Significant Seizure Reduction in Pediatric Participants with Early Onset SCN2A Developmental and Epileptic Encephalopathy following Treatment with Elsunersen, a Novel Antisense Oligonucleotide: Findings from the EMBRAVE Study

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Start Date: 24 September 2024
Start Time: 7:30 AM EDT
End Time: 1:00 PM EDT
Location: In-person and live-streamed from 99 High Street, 30th Floor, Boston, MA

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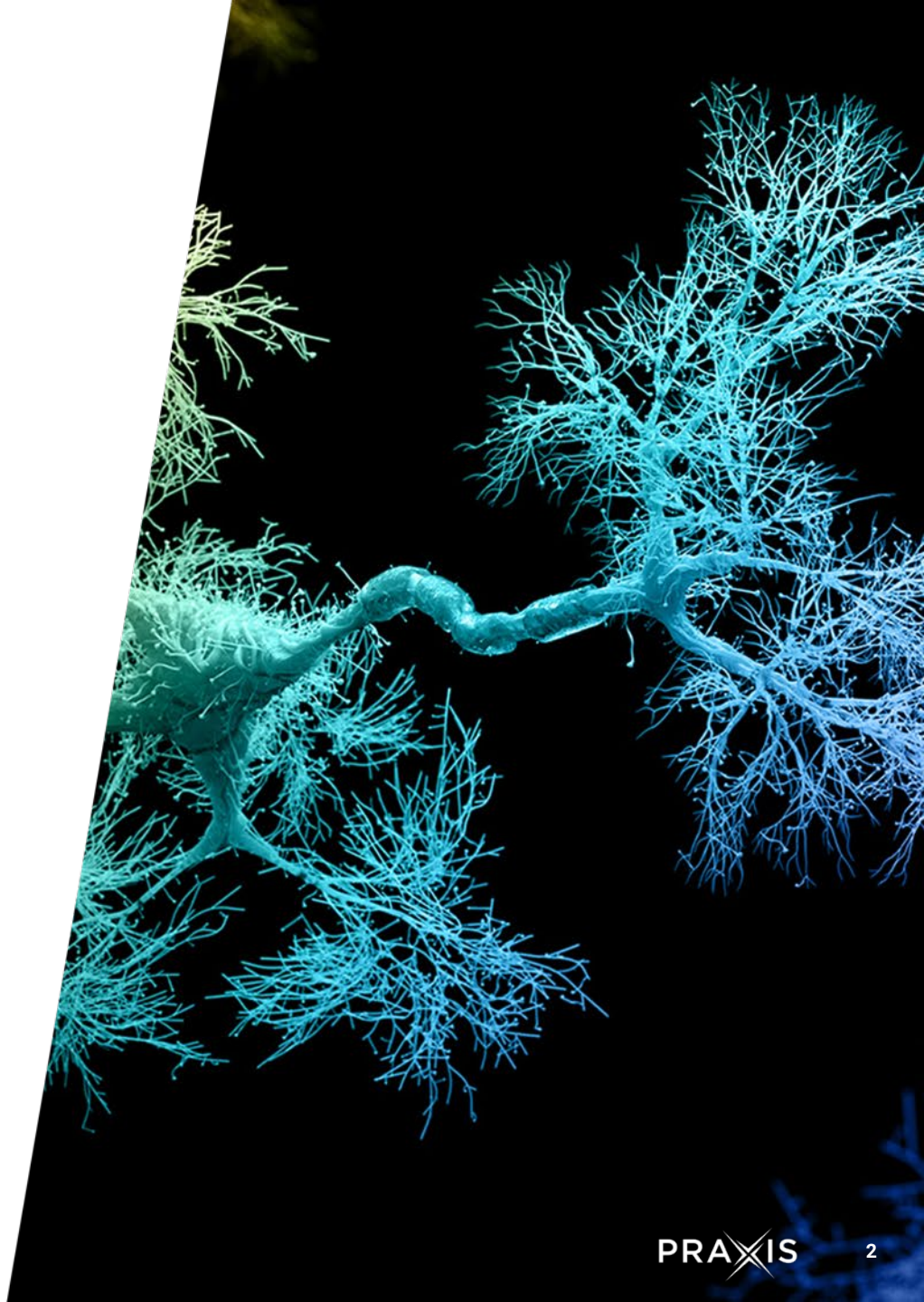


Conflict of Interest

Silvana Frizzo is a current employee of Praxis Precision Medicines and is a Praxis shareholder.

SCN2A-DEE is a rare and fatal disorder caused by gain-of-function mutations in the SCN2A gene encoding the voltage-gated sodium channel $Na_V1.2$

- **~2,300 SCN2A GoF patients in US**
- **Early onset seizures, refractory to existing treatment options**
- **No effective standard of care**
- **Trial-and-error treatment approach with multiple lines of therapy**

Patients with SCN2A-DEE have a debilitating and ultimately fatal trajectory

There are no effective treatment options

Patients are at high risk of death

- Rarely survive beyond teenage years
- Frequent, devastating seizures often beginning within days of birth
- Difficult to control with conventional ASMs

Comorbidities include profound impairment

- Motor, cognitive, language development delays, with most being non-verbal
- GI abnormalities
- Severe irritability
- Movement disorders, such as dystonia or ataxia
- Frequent hospitalizations leading to severely diminished QoL

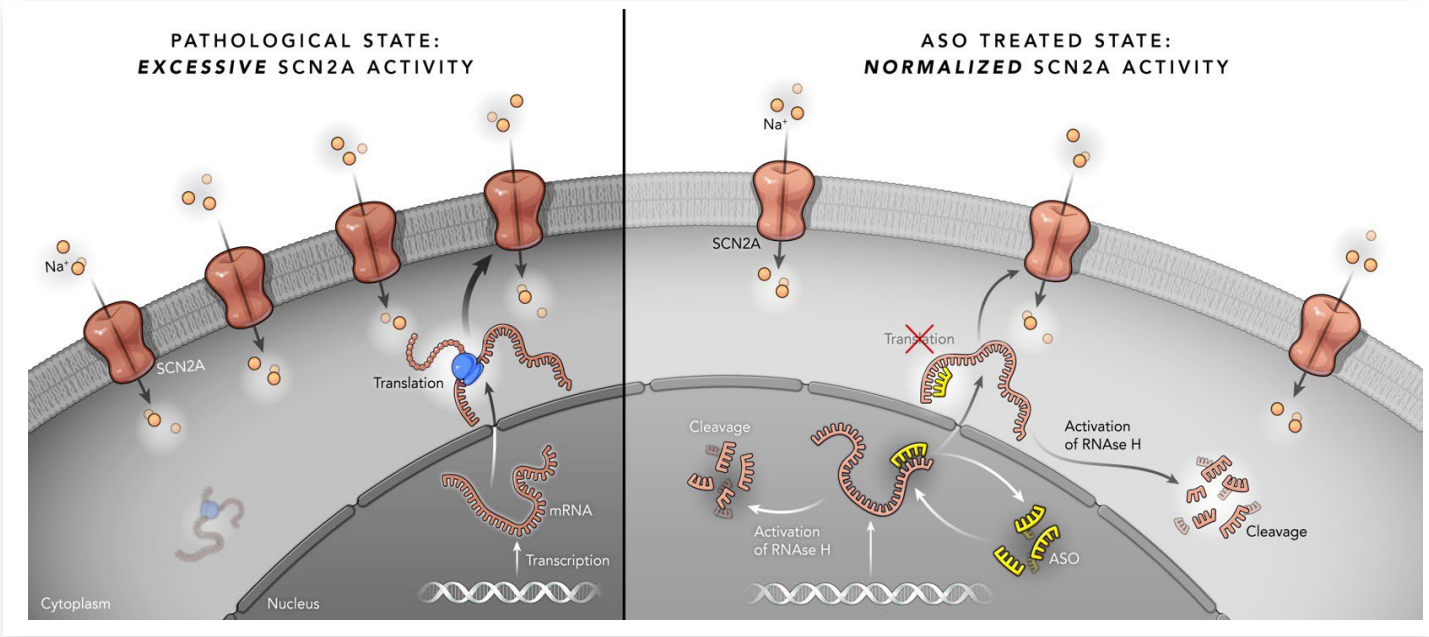
Elsunursen (PRAX-222) is an ASO designed to down-regulate SCN2A expression in patients with gain-of-function mutation

SCN2A disease variations are caused by random nucleotide base changes in the genome resulting in altered protein function[1,2]

An antisense oligonucleotide (ASO) is a short, synthetic strand of DNA or RNA designed to bind specifically to a target RNA molecule, typically to alter its function or expression[3]

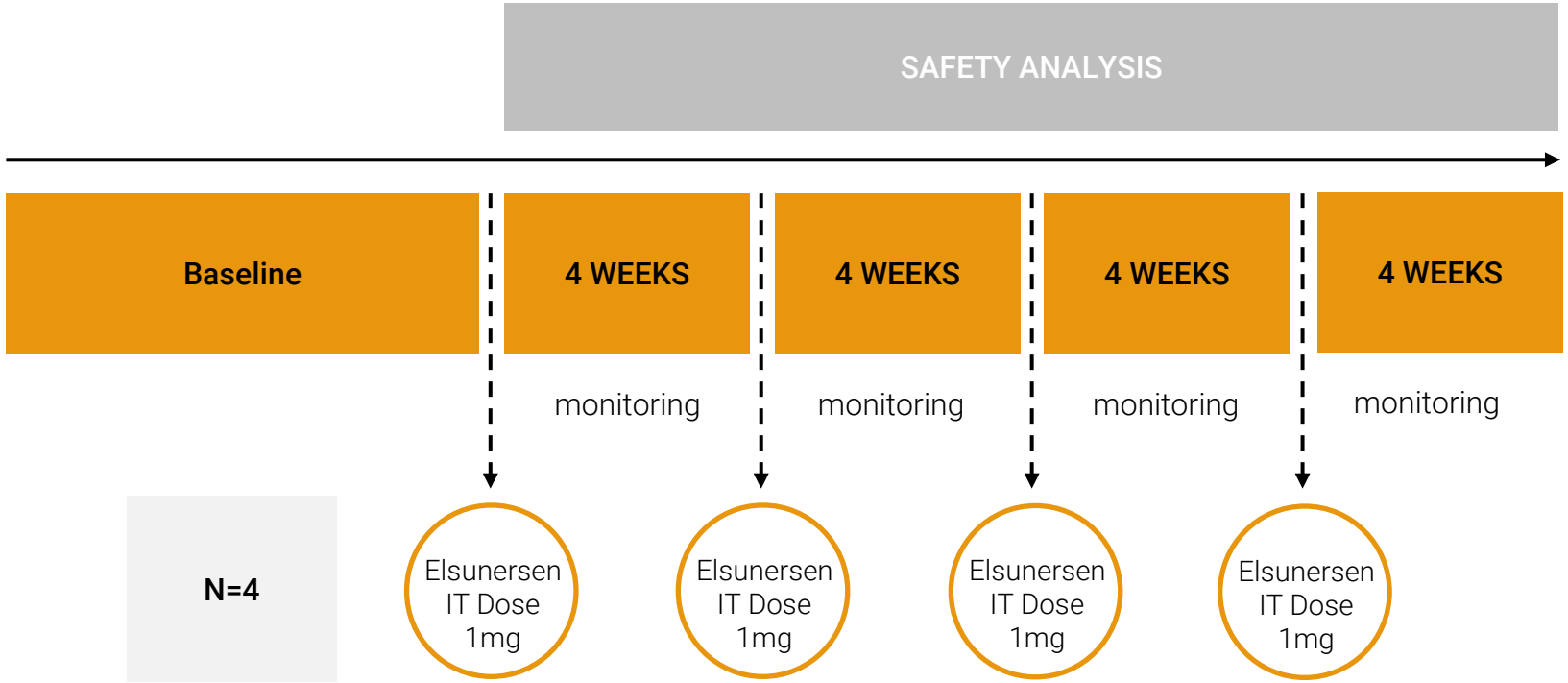
Elsunersen is a gapmer ASO with a modified core allowing it to bind to target mRNA and induce mRNA degradation via RNase H activation[3,4]

Preclinical data suggests that elsunersen has the potential to control seizures and to slow disease progression



1. Meisler MH, et al. *Nat Rev Neurosci.* 2021;22(3):152-166. 2. Carvill GL, et al. *Neurotherapeutics*. 2021;18(3):1500-1514. 3. Dhuri K, et al. *J Clin Med*. 2020;9(6):2004. 4. Li M, et al. *J Clin Invest*. 2021;131(23):e152079.

EMBRAVE Part 1 study design



EMBRAVE

GOAL:

Assess preliminary safety of elsunersen

Participant demographics

ID	Age at consent	Gender	Race	Ethnicity
2001	3 years	Female	White	Not Hispanic or Latino
2002	14 years	Male	White	Not Hispanic or Latino
2003	2 years	Female	White	Not Hispanic or Latino
2004	2 years	Female	Other (Hispanic)	Hispanic or Latino

Safety summary

- No TEAEs or SAEs considered related to study drug; all TEAEs recovered/resolved.
- Independent data monitoring committee provided opinion to continue dosing without modifications.

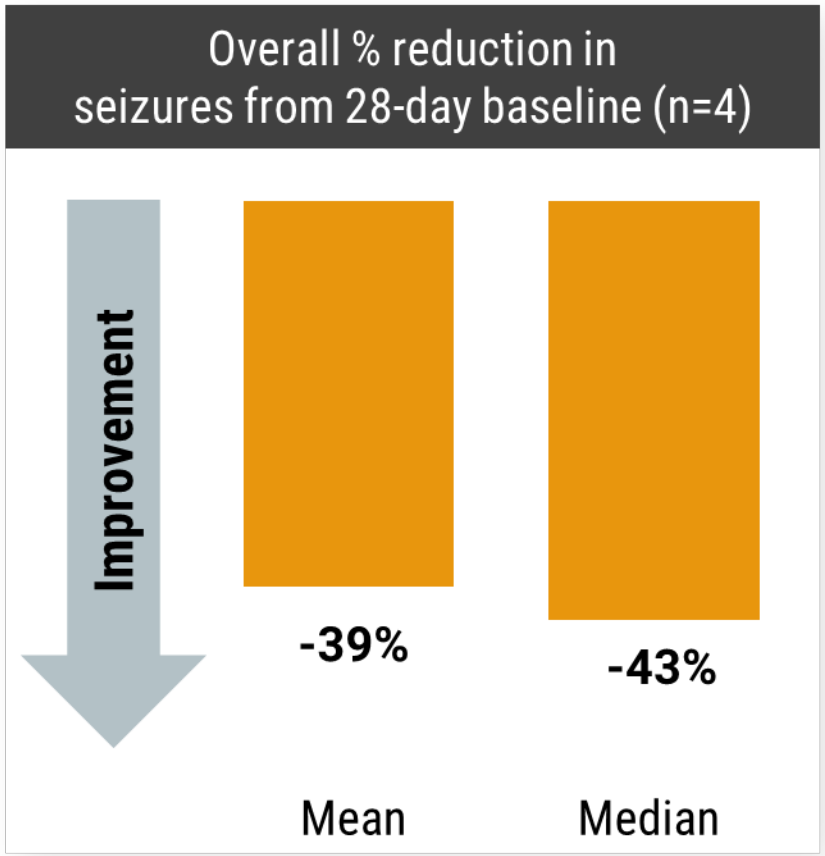
Assessment	Findings
Physical and neurological examinations	No clinically significant findings
Vital sign measurements	No clinically significant changes
Clinical laboratory results	No clinically significant changes in lab results except for 'elevated WBC' reported for 1 participant*
Electrocardiogram (ECG) parameters	No clinically significant changes

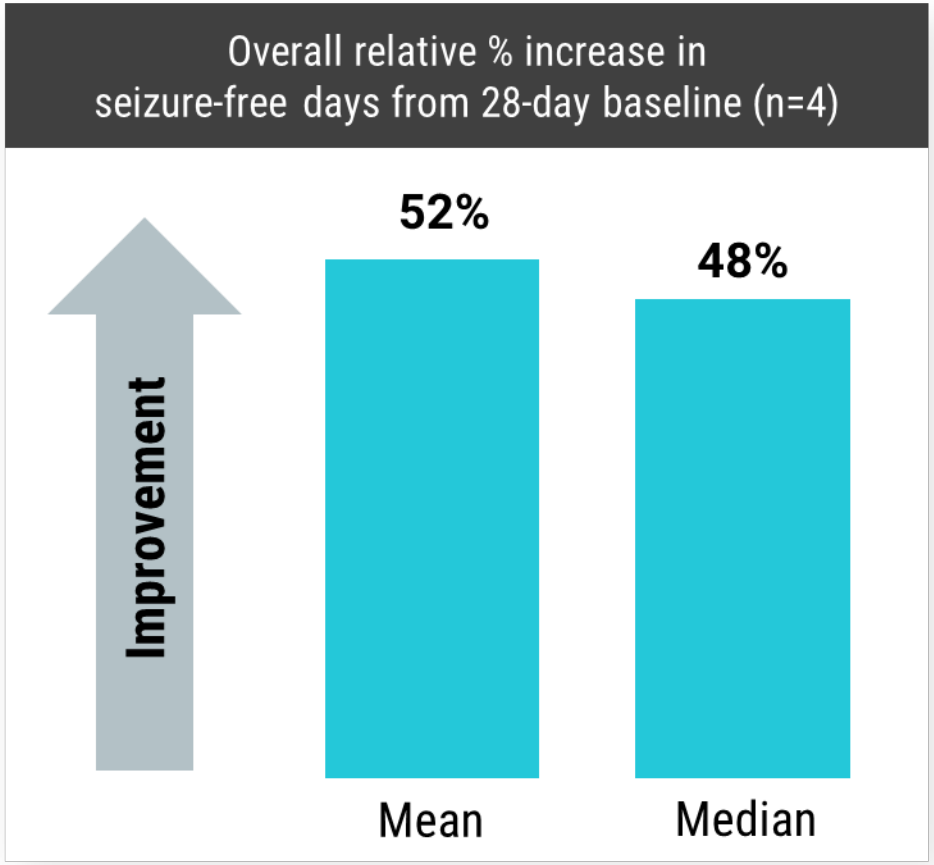
*Associated with rhino/enterovirus infection

Number of Participants with any TEAE (n=3)
Non serious TEAE (n=3)
Any serious TEAE (n=2)
Number of Individual TEAEs (n=10)
Non serious TEAE (n=5)
Any serious TEAE (n=5)*
TEAEs/SAEs considered related to study drug (n=0)

*Infection, common in this patient population

Significant seizure reduction observed for SCN2A patients





Elsunersen has the potential to be first disease-modifying treatment for early onset SCN2A GoF DEE

ELSUNERSEN

INTRATHECALLY-ADMINISTERED ASO for SCN2A GoF DEE

Significant and sustained seizure reduction at 1 mg dose levels

Unexpected benefits across all treated patients

Safe and well-tolerated with no drug related AEs

✓ **PRIME Designation from EMA for treatment of SCN2A GoF Developmental Epilepsies**

✓ ✓ **Orphan Drug Designation (ODD) and Rare Pediatric Disease Designation from FDA, and ODD from EMA for the treatment of SCN2A-DEE**

Acknowledgements

- Presented on behalf of The EMBRAVE Study Team
- We thank the patients of the EMBRAVE trial, and our collaborators, clinical sites and study investigators

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www.praxisepilepsyhcp.com

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For results from a first-in-human emergency use case in a preterm infant with refractory status epilepticus

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