ILAE EUROPE epilepsy congress

16th European Epilepsy Congress
5-9 September 2026 | Athens, Greece

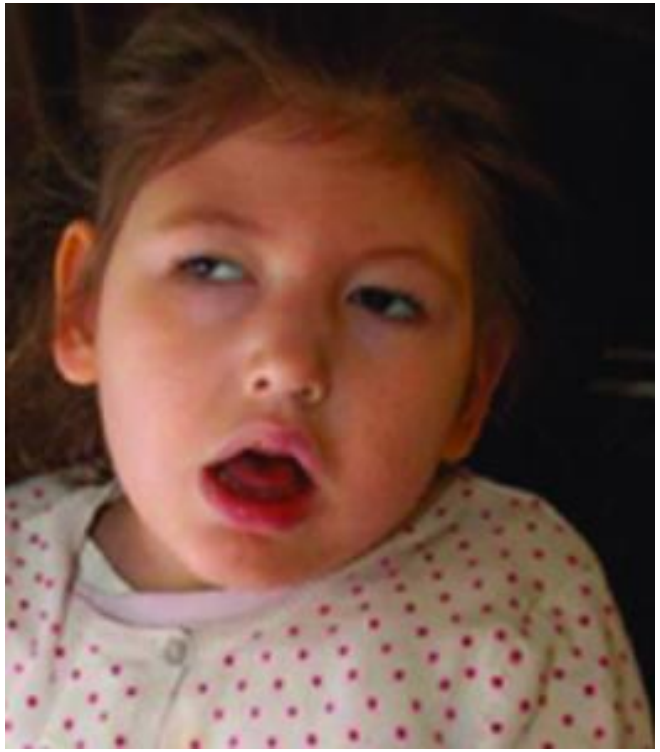
Elsunersen, a Novel Antisense Oligonucleotide, Shows Marked Seizure Reduction and Broad Functional Improvements Highlighting Disease-Modifying Potential in Early Onset SCN2A Developmental and Epileptic Encephalopathy: Results from the EMBRAVE Part A Study

Orrin Devinsky, MD
Praxis Precision Medicines, Boston, MA, USA

Disclosure: Orrin Devinsky is a current employee of Praxis Precision Medicines and is a Praxis stockholder

Early Onset *SCN2A*-DEE is Among the Most Severe Forms of DEE

- Patients frequently exhibit symptoms from birth, persevering throughout life
  - Severe, frequent seizures within the first days of life
  - Severe global developmental delays and intellectual disabilities
  - Movement disorders
  - Life-expectancy significantly shortened
- To date: Insufficient treatments, no targeted therapy, no established benefits for cognition or behavior

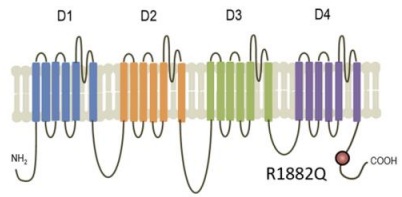


DEE=developmental and epileptic encephalopathy

Howell et al. *Neurology*. 2015;85(11):958-66; Scheffer et al. *Epilepsia*. 2017;58(4):512-21; Donnan et al. *Neurology*. 2023;100:e1712-22; Sanders et al. *Trends Neurosci.* 2018;41(7):442-56; Wolff et al. *Brain*. 2017;140:1316-36; Zeng et al. *Front Mol Neurosci.* 2022 Mar;15:809951

Mouse Model of *SCN2A*-DEE: $Na_V1.2$-R1882Q (Q/+)

Location of Variant



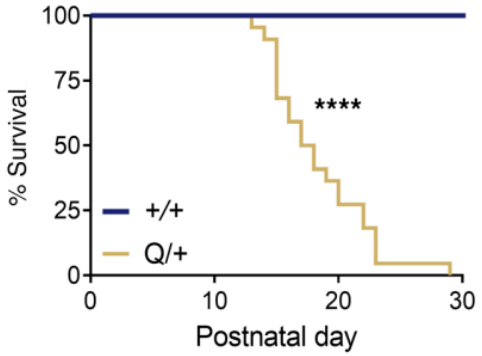
JCI The Journal of Clinical Investigation

Antisense oligonucleotide therapy reduces seizures and extends life span in an *SCN2A* gain-of-function epilepsy model

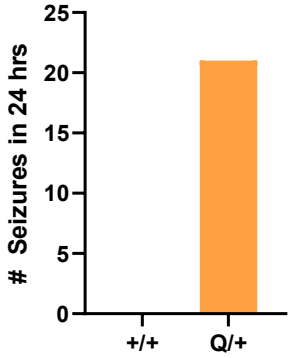
Melody Li, … , Frank Rigo, Steven Petrou

J Clin Invest. 2021;131(23):e152079. https://doi.org/10.1172/JCI152079.

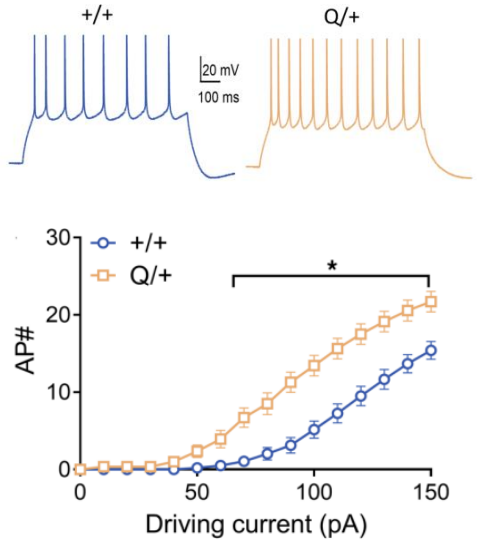
Premature Lethality



Spontaneous Seizure



Neuronal Hyperexcitability



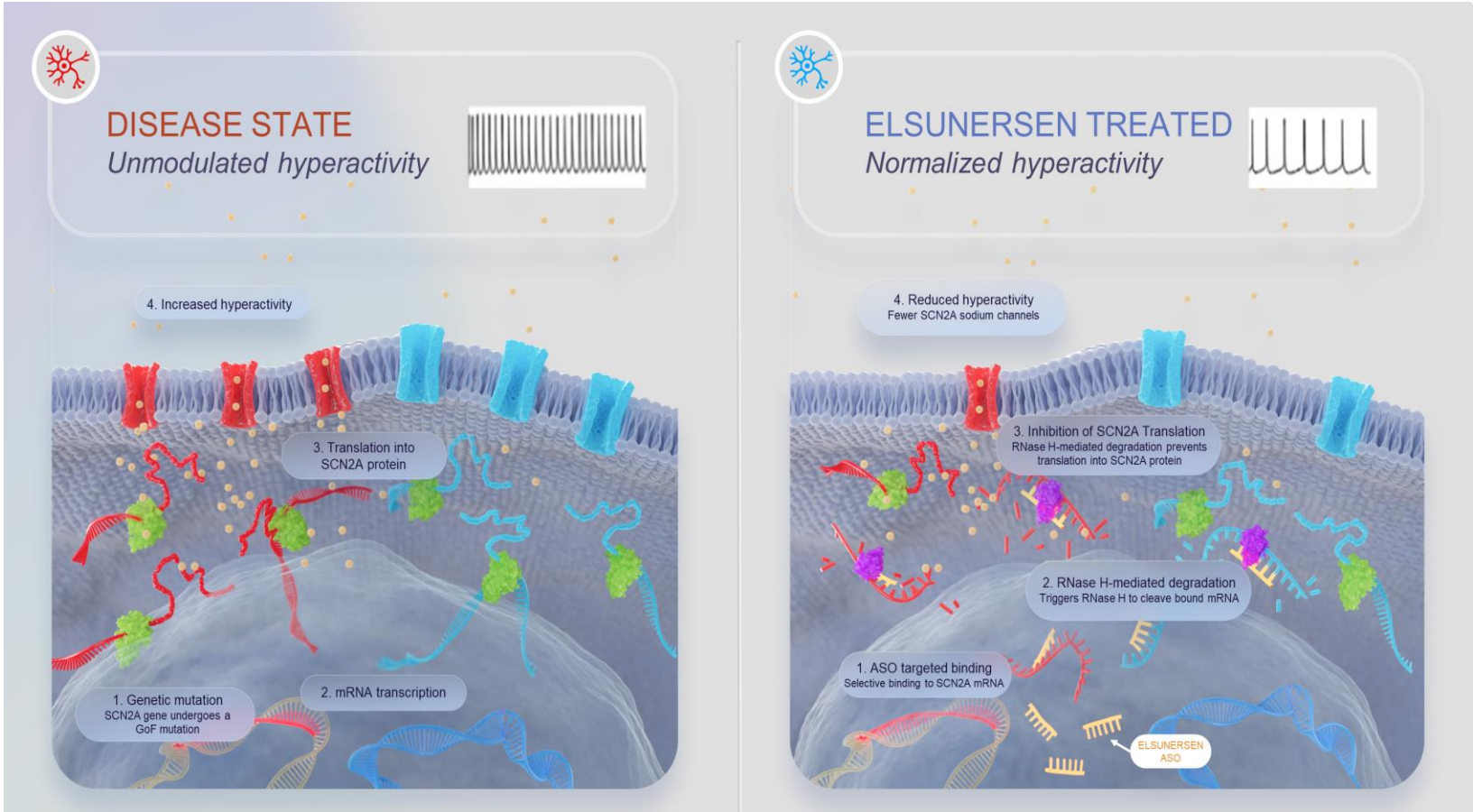
The SCN2A-DEE mouse model exhibits premature lethality due to spontaneous seizure driven by neuronal hyperexcitability

AP=action potential; DEE=developmental and epileptic encephalopathy; Na_V=voltage-gated sodium channel

Li et al. *J Clin Invest.* 2021;131(23):e152079

Elsunersen is an ASO Designed to Down-Regulate $Na_V1.2$ Expression in Patients with Early Onset *SCN2A*-DEE

By down regulating $Na_V1.2$ expression and normalizing pathological activity, elsunersen targets the genetic driver of disease in patients with early onset SCN2A-DEE



ASO=antisense oligonucleotide; Na_V=voltage-gated sodium channel

Li et al. *J Clin Invest.* 2021;131(23):e152079

Elsunersen: First Potential Disease-Modifying Therapy for Early Onset *SCN2A*-DEE

ELSUNERSEN

Antisense oligonucleotide (ASO)

Intrathecal administration

Once every 4 weeks

Designed for selective *SCN2A* mRNA reduction

Mechanistic Precision

- Designed to downregulate $Na_V1.2$ expression in early onset *SCN2A*-DEE
- Reduces $Na_V1.2$ hyperactivity, normalizing neuronal excitability

Clinical Profile

- Significant reduction in seizures achieved in patients with early onset *SCN2A*-DEE
- No adverse events were considered treatment-emergent or serious

Regulatory Designations

- FDA: BTD, ODD and Rare Pediatric Disease designation
- EMA: ODD and PRIME designation

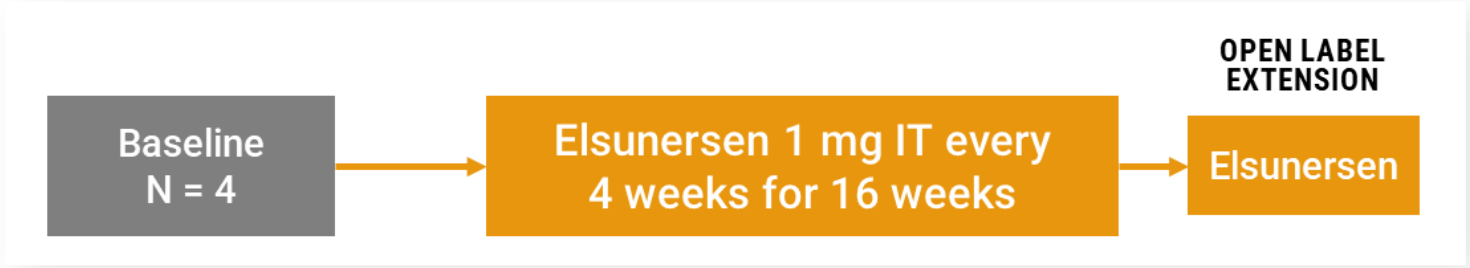
BTD=Breakthrough Therapy Designation; DEE=developmental and epileptic encephalopathy; Na_V=voltage-gated sodium channel; ODD=Orphan Drug Designation; PRIME=Priority Medicines
Elsunersen is an investigational drug and has not been approved by any regulatory body for use.
Frizzo et al. EEC 2024; Wagner et al. *Nature Medicine*. 2025;31:2174-8; Wagner et al. AAN 2026; Bialer et al. *Epilepsia*. 2026;00:1-51.

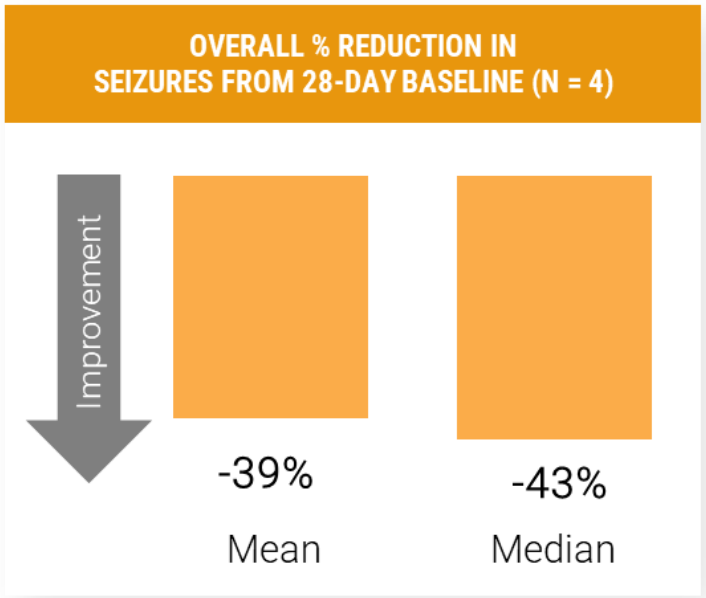
PHASE 2 CLINICAL EVIDENCE
EMBRAVE STUDY

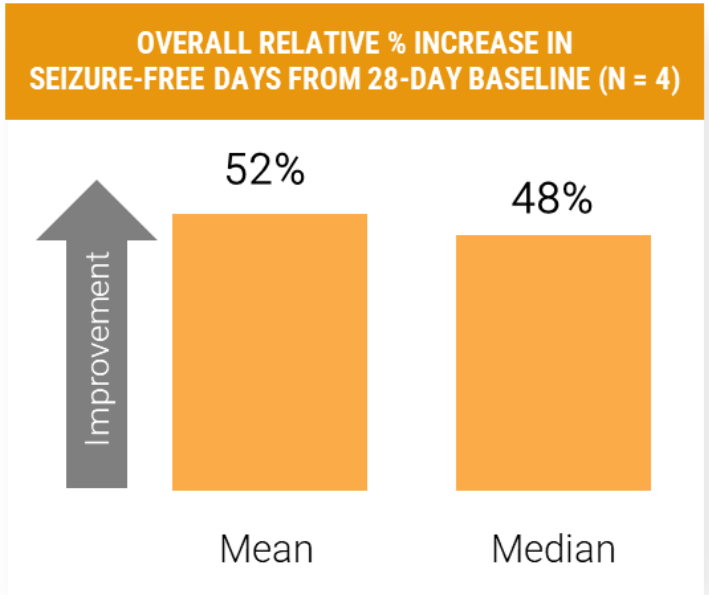
Elsunersen: Well-tolerated with clinically meaningful seizure reduction in patients with early onset SCN2A-DEE

Elsunersen is an investigational drug and has not been approved by any regulatory body for use.

EMBRAVE Part 1: Significant Seizure Reduction in Early Onset *SCN2A*-DEE







Key Endpoints

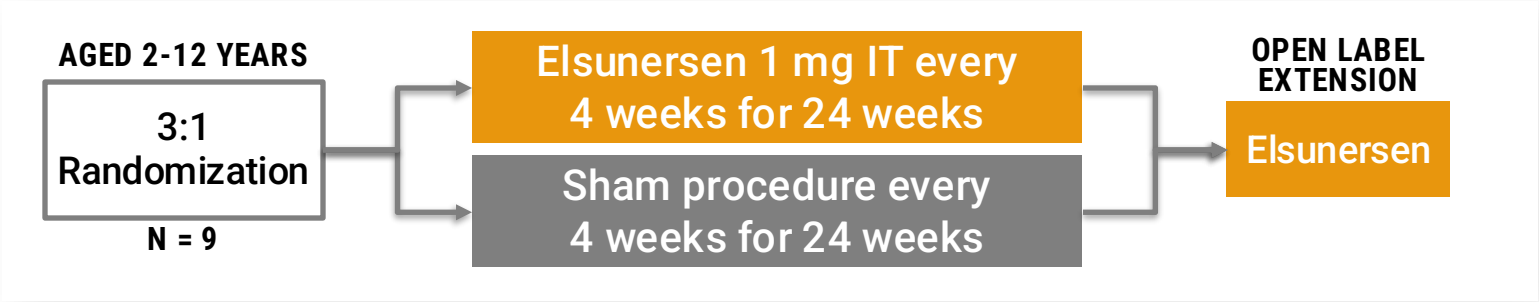
- Incidence and severity of treatment-emergent adverse events (TEAEs)
- Change from baseline in monthly (28-day) motor seizure frequency

Safety

- No TEAEs or SAEs considered related to study drug
- All TEAEs recovered/resolved

DEE=developmental and epileptic encephalopathy; IT=intrathecal; SAE=serious adverse event; TEAE=treatment-emergent adverse event
ClinicalTrials.gov Identifier: NCT05737784
Frizzo et al. EEC 2024; Bialer et al. *Epilepsia*. 2026;00:1-51

EMBRAVE Part A: Marked Seizure Reduction & Disease-Modifying Benefits in all Participants



EMBRAVE

Starting dose of 1 mg with optional dose escalation up to 8 mg based on individual tolerability at each dose

77% PRIMARY ENDPOINT

Placebo-adjusted seizure reduction from baseline, p=0.015

71%

>50% seizure reduction by period 6, with sustained benefit in OLE up to 1 year

57%

≥ One 28-day period of seizure freedom

100%

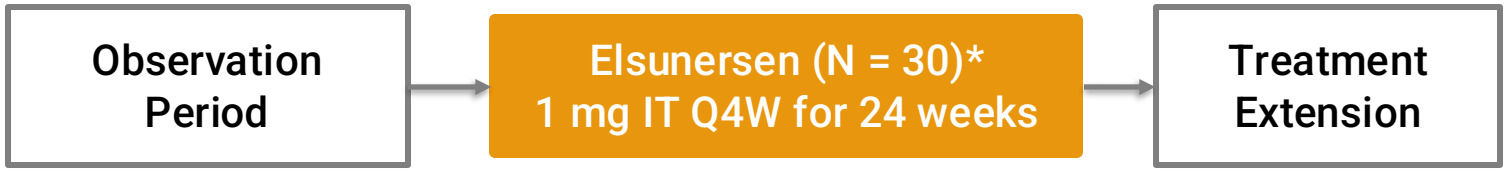
Broad functional improvements in sleep, motor function, muscle tone and attention

- Safety findings consistent with EMBRAVE Part 1
- No drug-related SAEs
- No discontinuations
- No neuroinflammation signals at doses up to 8 mg
- Most TEAEs mild to moderate

IT=intrathecal; OLE=open-label extension; SAE=serious adverse event; TEAE=treatment-emergent adverse event
ClinicalTrials.gov Identifier: NCT05737784
Wagner et al. AAN 2026; Bialer et al. *Epilepsia*. 2026;00:1-51.

EMBRAVE3 Registrational Trial

Phase 3 Study – ENROLLING



Expected to serve as registrational trial for NDA filing

Key Inclusion Criteria

- Documented early onset *SCN2A* variant with seizures prior to 3 months of age
- 0 to ≤18 years at Screening (ages 2-18 → Cohort 1; 1-2 → Cohort 2; 0-1 → Cohort 3)
- >4 countable motor seizures per 28-days during baseline

Primary Endpoint

- Median percent change in monthly motor seizure frequency from baseline

To learn more visit www.resiliencestudies.com/embrave

*Every participant will be assigned to receive elsunersen. There is no placebo group

IT=intrathecal; Q4W=every 4 weeks
ClinicalTrials.gov Identifier: NCT07019922

Elsunersen Clinical Experience To Date

- **Robust Therapeutic Impact.** Durable seizure reduction, resolution of *status epilepticus*, meaningful quality-of-life improvements across emergency use cases.
- **Strong Safety and Tolerability.** >250 doses across clinical studies and global Expanded Access Program. No severe or serious drug-related AEs; intrathecal dosing consistently well tolerated.
- **Promising Potential for Long-Term Benefits.** Early data suggest sustained seizure control and possible neurodevelopmental stabilization, with ongoing follow up poised to strengthen findings.
- **Disease-Modifying Potential.** Elsunersen represents a paradigm shift in early onset *SCN2A*-DEE treatment, with EMBRAVE Part A positive topline results positioning it as the first potential disease-modifying therapy for early onset *SCN2A*-DEE.
- **Global Trial Expansion.** Enrollment for the EMBRAVE3 registrational study is progressing, with topline results expected in 2027.

AE=adverse event; DEE=developmental and epileptic encephalopathy

Acknowledgements

Silvana Frizzo[1], Roberto Giugliani[2], Kette Valente[3], Orrin Devinsky[1,4], Brian Spar[1], Kelley Del Real[1], Dharit Patel[1], Henry Jacotin[1], Marcio Souza[1], Steven Petrou

[1]Praxis Precision Medicines, Boston, MA, USA; [2]Federal University of Rio Grande do Sul, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil; [3]Hospital das Clínicas, Faculty of Medicine, University of São Paulo, São Paulo, Brazil; [4]NYU Langone Comprehensive Epilepsy Center, New York, NY, USA

We thank the participants and families of the EMBRAVE studies without whom this work would not have been possible