Clinical Updates from the Elsunersen Emergency Use Program: A Novel ASO for Treatment of Early Onset SCN2A Developmental and Epileptic Encephalopathy

Steven Petrou, PhD

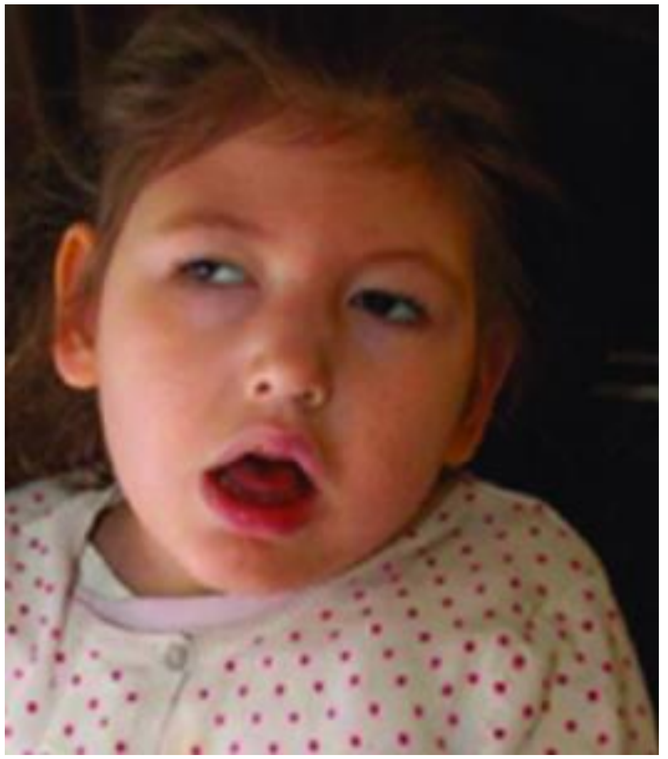
Chief Scientific Officer and President of Research & Development, Praxis Precision Medicines

Disclosure: Steven Petrou is a current employee of Praxis Precision Medicines and is a Praxis stockholder.

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SCN2A–DEE Is Among the Most Severe, Refractory Forms of DEE

- **Caused by gain-of-function (GoF) mutations in the SCN2A gene encoding the voltage-gated sodium channel $Na_V1.2$**
- **Patients frequently exhibit symptoms from birth, persevering throughout life**
  - Severe and uncontrollable seizures within the first days of life
  - Pronounced global developmental delays
  - Marked intellectual disabilities
  - Movement disorders
  - Refractory to treatment
  - Life-expectancy significantly shortened, rarely surviving beyond teenage years
- **To date: Insufficient treatment options, no targeted therapy, with very limited effect on cognitive and behavioral outcomes**

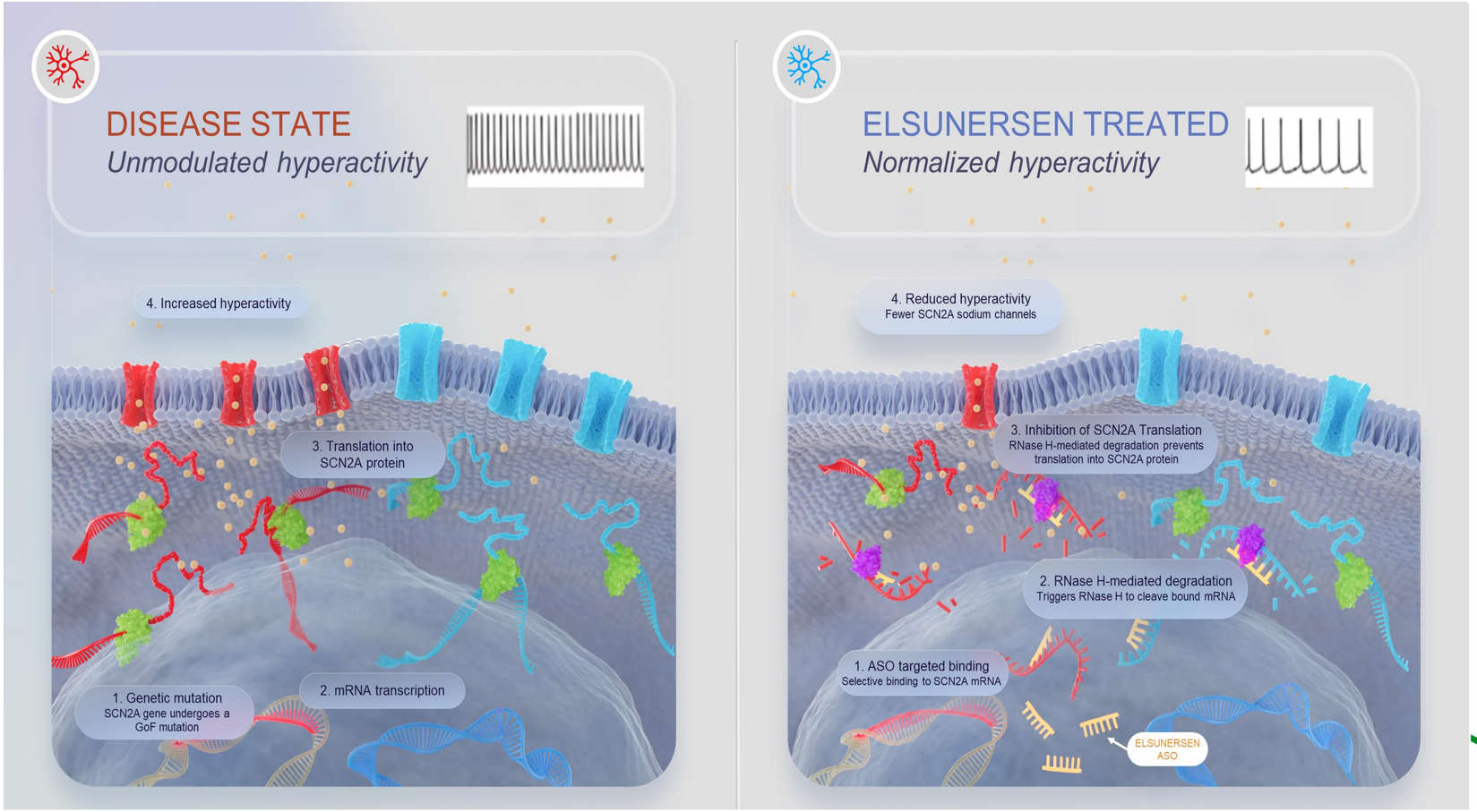


Sanders SJ, et al. *Trends Neurosci.* 2018;41(7):442–56; Wolff M, et al. *Brain.* 2017;140(5):1316–36; Wolff M, et al. *Epilepsia.* 2019;60(S3):S59–67; Zeng Q, et al. *Front Mol Neurosci.* 2022 Mar;15:809951

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Elsunersen Is an ASO Designed to Down-Regulate SCN2A Expression in Patients with GoF Mutation

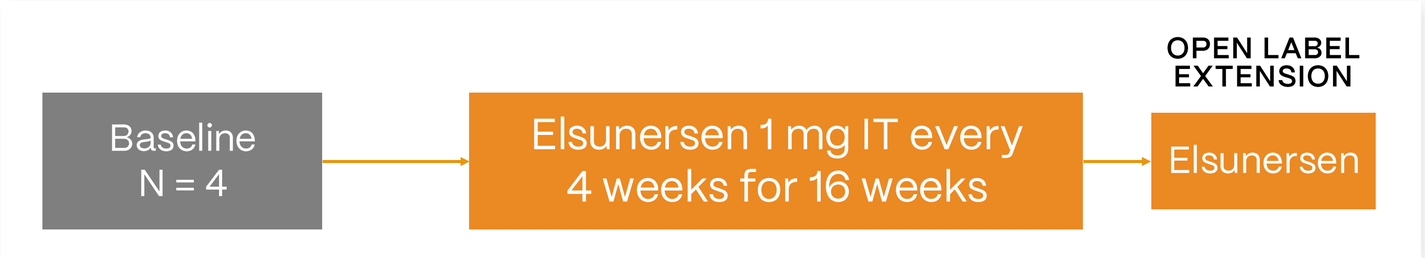
*By **down regulating SCN2A expression and normalizing pathological activity**, elsunersen targets the genetic driver of disease in patients with GoF mutation*

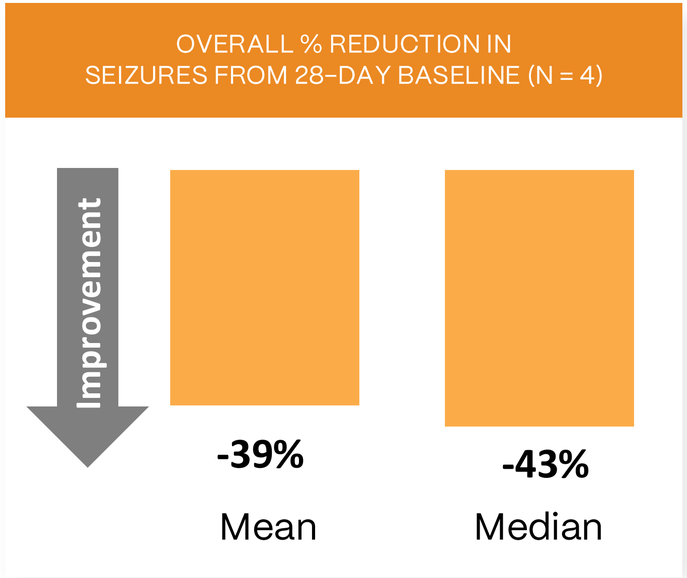


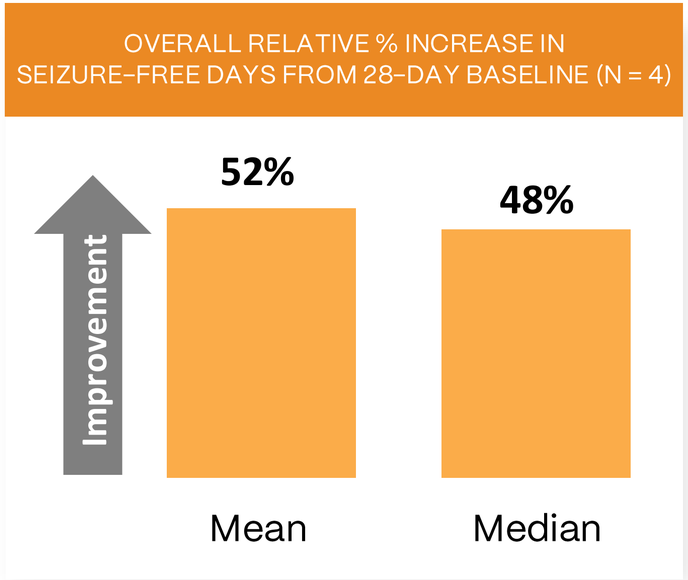
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EMBRAVE Part 1 Showed Clinically Meaningful Seizure Reduction in SCN2A GoF Patients







Key Endpoints

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

Safety

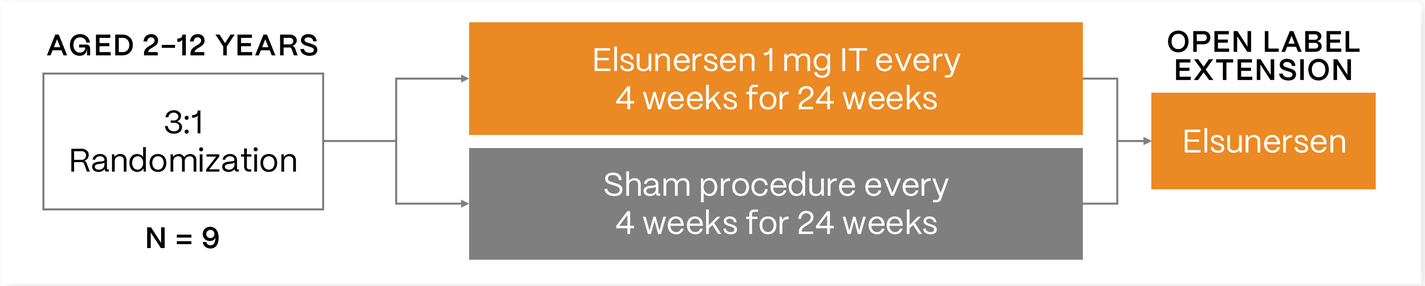
- No TEAEs or SAEs considered related to study drug
- All TEAEs recovered/resolved

Frizzo *et al.* EEC 2024, ClinicalTrials.gov Identifier: NCT05737784

IT=intrathecal; SAE=serious adverse event, TEAE=treatment emergent adverse event

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EMBRAVE Part A Topline Results Show Marked Seizure Reduction, with Disease-Modifying Benefit in All Participants



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%

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

57%

Had at least one 28-day period of seizure freedom

100%

All elsunersen-treated patients showed broad functional improvements including 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

Praxis Data on File, ClinicalTrials.gov Identifier: NCT05737784

IT=intrathecal; OLE=open label extension; SAE=serious adverse event, TEAE=treatment emergent adverse event

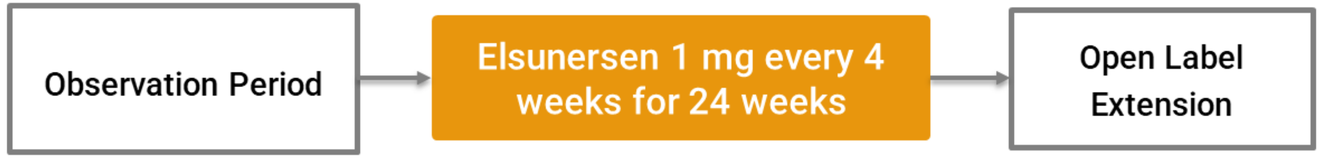
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EMBRAVE3 Registrational Trial

EMBRAVE③

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Cohort 1: ages >2-18 yrs (N = 30)



Key Inclusion Criteria
• Documented SCN2A GoF variant with seizures prior to 3 months of age • Between the ages of 0 to ≤18 years at Screening (ages 2-18 go to Cohort 1, 1-2 to Cohort 2, 0-1 to Cohort 3) • Seizure frequency of 4 or more countable motor seizures per 28-day during baseline
Primary Endpoint
• Median percent change in monthly motor seizure frequency from baseline

To learn more visit www.resiliencestudies.com/embrave

ClinicalTrials.gov Identifier: NCT07019922

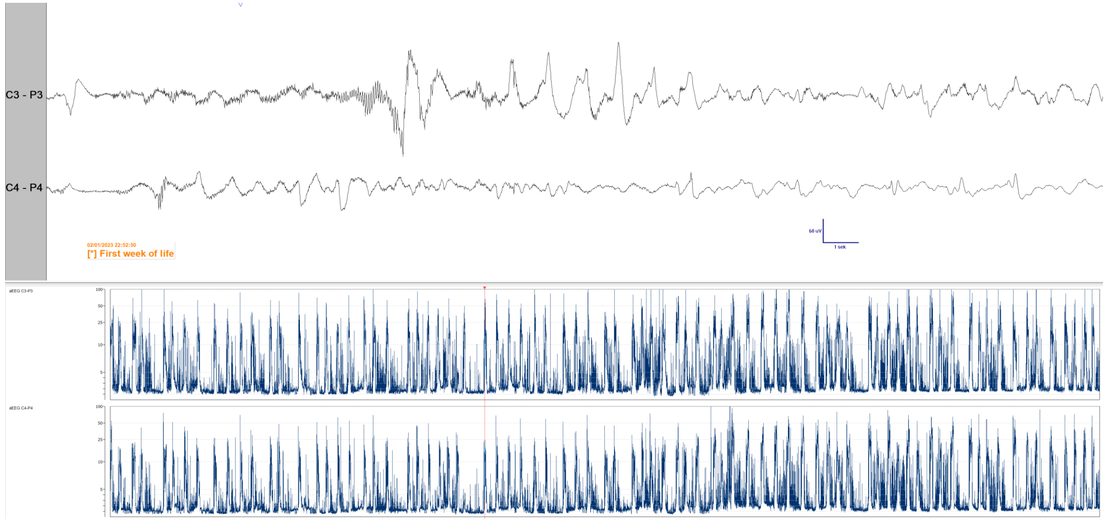
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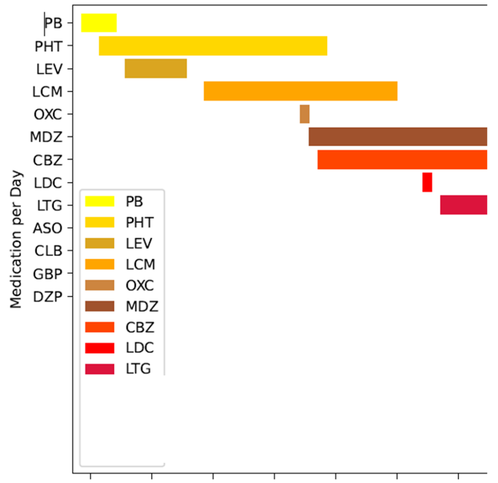
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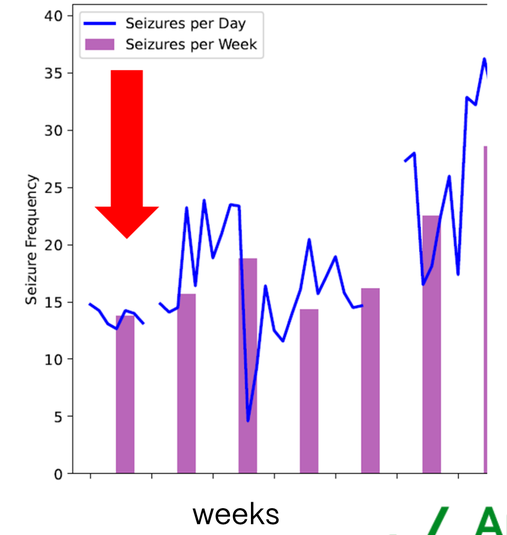
Elsunersen Emergency Use Case: Germany First-In-Patient

Case Details

- A preterm infant (29+4 weeks gestation; birthweight 1400g)
- Prenatally abnormal movements, arthrogryposis
- Prenatal exome sequencing SCN2A c.3986C>A p.(Ala1329Asp)
- Ongoing seizures since birth





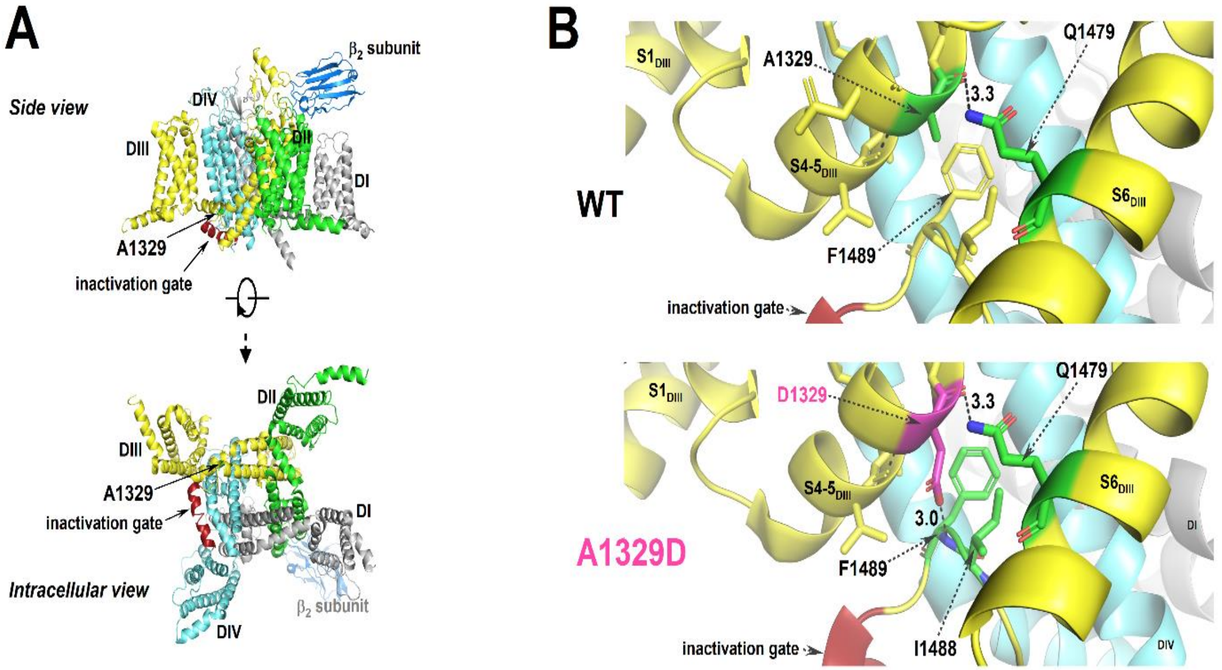


Wagner *et al. Nat Med* 31, 2174–2178 (2025)

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SCN2A: c.3986C>A p.Ala1329Asp



- Variant pathogenic
- Variant GoF

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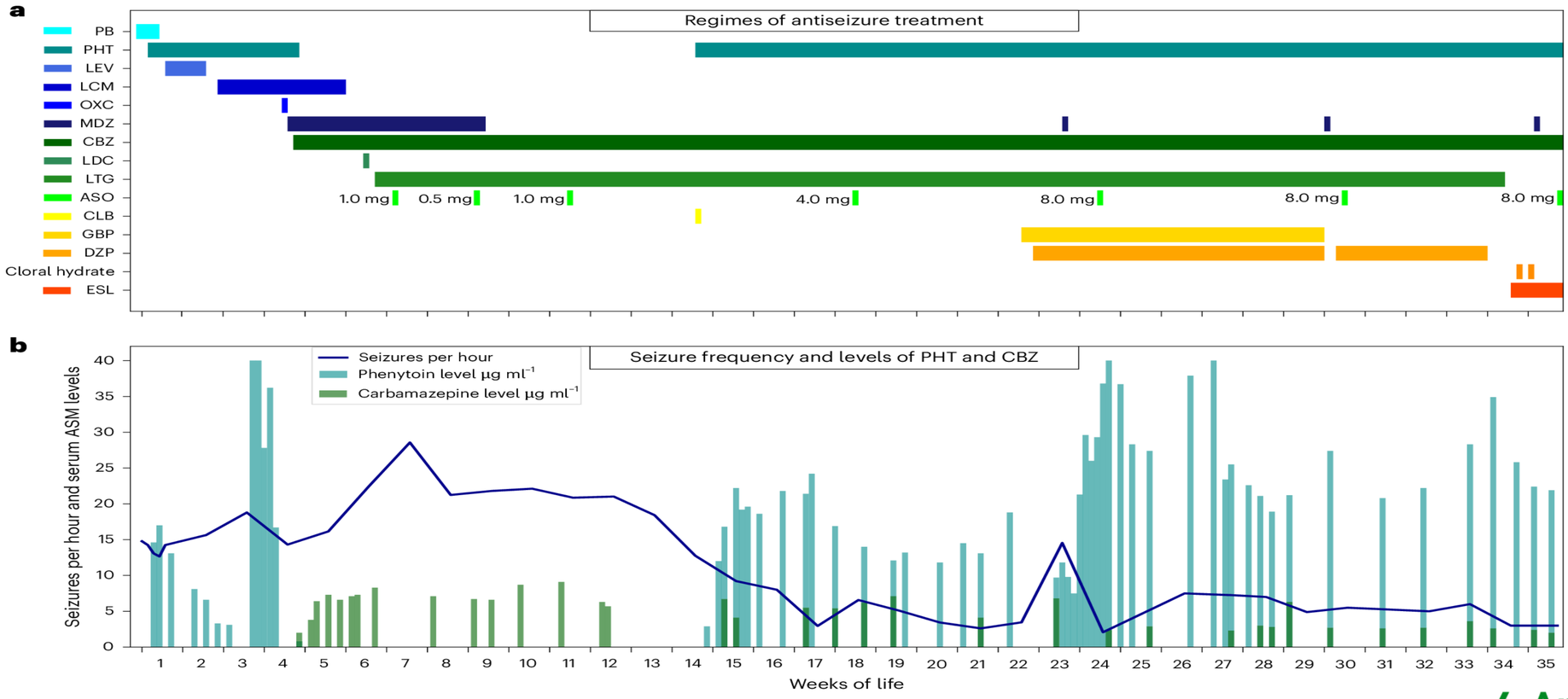
Elsunersen Emergency Use Case: Germany First-In-Patient

Clinical Course

nature medicine

Brief Communication https://doi.org/10.1038/s41591-025-03656-0

Antisense oligonucleotide treatment in a preterm infant with early-onset SCN2A developmental and epileptic encephalopathy



Wagner *et al. Nat Med* 31, 2174–2178 (2025)

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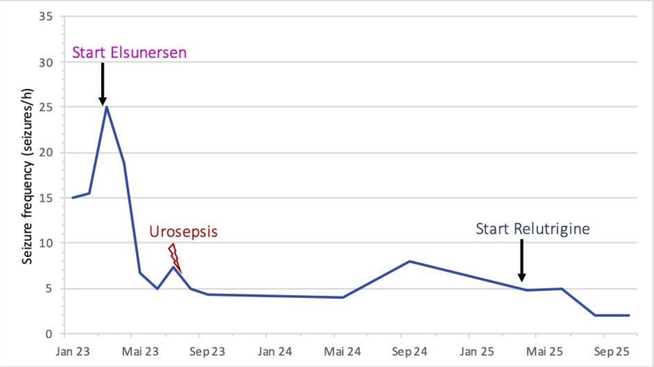
Elsunersen Emergency Use Case: Germany First-In-Patient Adjunctive Relutrigine Treatment

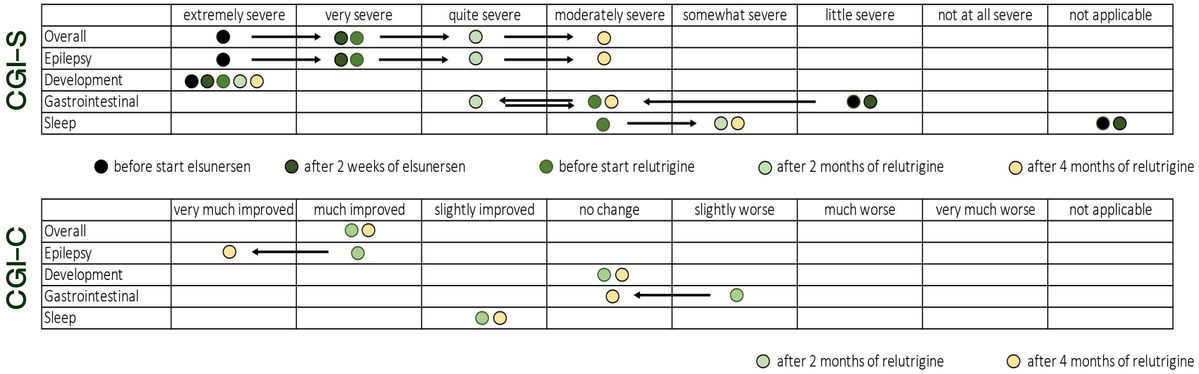
AGE AT FIRST ASO DOSE: 6 weeks

- Number of ASO administrations: 26 (182.5 mg total)
- Drug-related SAEs/AEs: None
- **>50% seizure reduction**
- **Phenytoin: tapered in Feb 2024, no seizure worsening**
- **Lacosamide: tapered in Jun 2024, out in Sep**
- Hammersmith score <10 at 8 months chronological age resembling severe disability; no further worsening through 2 years of age

EARLY CLINICAL EXPERIENCE: COMPLEMENTARY PRECISION SODIUM CHANNEL MODULATION FOR EARLY ONSET SCN2A-DEE

- 2 years after ASO commencement, adjunctive precision sodium channel modulation via relutrigine (0.5 mg/kg daily dose) commenced





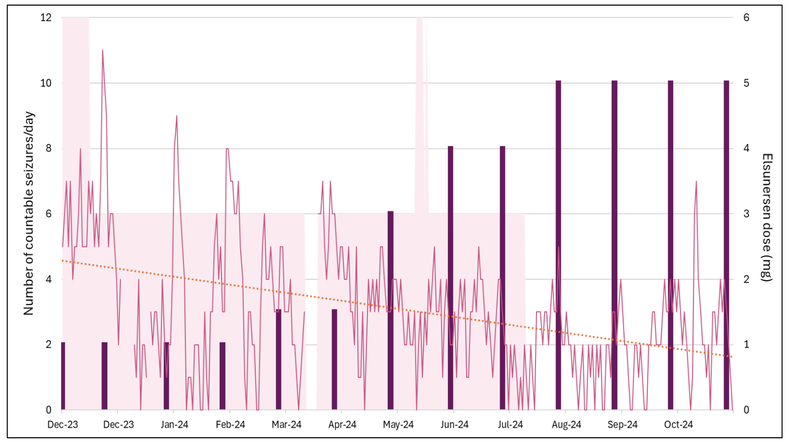
ASO=antisense oligonucleotide; CGI-C=Caregiver Global Impression of Change; CGI-S=Caregiver Global Impression of Severity

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Elsunersen Emergency Use Case: Australia

CURRENT AGE: 9 years old
AGE AT FIRST DOSE: 8 years

- Number of administrations to date: 25 (97 mg total), since December 2023
- History: refractory seizures, global cerebral atrophy, global developmental delay, frequent oculogyric movement, and severe dystonia while awake
- Drug-related SAEs/AEs: None
- CSF safety monitoring: no increase in CSF protein levels
- **>50% seizure reduction**



Caregiver and medical personnel reported notable improvements in a number of domains, with benefit for quality-of-life

Caregiver Global Impression of Severity

	Extremely severe	Very severe	Quite severe	Moderately severe	Somewhat severe	A little severe	Not at all severe	Not applicable
Overall		●				●		
Epilepsy		○	●			●		
Development	○			●				
Behaviour				○			●	
Movement disorder*	○	●	●					
Gastrointestinal						○	●●	
Sleep		○		●		●		

*i.e. dystonia, chorea, etc

○ baseline ● after dose 2 ● after dose 11

Caregiver Global Impression of Change (Ratings relative to baseline)

	Very much improved	Much improved	Slightly improved	No change	Slightly worse	Much worse	Very much worse	Not applicable
Overall		●●						
Epilepsy		●●						
Development			●	●				
Behaviour		●●						
Movement disorder*			●●					
Gastrointestinal		●						●
Sleep	●		●					

*i.e. dystonia, chorea, etc

● after dose 2 ● after dose 11

Significantly fewer clinical and electrographic seizures noted over the course of the first year of treatment

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Elsunersen Emergency Use Cases: United States

*Two participants from the EMBRAVE study demonstrated marked median **reduction in seizures from baseline** on top of best available standard of care during Part 1, as well as an **increased number of days without seizures**. They were granted emergency access to continue receiving elsunersen.*

CURRENT AGE: 5 years old
AGE AT FIRST DOSE: 3 years

- Number of administrations to date: 19 since April 2024
- Drug-related SAEs/AEs: None
- CSF safety monitoring: no increase in CSF protein levels
- **40% seizure reduction**
- **Weaned off oxygen supplementation**

EMBRAVE

CURRENT AGE: 4 years old
AGE AT FIRST DOSE: 2 years

- Number of administrations to date: 22 since March 2024
- Drug-related SAEs/AEs: None
- CSF safety monitoring: no increase in CSF protein levels
- **45% seizure reduction**
- **Weaned off ketogenic diet**

EMBRAVE

CURRENT AGE: 12 months old
AGE AT FIRST DOSE: 8 weeks

- Number of administrations to date: 12 since May 2025
- Drug-related SAEs/AEs: None
- CSF safety monitoring: no increase in CSF protein levels
- **>90% seizure reduction**

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Elsunersen Emergency Use Case: Spain

CURRENT AGE: ~4 months
AGE AT FIRST DOSE: ~2 months

- Number of administrations to date: 2 (2 mg total), since February 2026
- History: high seizure burden from first minutes of life (tremulous episodes, flexor rigidity, autonomic changes, eye deviation, occasional desaturation) → NICU admission and treatment with multiple ASMs
- Initial combination therapy (lidocaine, cenobamate, carbamazepine, clobazam, lacosamide + ketogenic diet) achieved first meaningful seizure control. Lidocaine discontinued due to right bundle branch block (cumulative exposure)
- Transitioned to phenytoin with good seizure control, but severe abnormalities remained on EEG (background disorganization, abundant multifocal spikes, fast activity)

Early Outcomes following ASO Initiation

- Drug-related SAEs/AEs: None
- **Last seizure recorded ~1 week after first elsunersen dose, shortly after lidocaine withdrawal and before phenytoin stabilization**
- **No longer using a nasogastric tube and discharged from hospital**
- **Progressive neurodevelopmental gains (social smile, improved eye fixation, good head control)**
- **Marked improvement on EEG; ~90% reduction in epileptiform activity vs pre-discharge recording**

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Elsunersen Clinical Experience To Date

- **Robust Therapeutic Impact.** Elsunersen demonstrates durable seizure reduction, resolution of *status epilepticus*, and meaningful quality-of-life improvements across emergency use cases.
- **Strong Safety and Tolerability.** >100 doses across global EAP. No severe or serious drug-related adverse events; intrathecal dosing consistently well tolerated even with repeated administrations.
- **Promising Potential for Long-Term Benefits.** Early data suggest sustained seizure control and possible neurodevelopmental stabilization, with ongoing follow up poised to strengthen these findings.
- **Global Trial Expansion.** EMBRAVE Part A positive topline results position elsunersen as the first potential disease-modifying therapy for early onset *SCN2A*-DEE. Enrollment for the EMBRAVE3 registrational study is underway, with topline results expected in 2027.
- **Pioneering Disease-Modifying Potential.** Elsunersen represents a paradigm shift in early onset *SCN2A*-DEE treatment, offering hope to patients and their families. Its potential may be further enhanced by precision sodium channel modulation to address residual network hyperexcitability.

EMBRAVE③

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SCAN TO LEARN MORE

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