ELSUNERSEN

AN ANTISENSE OLIGONUCLEOTIDE (ASO) IN DEVELOPMENT FOR
EARLY ONSET SCN2A DEVELOPMENTAL & EPILEPTIC ENCEPHALOPATHY (DEE)

Early Onset SCN2A DEE

SCN2A disease variations are caused by random genetic errors resulting in altered protein function and unmodulated sodium channel hyperactivity[1,2]

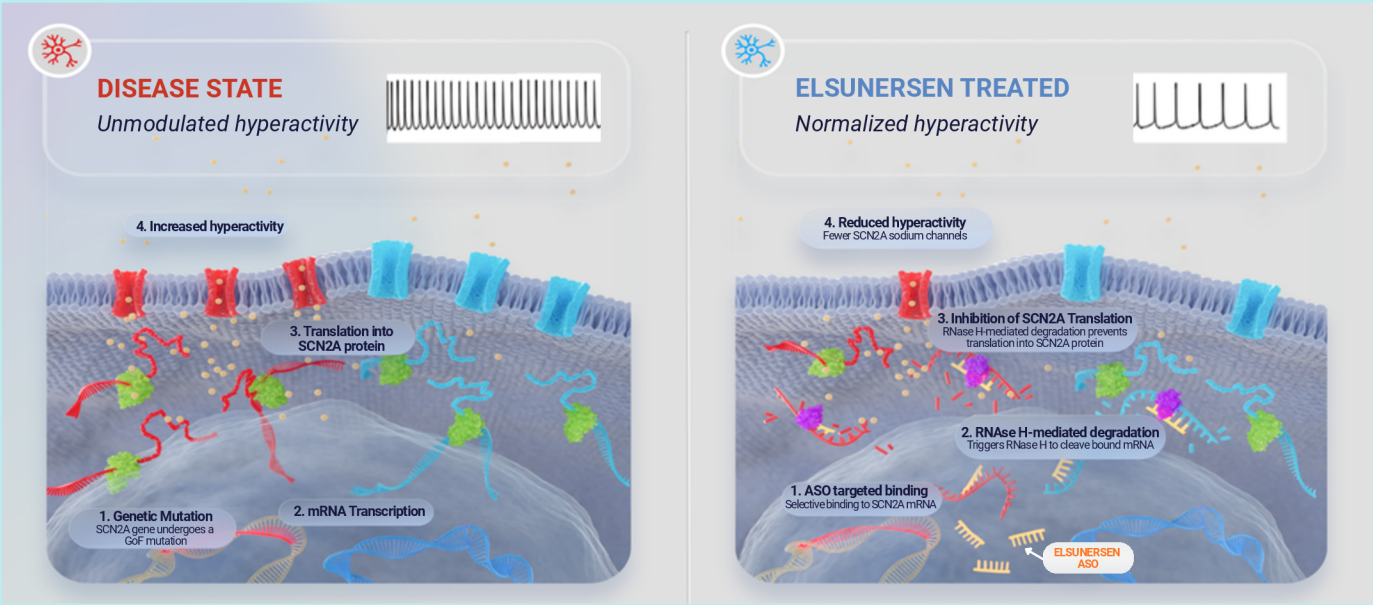
Antisense Oligonucleotide

An ASO is a short synthetic strand of DNA or RNA designed to bind specifically to target RNA to normalize its function or expression[3]

MECHANISM OF ACTION[3,4]

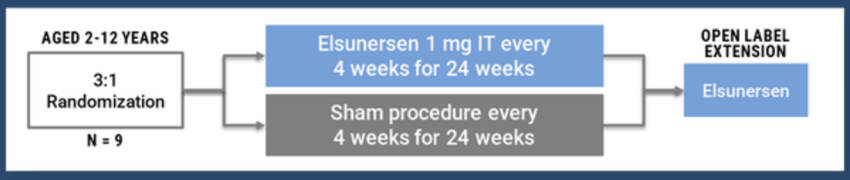
Elsunersen is a Gapmer ASO Designed to **Down Regulate SCN2A Expression and Normalize Pathological Activity**, Targeting the Genetic Driver of Disease in Patients with Gain-of-Function (GoF) Mutation

Selectively binds target RNA→ Induces RNA degradation → Decreased number and hyperactivity of sodium channels



PHASE 2 CLINICAL FINDINGS – EMBRAVE PART A STUDY

This profile translated into well-tolerated, marked seizure reduction with disease-modifying benefit in patients with early onset SCN2A GoF DEE, consistent with earlier findings from EMBRAVE Part 1.[5,6]



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

- Part A safety findings consistent with Part 1[5]
- No drug-related SAEs
- No discontinuations
- No neuroinflammation signals at doses up to 8 mg
- Most TEAEs mild to moderate

[1]Meisler et al *Nat Rev Neurosci* 2021; [2]Carvill et al *Neurotherapeutics* 2021; [3]Dhuri et al *J Clin Med* 2020; [4]Li et al *J Clin Invest* 2021; [5]Frizzo et al. EEC 2024; [6]Petrou et al. AAN 2026
ASO=antisense oligonucleotide; DEE=developmental and epileptic encephalopathy; GoF=gain of function; IT=intrathecal; OLE=open label extension; SAE=serious adverse event; TEAE=treatment emergent adverse event

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Antisense oligonucleotide (ASO)

Intrathecal administration

Once every 4 weeks

The EMBRAVE3 Study

- **Design:** Phase 3, single arm study*
- **Population:** Ages 0-18 years with early onset SCN2A DEE
- **Duration:** 24-weeks single arm + 24-week open-label extension
- **Primary Endpoint:** Change in monthly motor seizure frequency
- **Dosing:** 1 mg, every 4 weeks

Key Eligibility Criteria

- ✓ Documented SCN2A mutation with seizure onset in the first 3 months of life
- ✓ Between the ages of 0 to ≤18 years at Screening (Cohort 1, ages 2-18; Cohort 2, ages 1-2; Cohort 3, ages 0-1)
- ✓ >4 countable motor seizures in the 4 weeks prior to screening
- ✓ ASMs on stable doses (no dose changes) 1 month before screening

EMBRAVE3 offers a combination of in-clinic visits and at-home telehealth visits reducing the burden of participation

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

EMBRAVE③

To learn more about the EMBRAVE3 study, visit

www.resiliencestudies.com/embrave

ELSUNERSEN REGULATORY DESIGNATIONS

- **FDA:** Rare Pediatric Disease Designation for SCN2A GoF DEE
- **EMA:** PRIME and Orphan Drug Designations for SCN2A GoF DEE