly prevalent neurological disorder.

Poster Presentation Details

European Society of Gene & Cell Therapy 32nd Annual Congress, October 7 – 10, 2025, in Seville, Spain
Title: *Non-opioid AAV9-miRNA Gene Therapy to Silence SCN9A Achieves Durable Pain Control and Target Engagement in Non-human Primates*
Session Date & Time: October 9, 14:00 – 15:30 CEST
Presenter: Chao Tai, PhD, Senior Scientist, Encoded Therapeutics
Poster Number: 252
Location: Seville Exhibition and Conference Centre, Fibes 2

19th Annual Pain Therapeutics Summit, October 13 – 14, 2025, in San Diego, CA
Title: *Non-opioid AAV9-miRNA Gene Therapy to Silence SCN9A Achieves Durable Pain Control and Target Engagement in Non-human Primates*
Session Dates: October 13 – 14
Presenter: Sheila Sears, PhD, Associate Director, Translational Research, Encoded Therapeutics
Location: DoubleTree by Hilton – Mission Valley, Great Room

About Intractable Chronic Pain

Intractable chronic pain is defined by persistent, severe discomfort that resists conventional treatments and profoundly disrupts quality of life. It affects millions of people worldwide, yet current therapies-including opioids-often provide limited relief and are associated with significant side effects and risk of dependency. Despite its widespread impact, there remains a lack of therapies that target the underlying mechanisms of chronic pain. This underscores an urgent need for innovative, safe, and effective approaches to address this persistent and debilitating condition.

About Encoded Therapeutics

Encoded Therapeutics is a clinical-stage genetic medicines company developing one-time therapies for severe neurological disorders. Our vector engineering platform enables highly selective, potent, and durable gene modulation. ETX101, our lead program, is designed to address the underlying cause of Dravet syndrome by selectively upregulating *SCN1A* and is currently in Phase 1/2 clinical trials. Building on this foundation, we are advancing additional programs to selectively modulate highly validated genetic targets in chronic pain, Angelman syndrome, and Alzheimer's disease/tauopathies. With integrated discovery, development, and manufacturing capabilities, we are positioned to efficiently move programs from concept through the clinic. We are driven by a mission to pioneer transformative therapies that meaningfully improve the lives of patients and families affected by devastating neurological conditions. For more information, please visit www.encoded.com.

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