Developmental & Epileptic Encephalopathies (DEE) Portfolio Update

May 2, 2025

Forward-looking statements

This presentation may contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial conditions, including but not limited to express or implied statements regarding the current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, statements regarding the estimated market for our product candidates, if approved, our development plans, our preclinical and clinical results and other future conditions, including our cash runway, and the safety, efficacy, and regulatory and clinical design or progress, potential regulatory submissions, approvals and timing thereof of any of our product candidates. Any forward-looking statements in this presentation are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, risks relating to: (i) the success and timing of our ongoing clinical trials, (ii) the success and timing of our product development activities and initiating clinical trials, (iii) the success and timing of our collaboration partners' product development activities, (iv) the timing of and our ability to obtain and maintain regulatory approval of any of our product candidates, (v) our plans to research, discover and develop additional product candidates, (vi) our ability to enter into collaborations for the development of new product candidates, (vii) our ability to establish manufacturing capabilities, and our collaboration partners' abilities to manufacture our product candidates and scale production, (viii) our ability to meet any specific milestones set forth herein, and (ix) the potential addressable market sizes for product candidates. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements.

For further information regarding the risks, uncertainties and other factors that may cause differences between our expectations and actual results, you should review the "Risk Factors" section of our Annual Report on Form 10-K for the year ended December 31, 2024 filed with the Securities and Exchange Commission ("SEC") and our other filings with the SEC.

Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and make no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

PRAXIS' MISSION

The needs of patients with CNS disorders are devastatingly urgent. Our mission is to help patients by delivering life-altering treatments faster and more effectively than has ever been done before — and to do it again and again.

Overview

TODAY'S PRESENTERS

Marcio Souza,
President & CEO

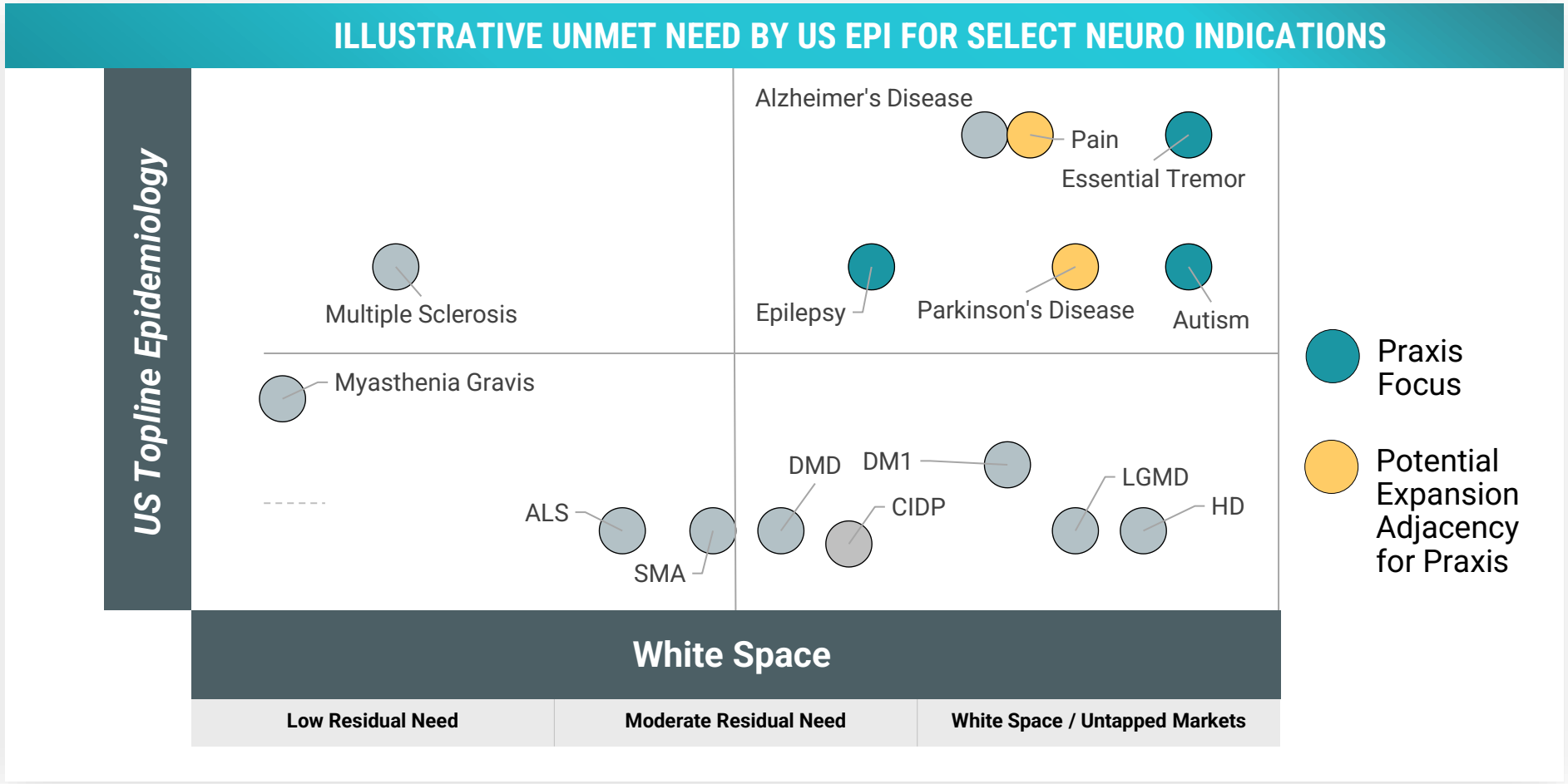
Steven Petrou, PhD,
CSO

INTRODUCTION

- Developmental and Epileptic Encephalopathies (DEEs)
- Commercial Opportunity
- Relutrigine program
- Solidus platform
  - Elsunersen clinical program and commercial potential
  - ASO Pipeline: PRAX 80, 90, 100
- Conclusion and Q&A

Neurology is a large TA – much of which is “white space”

Praxis is strategically positioned to target important unmet needs with large potential



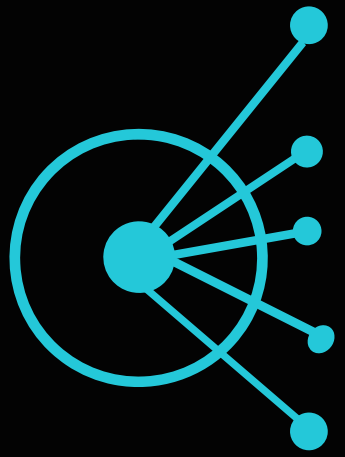
ALS=amyotrophic lateral sclerosis, CIDP=chronic inflammatory demyelinating polyneuropathy, DM1=myotonic dystrophy type 1, DMD=Duchenne muscular dystrophy,, HD=Huntington’s disease, LGMD=limb-girdle muscular dystrophy, TA=therapeutic area, SMA=spinal muscular atrophy

Two platforms to generate optimized therapies

CEREBRUM™

SMALL MOLECULE PLATFORM

Cerebrum™ utilizes deep understanding of neuronal excitability and neuronal networks and applies a series of computational and experimental tools to develop orally available precision therapies



Molecule	Indication	Mechanism
ulixacaltamide	Essential Tremor	T-type calcium channel modulator
vormatrigine	Focal Onset Seizures & Generalized Epilepsy	Sodium channel functional state modulator for broad use
relutrigine*	DEE Epilepsies	Sodium channel functional state modulator for broad use
PRAX-020^	KCNT1 Epilepsy	KCNT1 specific inhibitor
PRAX-050	Not disclosed	Not disclosed

SOLIDUS™

ANTISENSE OLIGONUCLEOTIDE (ASO) PLATFORM

Solidus™ is an efficient, targeted precision medicine discovery and development engine for ASOs anchored on proprietary, computational methodology

Molecule	Indication	Mechanism
elsunersen*	SCN2A GoF	Gapmer ASO
PRAX-080	PCDH19 Mosaic expression	Gapmer ASO
PRAX-090	SYNGAP1 LoF	Splice switching ASO
PRAX-100	SCN2A LoF	Undisclosed mechanism ASO

* Relutrigine has received Orphan Drug Designation (ODD) and Rare Pediatric Disease (RPD) designation from the FDA, and ODD from the European Medicines Agency (EMA) for the treatment of SCN2A and SCN8A-DEE and RPD designation for Dravet Syndrome

^ PRAX-020 (KCNT1) has been licensed to UCB

** Elsunersen has received ODD and RPD designation from the FDA, and ODD and PRIME designations from the EMA for the treatment of SCN2A GoF

DEE=developmental & epileptic encephalopathy, GoF=gain-of-function, LoF=loss-of-function, PRIME=Priority Medicines

Two platforms to generate optimized therapies

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Today's Focus

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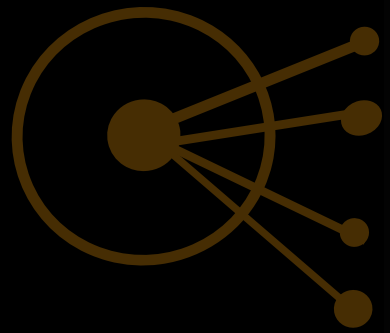

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DEE=developmental & epileptic encephalopathy, GoF=gain-of-function, LoF=loss-of-function, PRIME=Priority Medicines

- Developmental and Epileptic Encephalopathies (DEEs)
- Commercial Opportunity

A common, phenotypically driven definition of DEEs

DEEs are a group of severe brain disorders characterized by early-onset epilepsy combined with developmental delay or regression, where both the epilepsy and the underlying brain dysfunction contribute to impaired development

Pictures are from stories shared at Praxis 2024 DEEp Dive Day event

DEEs are amongst the most severe pediatric conditions

Caused by diverse etiologies which all converge on the same neurobiological mechanism of network hyperexcitability

Significant comorbidities and need for long-term supportive care contribute to lifelong burden for the caregiver community

Often presenting with frequent seizures and developmental disability in infancy

Early mortality is common, with many rarely surviving beyond teenage years

Majority of patients without an approved treatment option

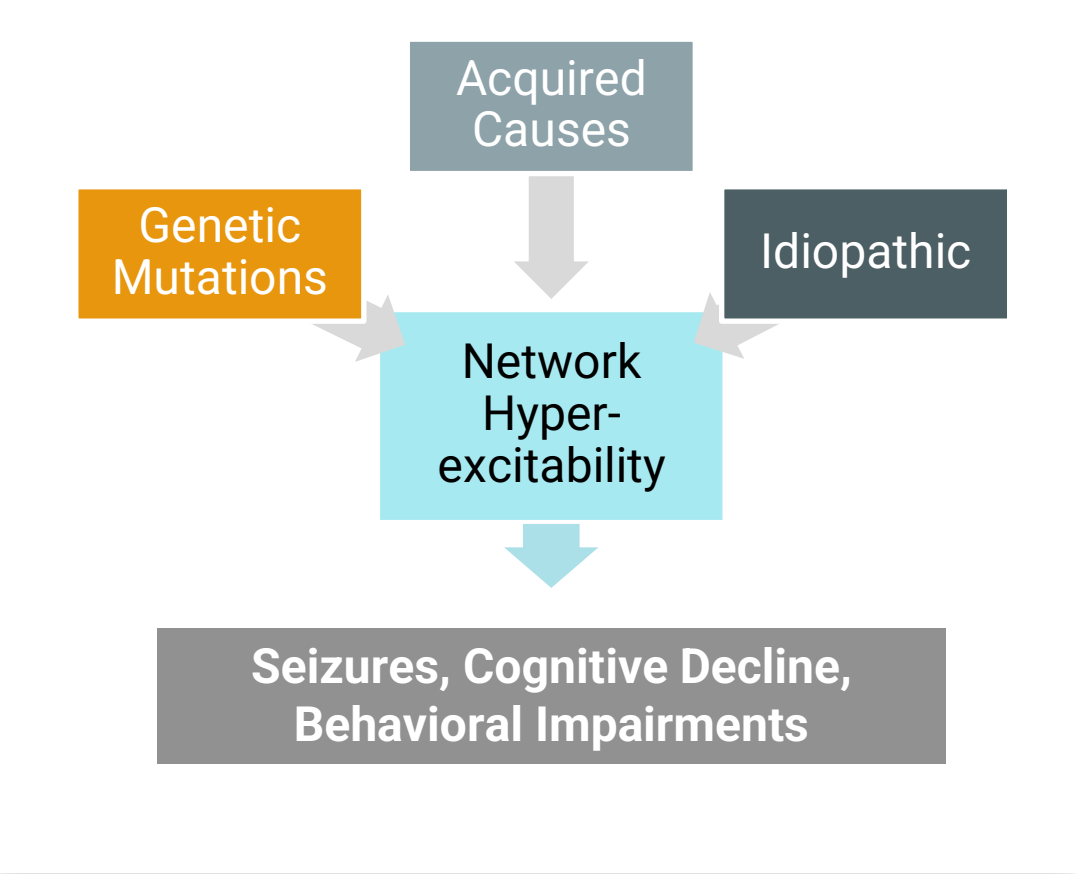
Zuberi SM, et al. Epilepsia. 2022;63(6):1349-1397, Helbig KL, et al. Am J Hum Genet. 2018;103(5):666-678., Takai A, et al. Int J Mol Sci. 2020;21(17):6442, Gallop K, et al. Epilepsy Behav. 2021;124:108324, Johannessen Landmark C, et al. Epilepsia. 2021;62(4):857-873.,Thurman DJ, et al. Epilepsia. 2014;55(10):1479-1485 7., Li M, et al. J Clin Invest. 2021;131(23):e152079.

SUDEP=sudden unexpected death in epilepsy

Neuronal hyperexcitability is a common mechanism of seizures

Praxis' Approach

- **While the underlying etiology may vary, hyperexcitability of neurons that lead to uncontrolled seizures and devastating outcomes is a common manifestation**
- **Targeting the hyperactivated voltage-gated ion channels offers a unified therapeutic approach across DEEs**



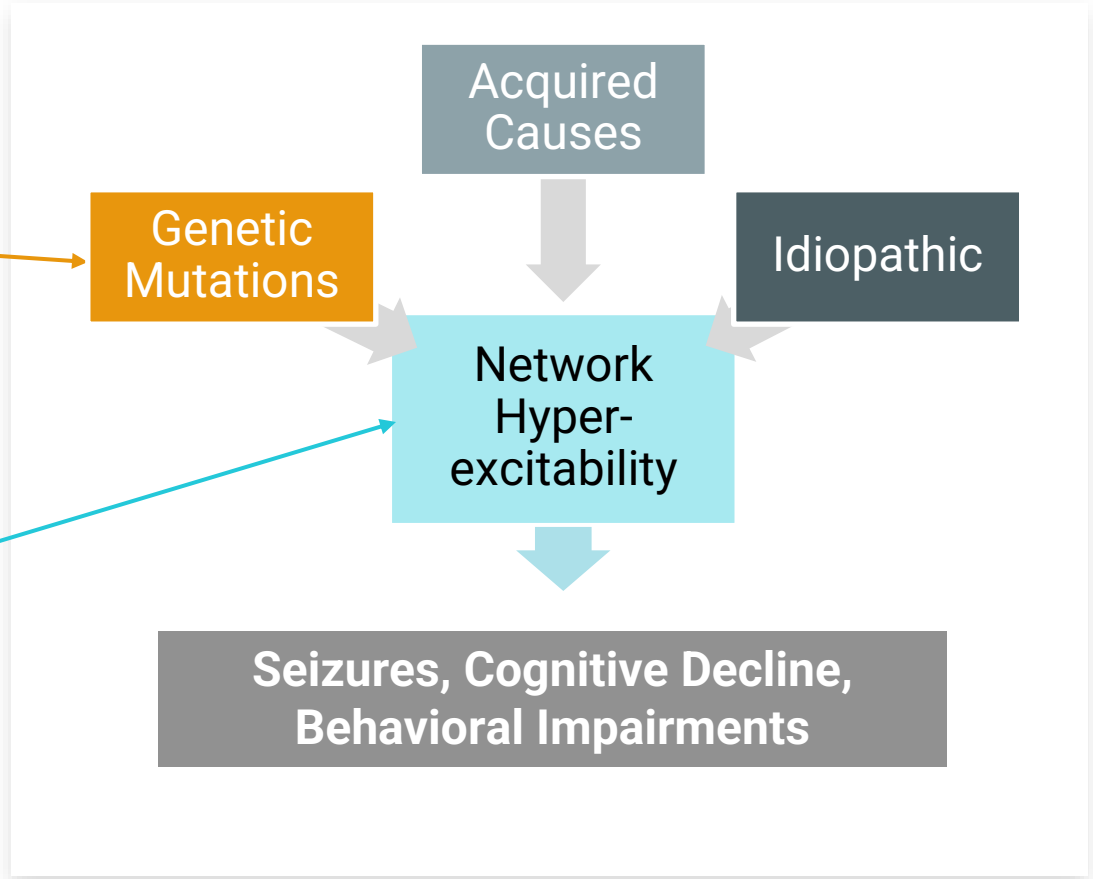
Guerrini R, et al. Physiol Rev.2023;103(1):433-513.
DEE=developmental & epileptic encephalopathy

Addressing the unmet need with multiple approaches

SOLIDUS PLATFORM FOCUS

- **Elsunersen**
- **PRAX-80**
- **PRAX-90**
- **PRAX-100**

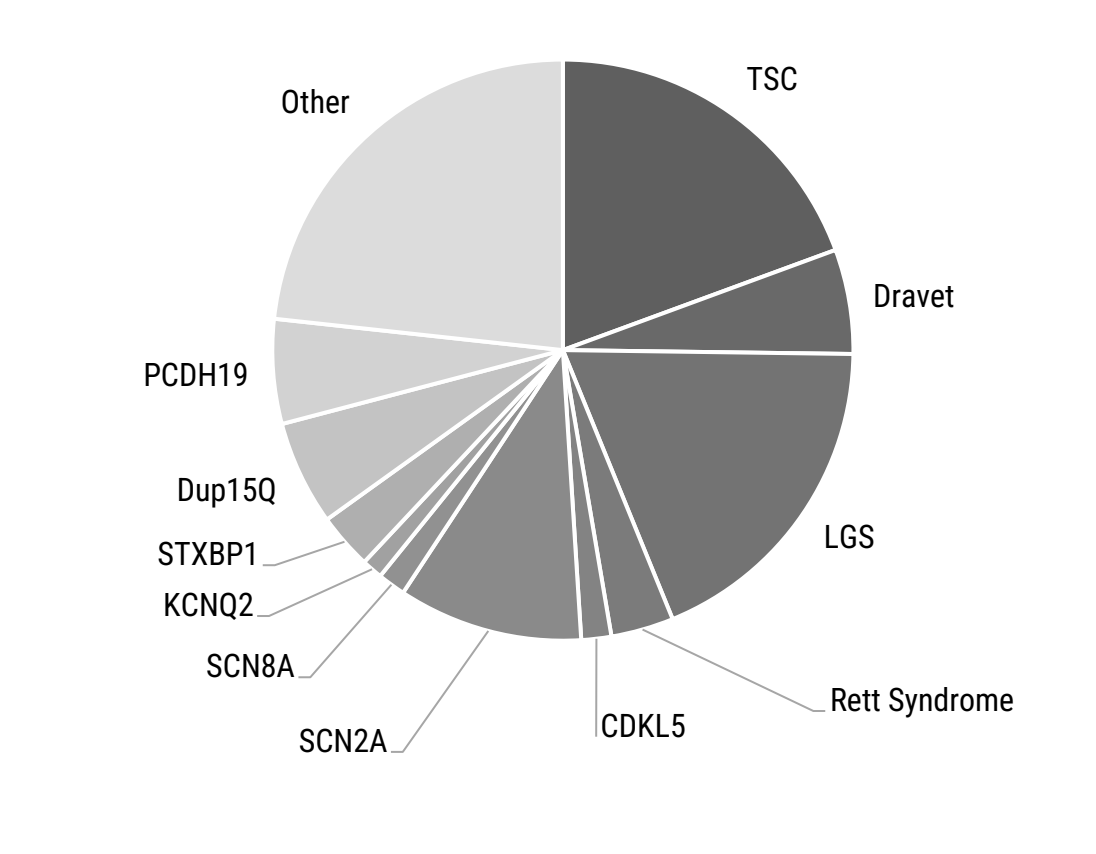
Relutrigine



DEE=developmental & epileptic encephalopathy

Current US DEE market is over 200,000 patients

Expected to increase in coming years as care and diagnosis improve

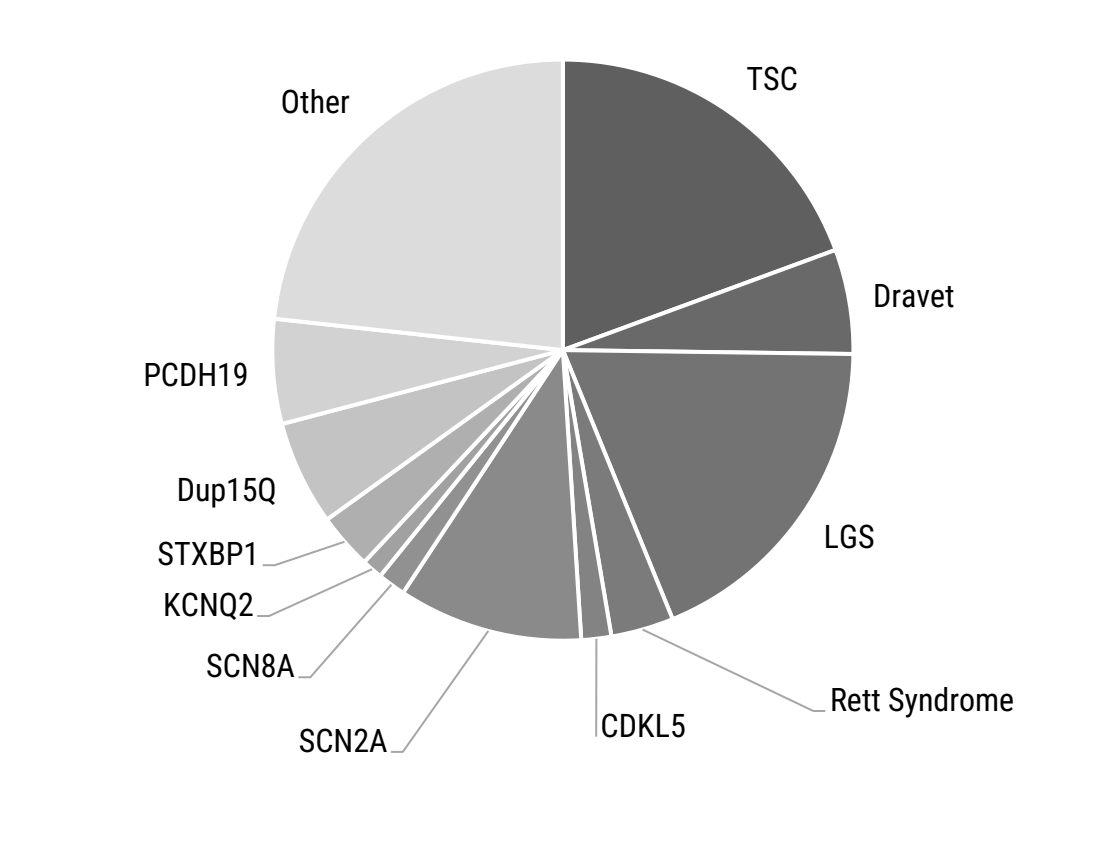


- **Different levels of severity along the disease spectrum**
- **Opportunity for multiple approaches to address unmet need**

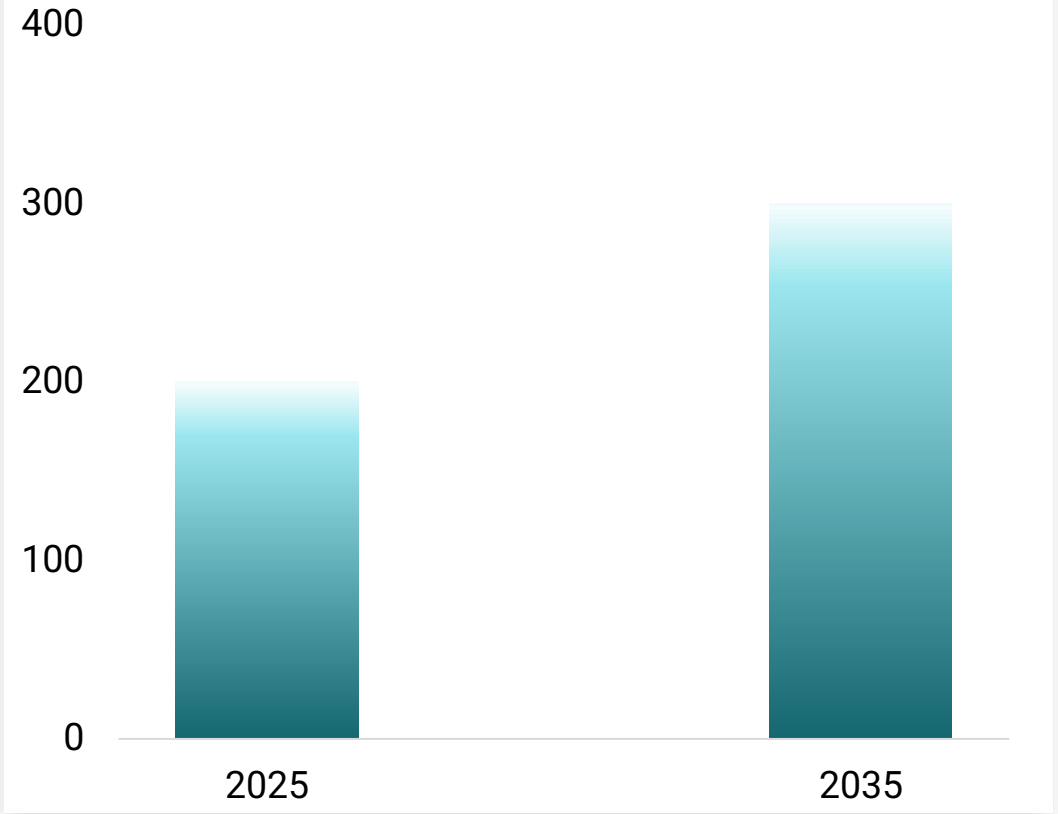
Poke G, et al. Neurology. 2023;100(13)e.1363-75., Lopez-Rivera JA, et al. Brain.2020;143(4):1099-1105., Wu YW, et al. Pedatrics.2015;136(5):e1310-15., Scheffer IE, et al. Nat Rev Dis Primers.2024;10(61)1-19., LGS Foundation. "How Many People Have LGS?", Boston Children's Hospital. "Tuberous Sclerosis Complex (TSC).", SCN8A Alliance. "What Is SCN8A?", Stoke Therapeutics. "SYNGAP1", Roche. "Dup15q Syndrome Clinical Trials,", Angelman Syndrome Foundation. "What Is Angelman Syndrome?", Acadia Pharmaceuticals Inc. "Rett Syndrome Overview.", The Cute Syndrome Foundation. "PCDH19 Epilepsy Overview", FamilieSCN2A Foundation. "SCN2A-Related Autism."

DEE=developmental & epileptic encephalopathy, LGS=lennox gastaut syndrome, TSC=tuberous sclerosis complex

DEE population is expected to continue to increase



INCREASED DIAGNOSIS, TREATMENT AND SURVIVAL AS DRIVERS OF GROWTH



Poke G, et al. Neurology. 2023;100(13)e.1363-75., Lopez-Rivera JA, et al. Brain.2020;143(4):1099-1105., Wu YW, et al. Pedatrics.2015;136(5):e1310-15., Scheffer IE, et al. Nat Rev Dis Primers.2024;10(61)1-19., LGS Foundation. "How Many People Have LGS?", Boston Children's Hospital. "Tuberous Sclerosis Complex (TSC).", SCN8A Alliance. "What Is SCN8A?", Stoke Therapeutics. "SYNGAP1", Roche. "Dup15q Syndrome Clinical Trials,", Angelman Syndrome Foundation. "What Is Angelman Syndrome?", Acadia Pharmaceuticals Inc. "Rett Syndrome Overview.", The Cute Syndrome Foundation. "PCDH19 Epilepsy Overview", FamilieSCN2A Foundation. "SCN2A-Related Autism."

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Relutrigine is well positioned to address the broad DEE market

>200,000 ELIGIBLE PATIENTS

EMERALD study expected to provide evidence to support a broad label

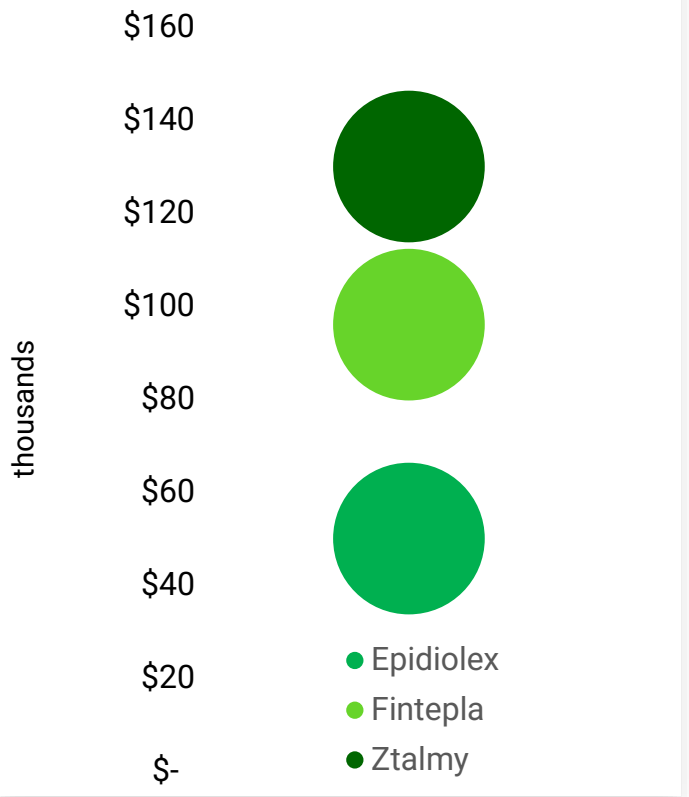
DEE=developmental & epileptic encephalopathy

Modest assumptions on market share and pricing support a large commercial opportunity

>200,000 ELIGIBLE PATIENTS

X

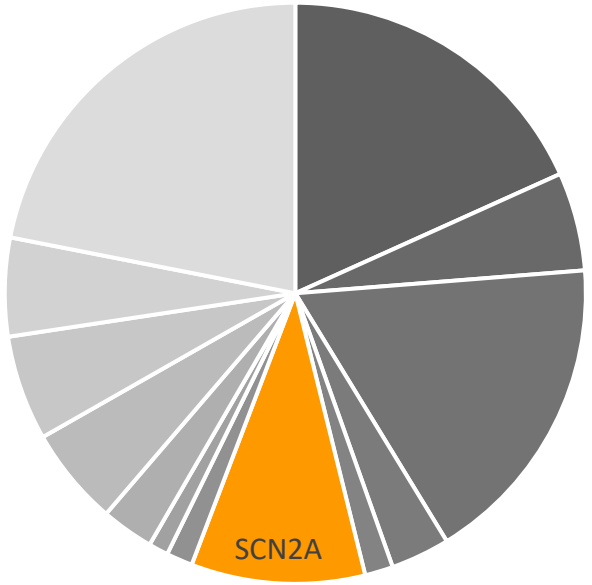
CURRENT PRICING ANALOGS



~$3B opportunity

Elsunersen represents a significant global opportunity

~5,000 ELIGIBLE PATIENTS



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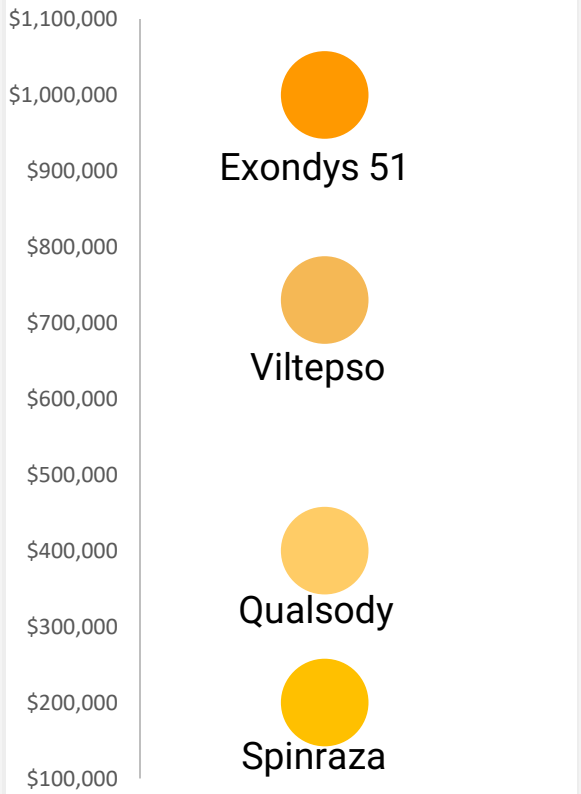
ASO PRICING ANALOGS



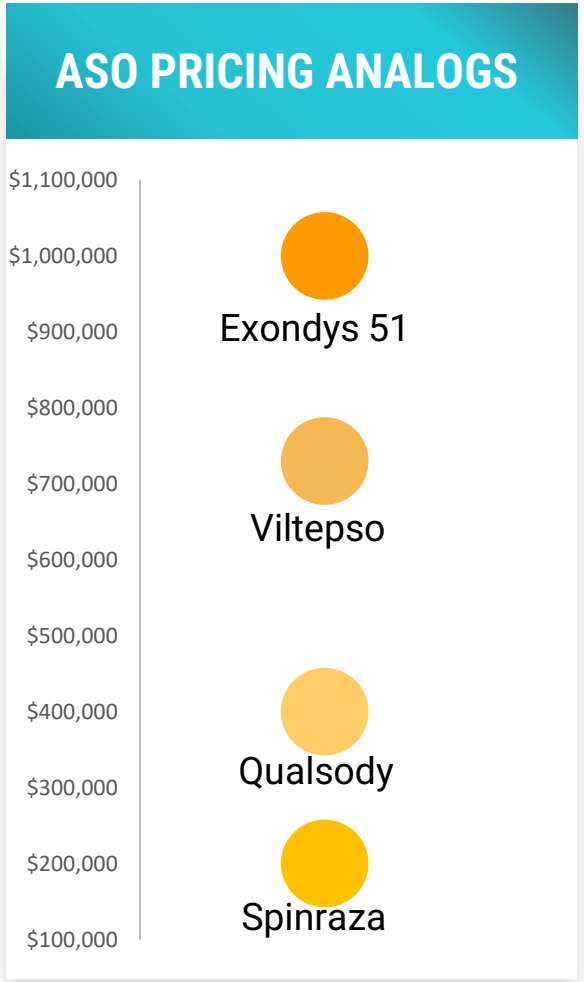
~$1B opportunity

FamilieSCN2A Foundation. "SCN2A-Related Autism."
ASO=antisense oligonucleotide

PRAX-100 addresses an untapped opportunity in genetically defined autism

>20,000 ELIGIBLE PATIENTS*

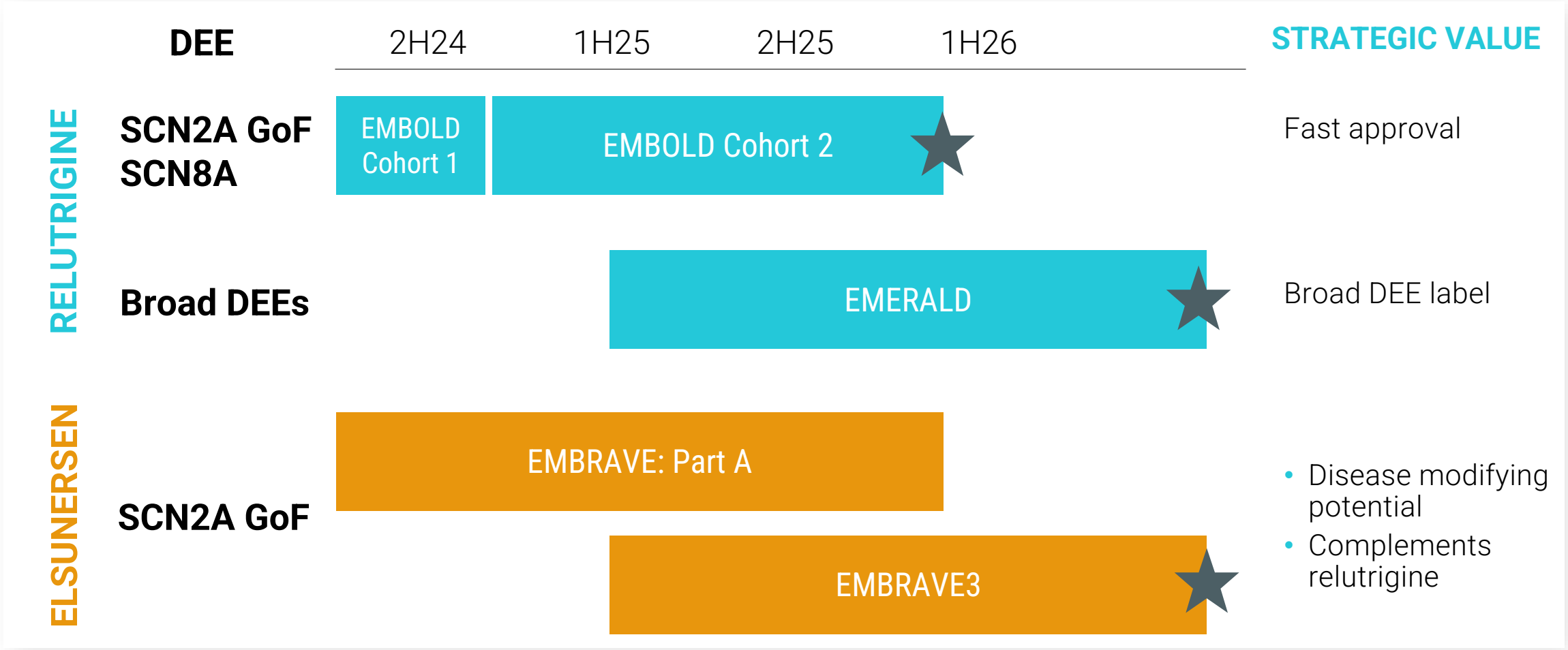
X



>$4B opportunity

FamilieSCN2A Foundation. "SCN2A-Related Autism."
ASO=antisense oligonucleotide, LoF=loss-of-function

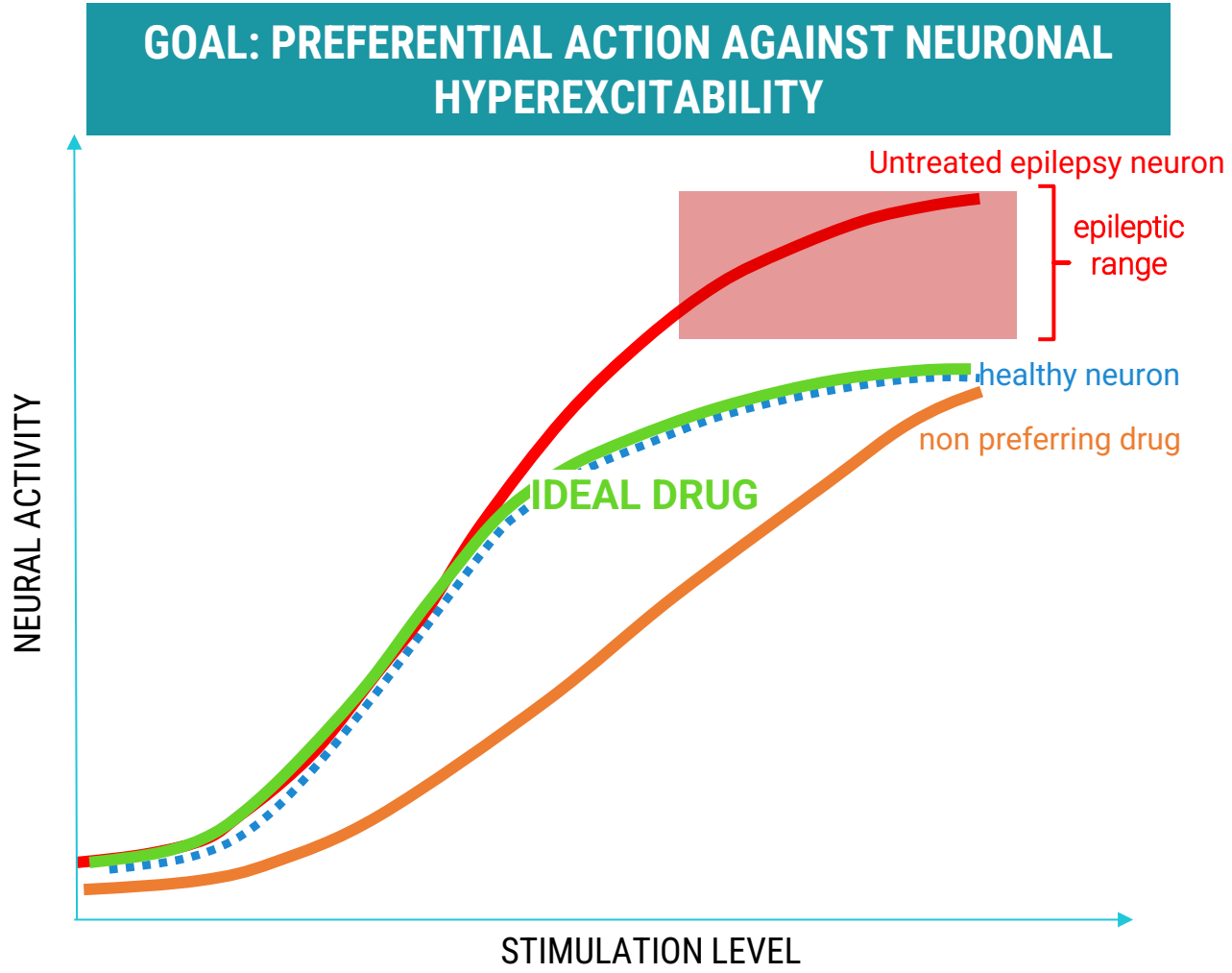
Praxis DEE clinical program: stepwise approach to broad DEE impact



DEE=developmental & epileptic encephalopathy, GoF=gain-of-function

- Relutrigine program

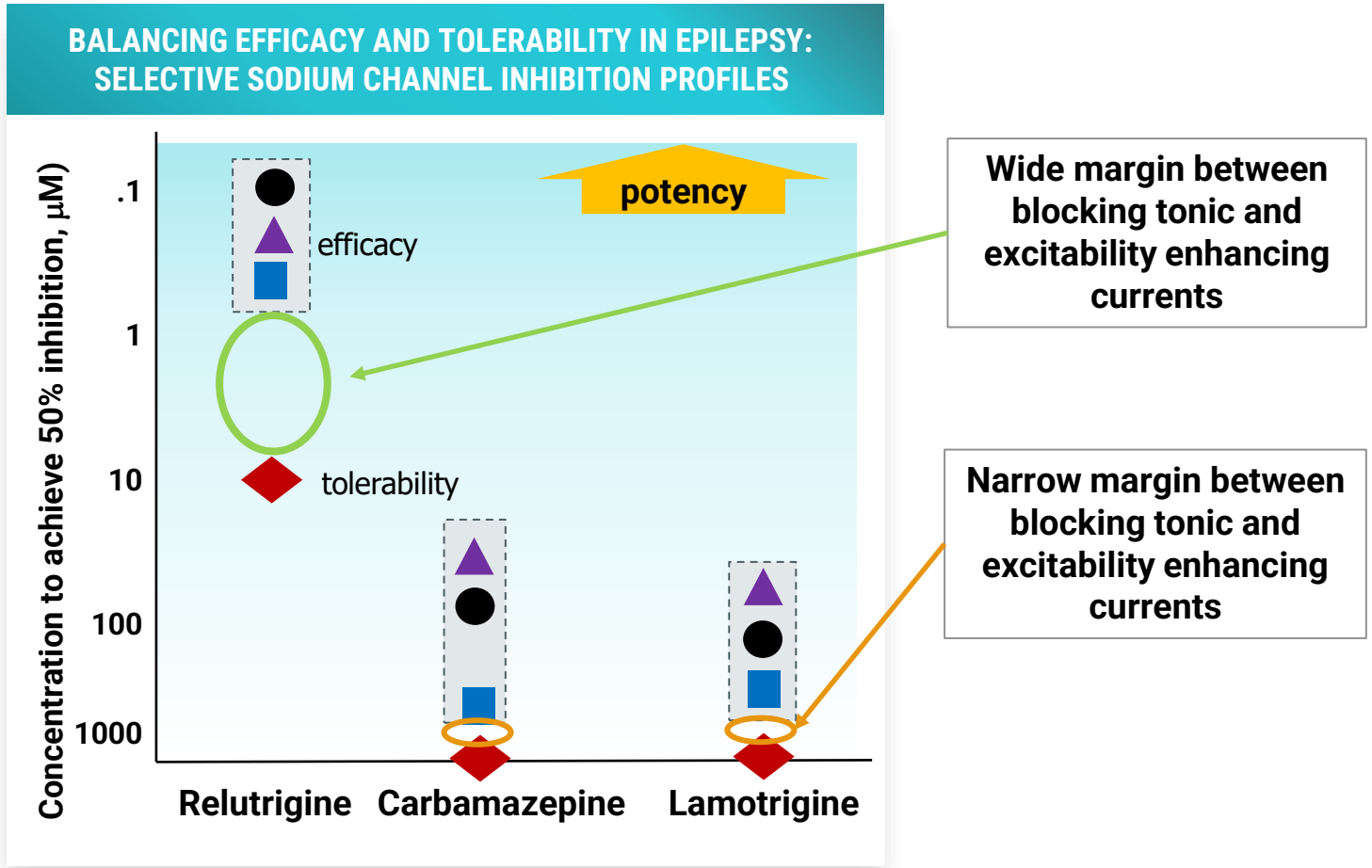
Selectively targeting pathologic neuronal hyperexcitability



Differentiated profile enabling wide therapeutic index

Tolerability-Supporting Current
- Physiological (Tonic) Sodium Current
- Maintains normal neuronal function
- Inhibition leads to side effects

Pathological Excitability Currents
- Currents:
  - Persistent
  - Voltage
  - Use-dependent
- Promote hyperexcitability
- Inhibition drives anti-seizure efficacy

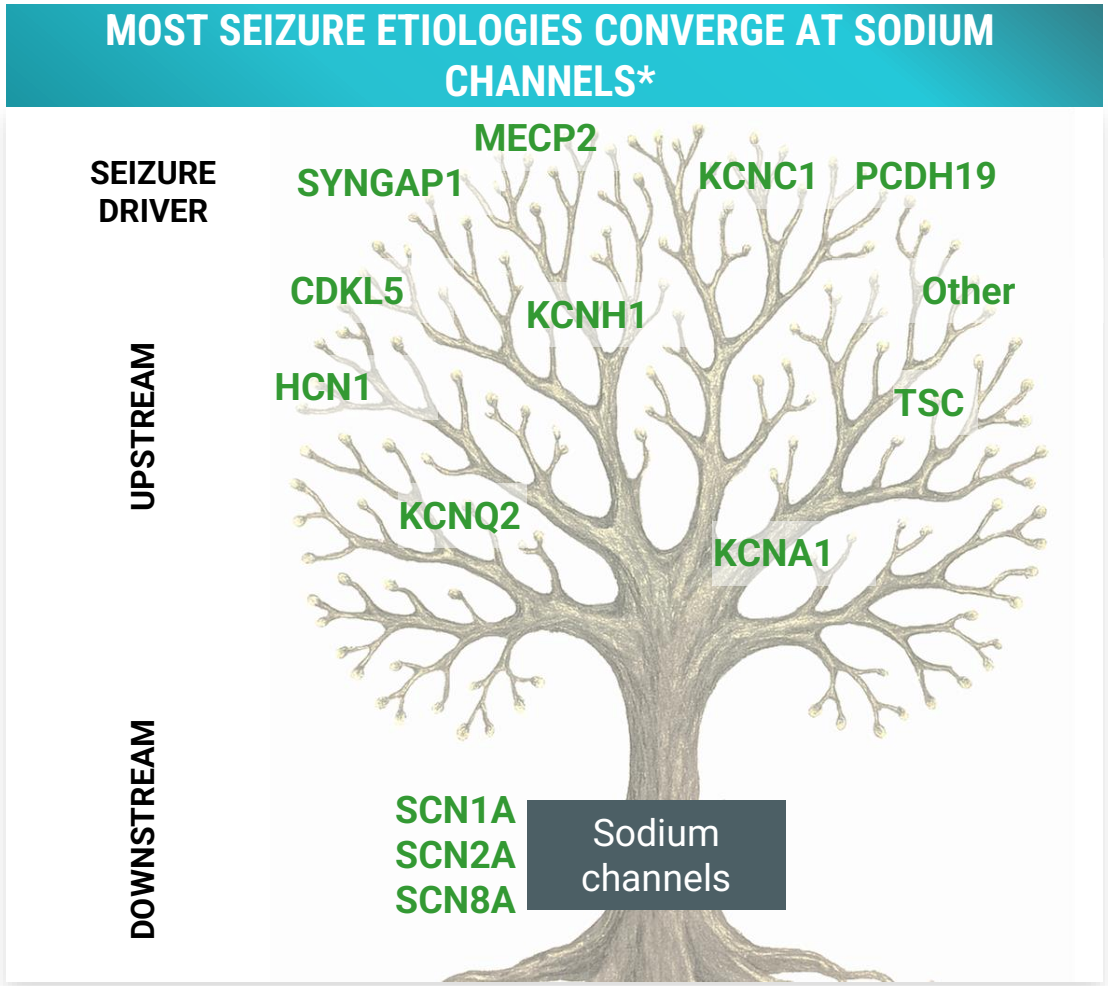


Praxis data on file

hNav=human voltage-gated sodium channel, μM = micromolar, TI=therapeutic index

Broad applicability across multiple etiologies

- All genetically driven DEEs result in hyperactivation of sodium channels, manifesting in epilepsy syndromes
- Relutrigine's mechanism of action is to target hyperactive Na_V channels to address the neuronal hyperexcitability driving seizures
- Targeting the root cause of DEE symptomology allows for broad use of relutrigine not seen in other therapies before

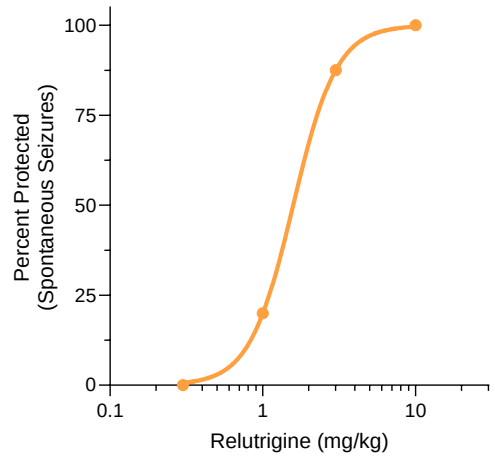


*Illustrative etiologies, not limited by examples shown
DEE=developmental & epileptic encephalopathy, Na_V=voltage-gated sodium channel

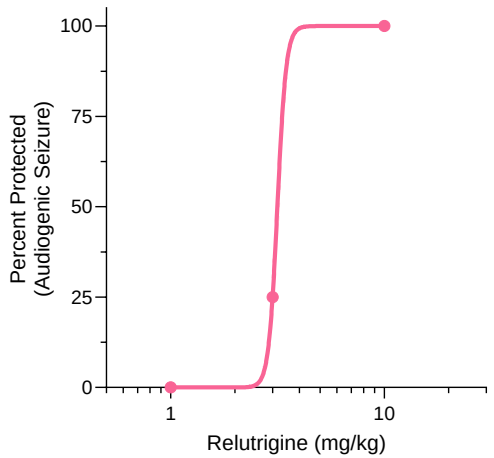
Robust anticonvulsant activity across multiple genetic DEE models

ACTIVITY IN SODIUM CHANNEL DEE MODELS

PROTECTS *SCN2A*^{Q54} MICE

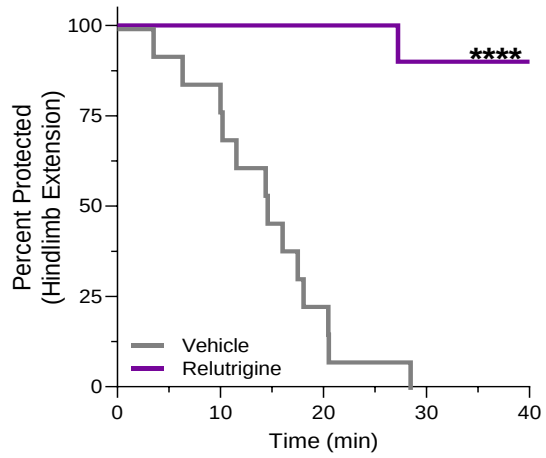


PROTECTS *SCN8A*$^{N1768D/+}$ MICE



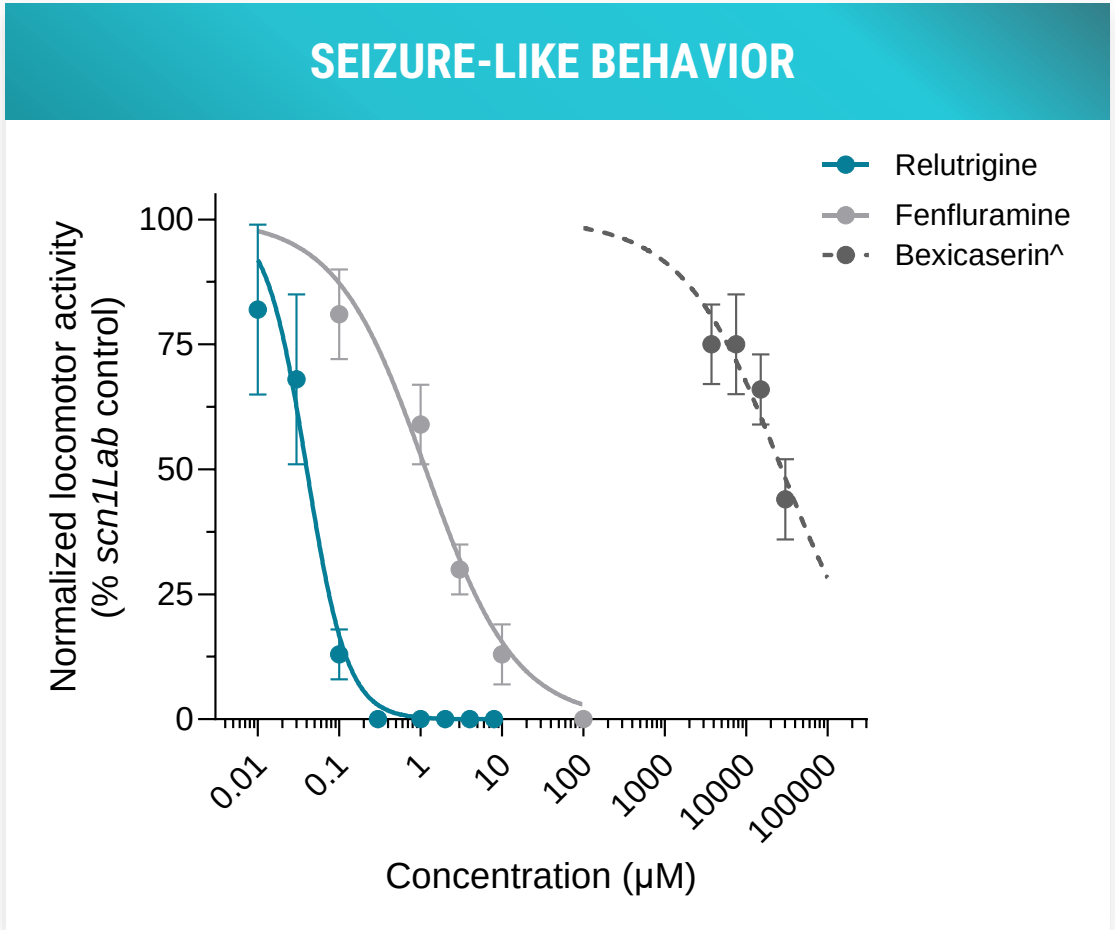
ACTIVITY IN NON-SODIUM CHANNEL DEE MODELS

KCNC1$^{R320H/+}$ MICE PTZ MODEL



Praxis data on file., Anderson LL. Epilepsia. 2014;55(5):1274-83., Baker EM, et al. Epilepsia. 2018;59(60):1166-76.
DEE=developmental & epileptic encephalopathy

Relutrigine outperforms: competitive profile in Dravet model



Agent	Antiseizure Activity EC_{50} (µM)
Relutrigine	**0.04**
Fenfluramine	1.2
Bexicaserin	~25,000^

^Estimated from AES 2023 poster

Praxis data on file
dpf=days post-fertilization, EC_{50}=half maximal effective concentration, mm/s=millimeters per second, µM=micromolar

Consistent efficacy in diverse number of DEE models

DEE Model	Relutrigine and Analogs
Scn2a^{R1882Q}	
Scn2a^{Q54}	
Scn8a$^{N1768D/+}$	
Scn1a$^{+/-}$ Dravet	
scn1Lab (fish) Dravet	
Kcnh1^{R357Q}	
Kcnc1$^{R320H/+}$	
Kcnq2$^{K556E/+}$	
Kcna1$^{T401I/+}$	
Hcn1$^{M294L/+}$	

1. Effect in 2A/8A epilepsy models ✓

2. Effect in Dravet (1A) epilepsy models ✓

3. Effect in non-sodium channel epilepsy models ✓

Praxis data on file, Anderson LL, et al. Epilepsia. 2014;55(5):1274-83., Baker EM, et al. Epilepsia. 2018;59(60):1166-76.; Anderson LL, et al. Sci Rep. 2017;7(1):1682., Johnson JP, et al. Elife. 2022:11:e72468., Hawkins NA, et al. Ann Clin Transl Neurol. 2017;4(5):326-339., Bleakley LE, et al. Epilepsia. 2023;64(1):e1-e8., Merseburg A, et al. Elife. 2022:11:e70826., Prof Kearney Lab 2025.

Relutrigine: Potential for class leading efficacy and tolerability

RELUTRIGINE

ORAL SOLUTION, NO TITRATION, ONCE DAILY ADMINISTRATION

FORMULATED FOR PEDIATRIC USE

SMALL MOLECULE

FUNCTIONAL STATE MODULATOR

- Demonstrated robust seizure reduction and unprecedented seizure-free status per 28-day period
- Superior selectivity for hyperactive Na_V channels, a known cause of seizure manifestation in all DEEs regardless of etiology
- Generally well-tolerated with mostly mild to moderate AEs, no drug-related SAEs and no relutrigine dose reduction required
- Three Rare Pediatric Drug designations for SCN1A (Dravet Syndrome), SCN2A DEE and SCN8A DEE

AE=adverse event, DEE=developmental & epileptic encephalopathy, Na_V=voltage-gated sodium channel, SAE=serious adverse event

Relutrigine Phase 1: favorable safety and pharmacodynamics

Relutrigine has been generally well tolerated in over 130 healthy volunteers

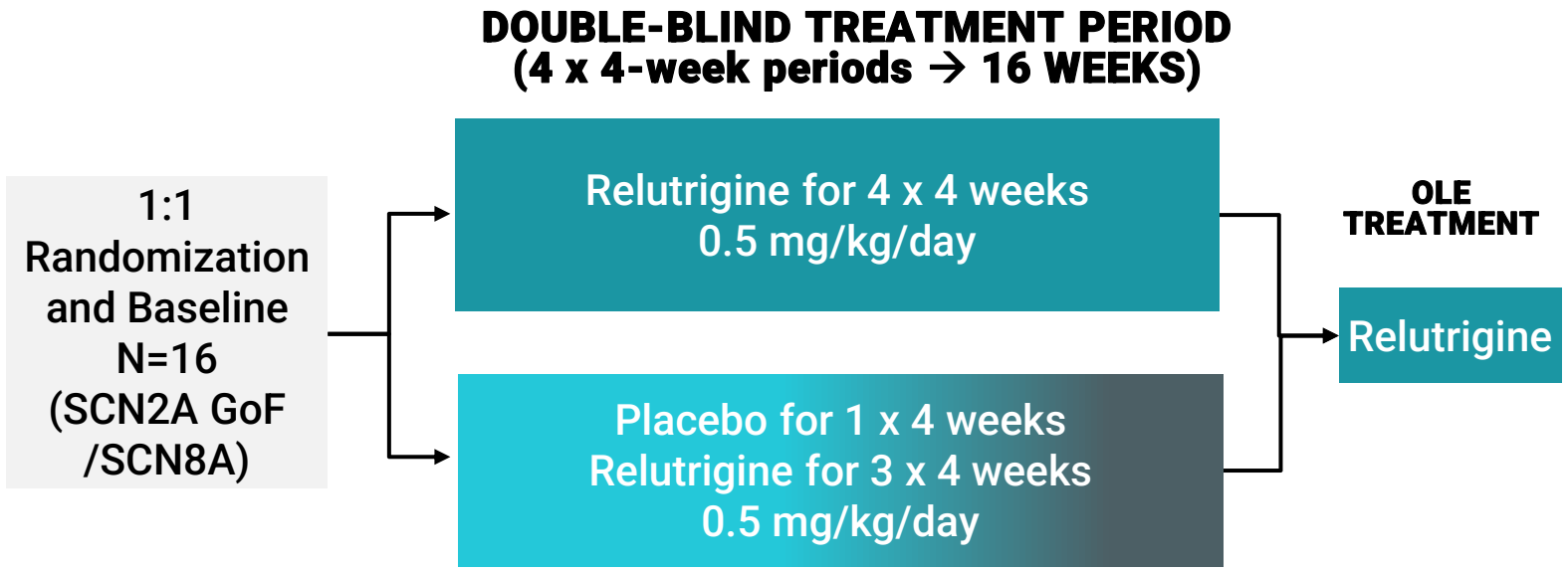
All TEAEs mild to moderate as stand-alone therapy, with headache & dizziness most common TEAEs

No MTD at exposures multiple fold above therapeutic range indicates potential for superior therapeutic index

Significant changes observed between placebo and relutrigine on qEEG biomarkers

MTD=maximum tolerated dose, qEEG=quantitative electroencephalography, SAE=serious adverse event, TEAE=treatment emergent adverse event

EMBOLD study design: controlled trial targeting DEE seizure burden in patients receiving standard of care ASMs



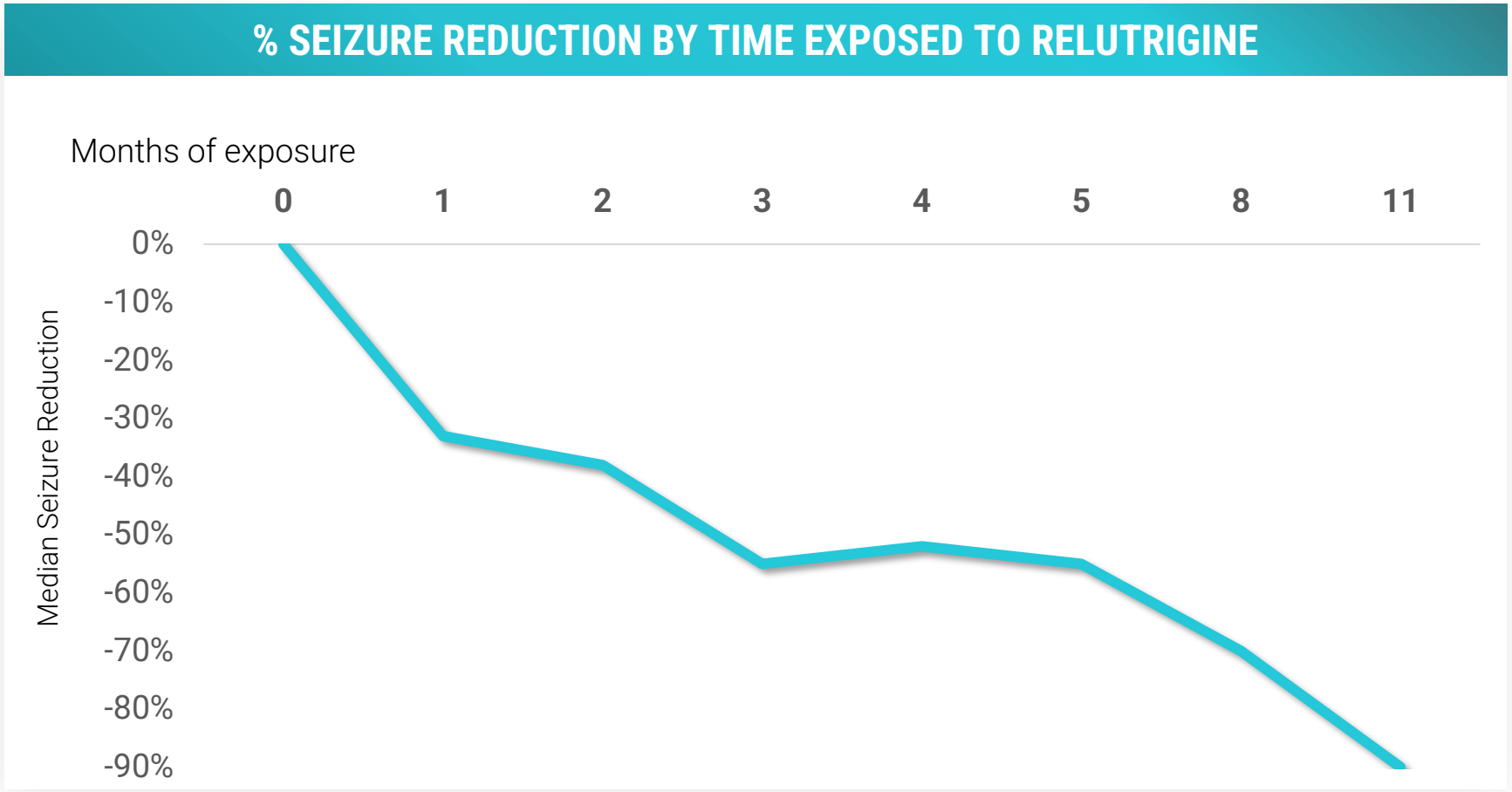
KEY ENDPOINTS:

- Incidence and severity of treatment-emergent adverse events
- Change from baseline in monthly motor seizure frequency
- Length of seizure freedom achieved over a 28-day period
- Clinical and Caregiver Global Impression of Improvement and Severity

EMBOLD

ClinicalTrials.gov Identifier: NCT05818553.
ASM=anti-seizure medication, QD=daily

EMBOLD Cohort 1 results: sustained seizure reduction with continued exposure on top of SOC



70% of patients were at stable doses of Sodium Channel Blockers at baseline

AEs were mostly mild to moderate

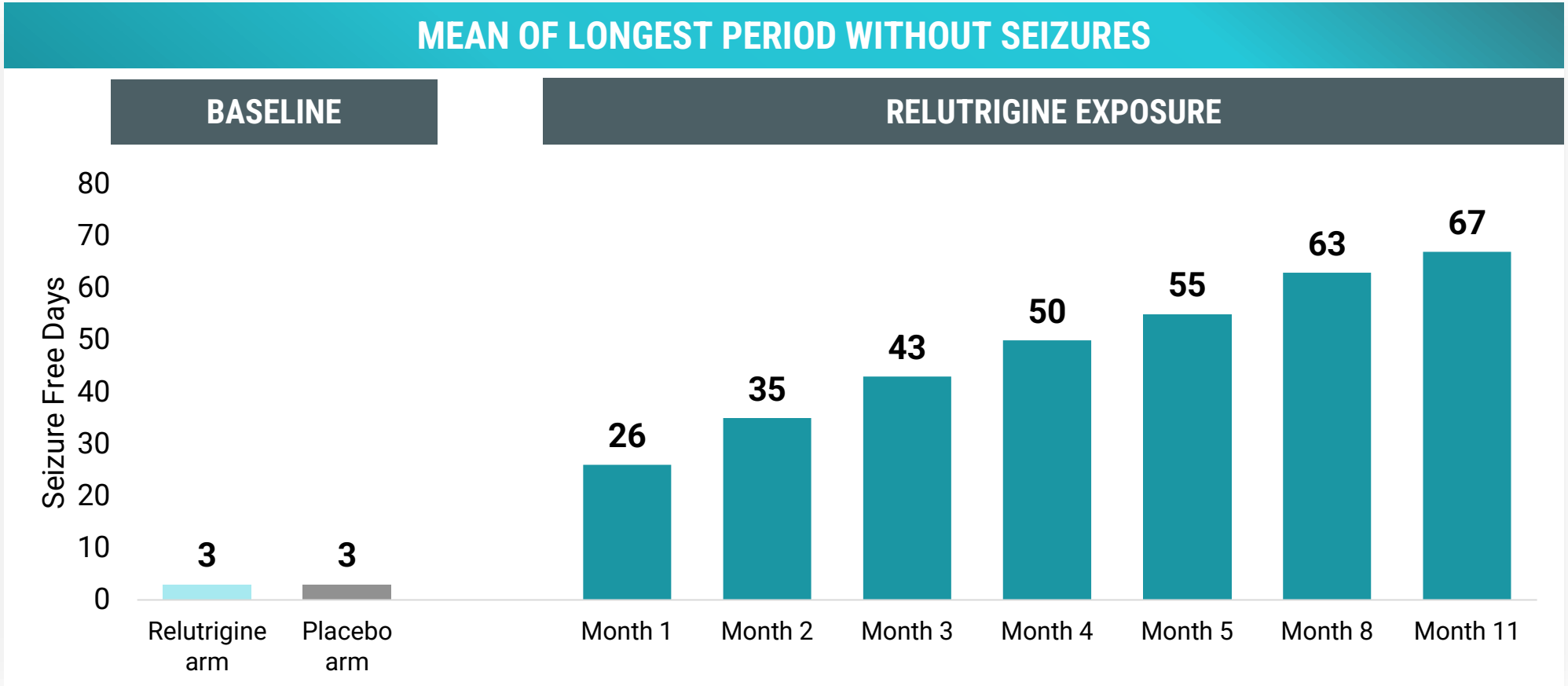
No drug-related SAEs

No dose reduction of relutrigine required

EMBOLD

*Inclusive of open-label extension period as of April 24, 2025
Praxis Data on File
AE=adverse event, SAE=serious adverse event

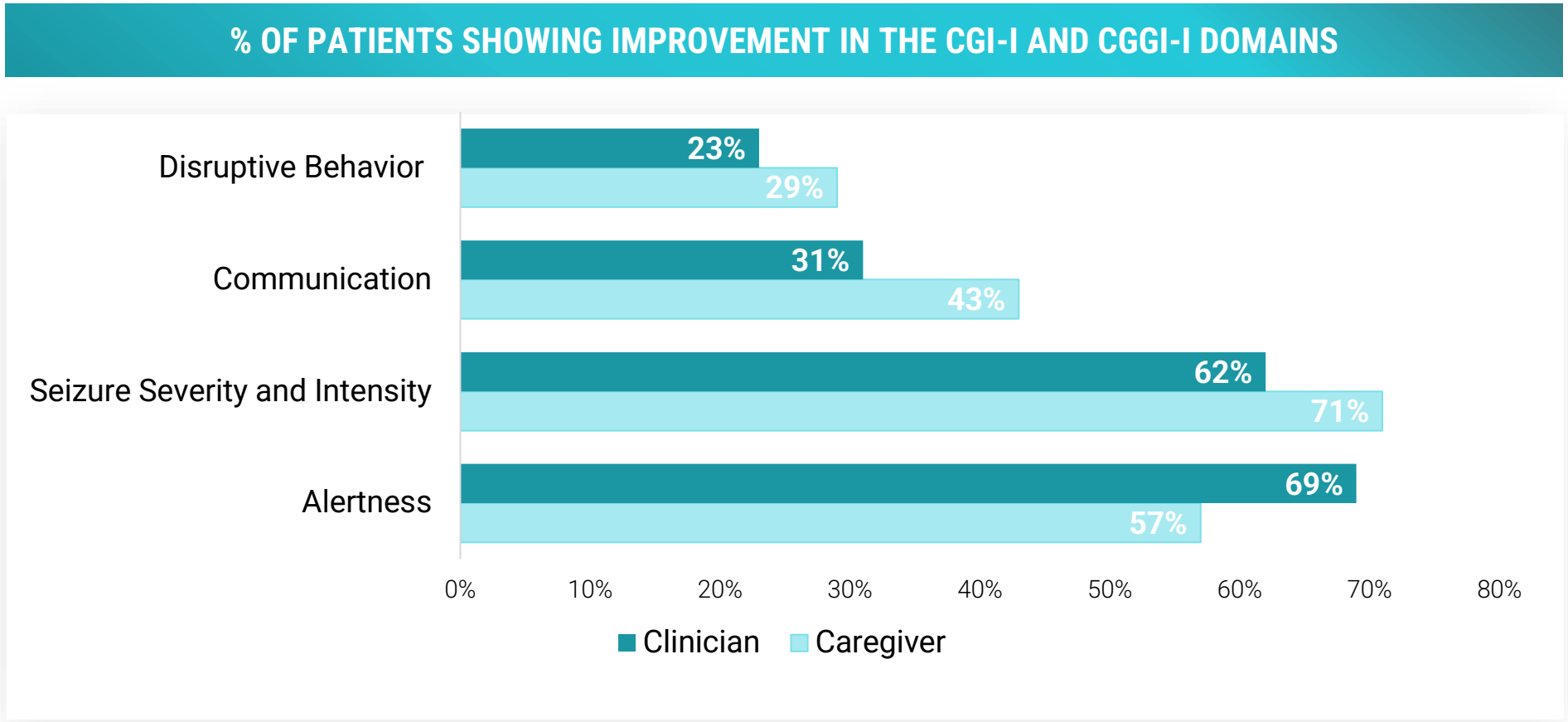
EMBOLD Cohort 1 results: sustained seizure-free periods reflect both clinical and daily life improvements



EMBOLD

*Inclusive of open-label extension period at data cutoff as of April 24, 2025
Praxis Data on File

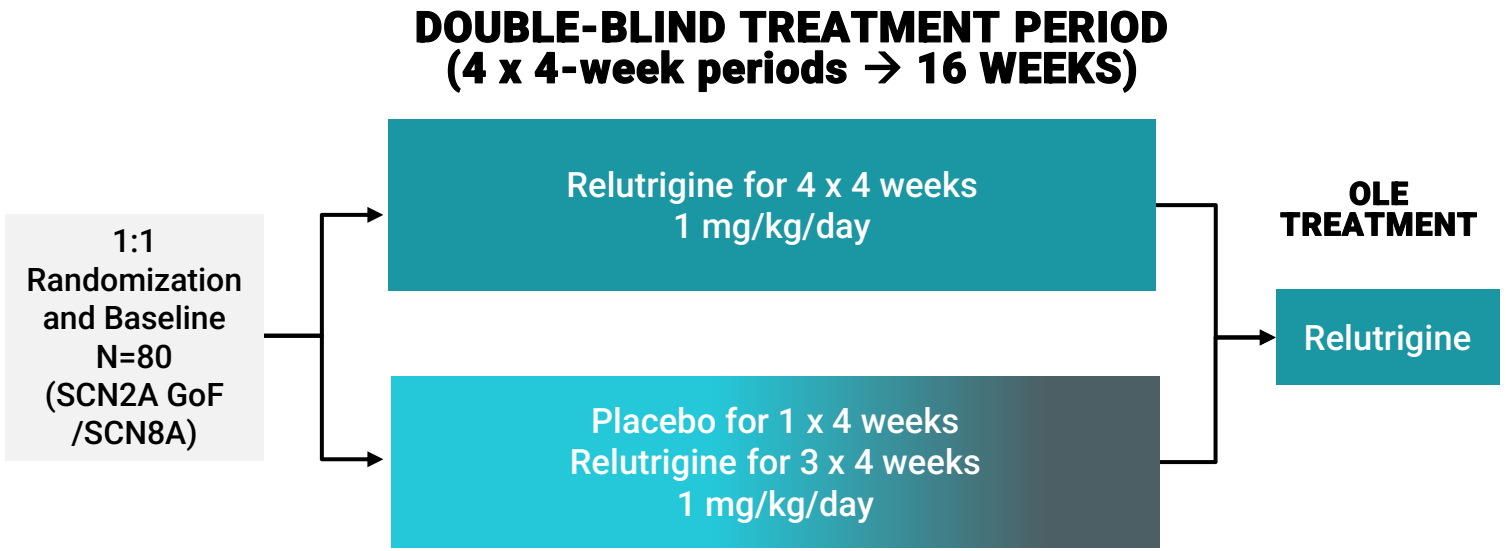
EMBOLD Cohort 1 results: relutrigine demonstrates disease modification with broad functional improvement



EMBOLD

Clinical Global Impression of Improvement (CGI-I) and Caregiver Global Impression of Improvement (CgGI-I) assessed at Week-16 visit

EMBOLD Cohort 2 is designed as a pivotal study to confirm relutrigine's efficacy



KEY ENDPOINTS:

- Change from baseline in monthly motor seizure frequency
- Length of seizure freedom achieved over a 28-day period
- Incidence and severity of treatment-emergent adverse events
- Clinical and Caregiver Global Impression of Improvement and Severity

EMBOLD

ClinicalTrials.gov Identifier: NCT05818553.
ASM=anti-seizure medication, QD=daily

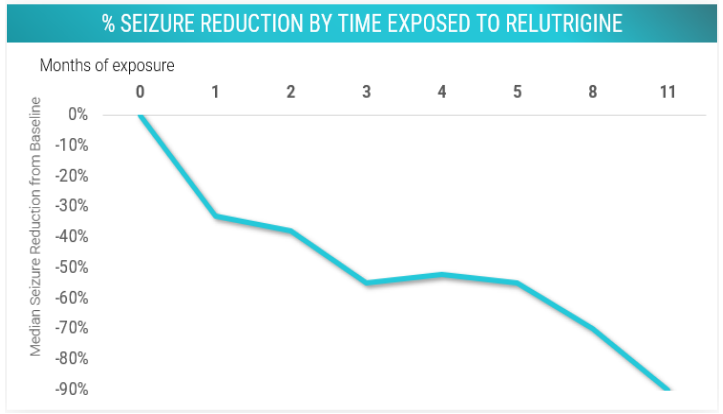
Relutrigine's clinical profile expanding with EMERALD study

Broad biologic rationale

DEE Model	Relutrigine and Analogs
Scn2a^{R1882Q}	
Scn2a^{Q54}	
Scn8a$^{N1768D/+}$	
Scn1a$^{+/-}$ Dravet	
scn1Lab (fish) Dravet	
Kcnh1^{R357Q}	
Kcnc1$^{R320H/+}$	
Kcnq2$^{K556E/+}$	
Kcna1$^{T401I/+}$	
Hcn1$^{M294L/+}$	

1. Effect in 2A/8A driven epilepsy models
2. Effect in Dravet (SCN1A) epilepsy models
3. Effect in non-sodium channel epilepsy models

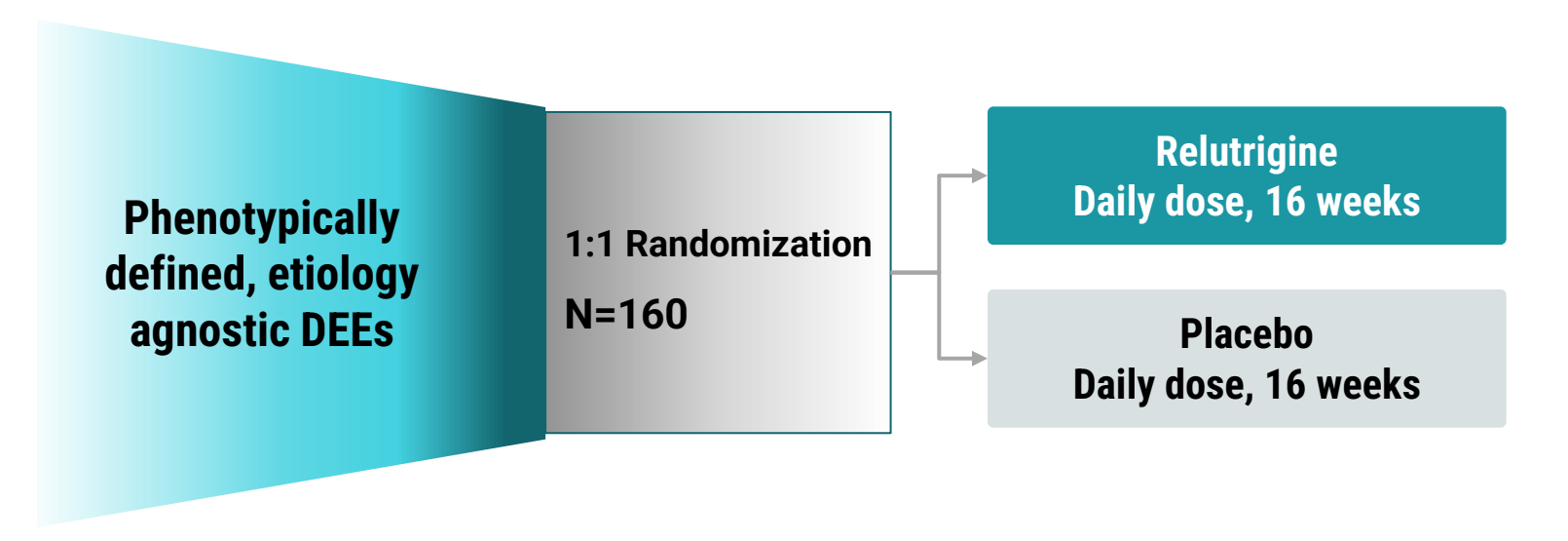
Clinical proof of concept data



Large, unmet need

EMERALD

EMERALD targets phenotypic DEEs regardless of etiology



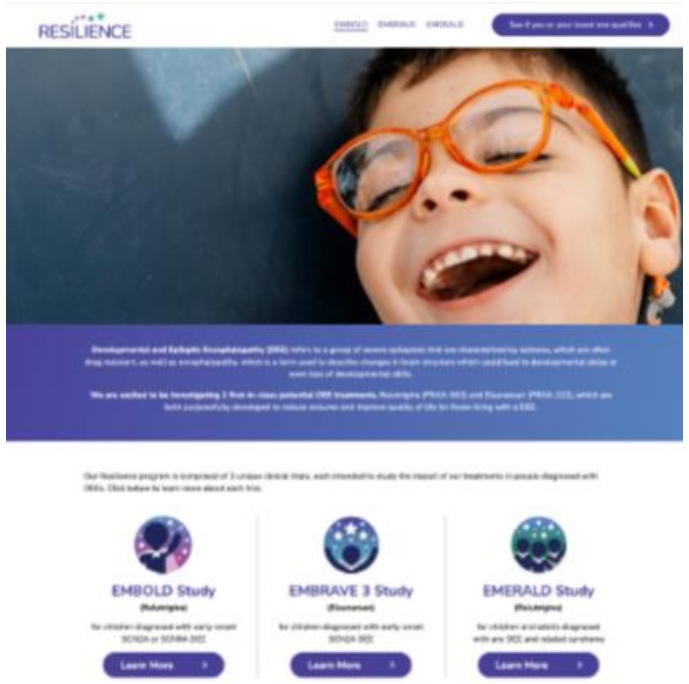
Primary endpoint: Change from baseline in monthly motor seizure frequency

- No titration period
- Once-daily, oral-dose

Key Inclusion Criteria
• Ages ≥2 and ≤65 years • Has a documented diagnosis of a developmental and epileptic encephalopathy in childhood • Has 4 or more countable motor seizures during the 28-day observation period
Treatment
• Relutrigine or matching placebo 1mg/kg/day. At day 35, the dose may be escalated to 1.5 mg/kg/day

EMERALD global footprint enabling efficient trial execution

A single online portal for all DEE studies



- Solidus platform
  - Elsunersen clinical program and commercial potential
  - ASO Pipeline: PRAX 80, 90, 100

SOLIDUS platform delivers genetically targeted therapies

SOLIDUS™

ANTISENSE OLIGONUCLEOTIDE (ASO) PLATFORM

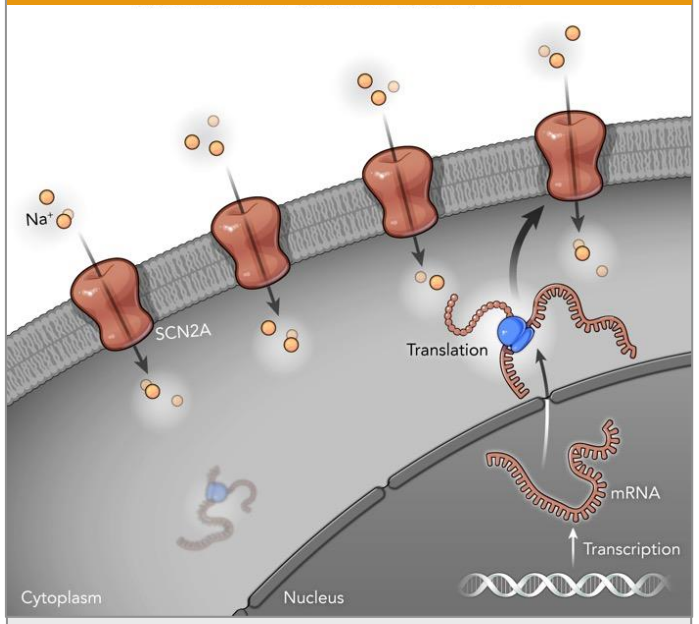
Solidus™ is an efficient, targeted precision medicine discovery and development engine for ASOs anchored on proprietary, computational methodology

Molecule	Indication	Mechanism
elsunersen **	SCN2A GoF	Gapmer ASO
PRAX-080	PCDH19 Mosaic expression	Gapmer ASO
PRAX-090	SYNGAP1 LoF	Splice switching ASO
PRAX-100	SCN2A LoF	Undisclosed mechanism ASO

** Elsunersen has received Orphan Drug Designation (ODD) and Rare Pediatric Disease (RPD) designation from the FDA, and ODD and PRIME designations from the EMA for the treatment of SCN2A GoF
GoF=gain-of-function, LoF=loss-of-function, PRIME=Priority Medicines

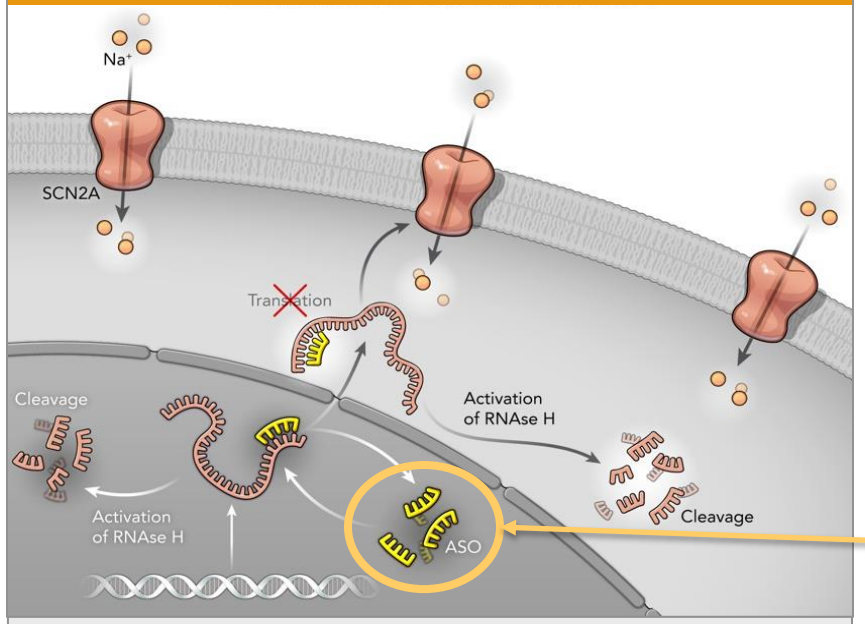
Precision targeting of SCN2A GoF patients positions elsunersen as a potential disease-modifying therapy

DISEASE STATE: EXCESSIVE SCN2A ACTIVITY



- SCN2A mutation leads to hyperactive $Na_V1.2$ sodium channels
- Hyperactive channels leads to an increased ion flow leading to seizure

ASO TREATED: NORMALIZED SCN2A ACTIVITY



elsunersen

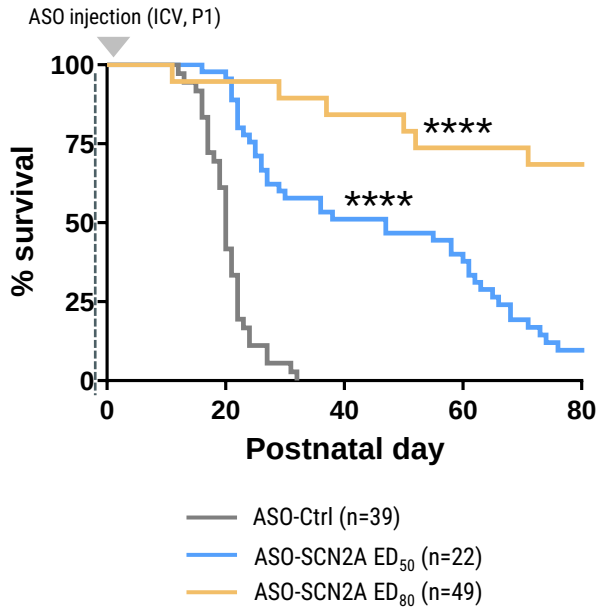
- Elsunersen selectively interacts with SCN2A mRNA causing RNase H1 mediated degradation
- The number of SCN2A sodium channels is reduced, which normalizes ion flow and reduces seizure activity

ASO=antisense oligonucleotide, DEE=developmental & epileptic encephalopathy, Na_V=voltage-gated sodium channel

Elsunersen extends survival of SCN2A GoF mice even when treatment begins well after disease onset

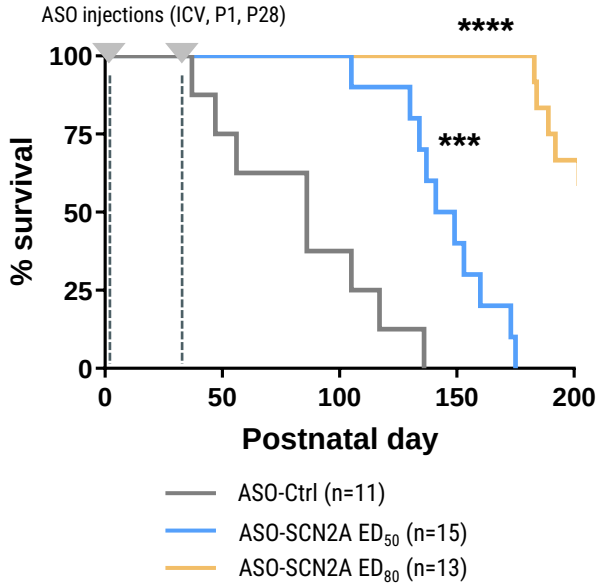
SCN2A ASO INCREASES SURVIVAL WITH A SINGLE DOSE INJECTION

SCN2A GoF model



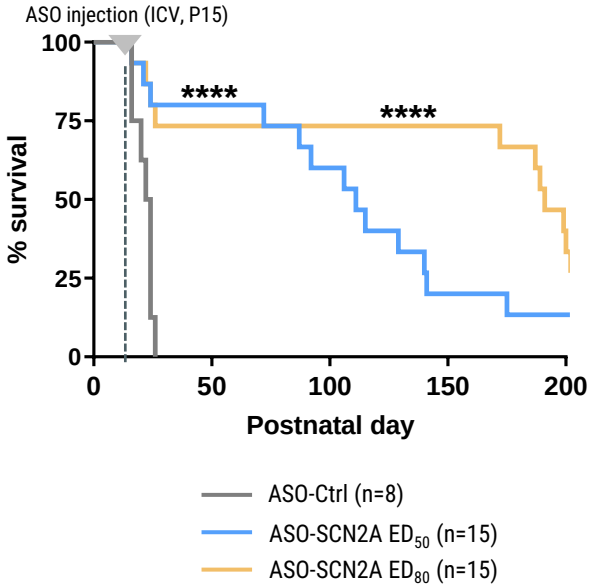
RE-DOSING SIGNIFICANTLY EXTENDS SURVIVAL

SCN2A GoF model



ADMINISTRATION POST-DISEASE ONSET ALSO EXTENDS SURVIVAL

SCN2A GoF model



***p<0.001; ****p<0.0001
All experiments conducted with SCN2A R1882Q mouse model
ASO=antisense oligonucleotide, Ctrl=control, ED_{50}=median effective dose, GoF=gain-of-function, ICV=Intracerebroventricular

Elsunersen is the first drug designed for SCN2A GoF DEE

ELSUNERSEN

SCN2A GoF

INTRATHECAL

ANTISENSE OLIGONUCLEOTIDE (ASO)

Designed to selectively decrease SCN2A gene expression

Significant reduction in seizures achieved in SCN2A GoF patients

No adverse events related to the study were considered treatment-emergent or serious

Orphan Drug Designation (ODD) and Rare Pediatric Disease (RPD) designation from the FDA, and ODD and PRIME designations from the EMA

DEE=developmental & epileptic encephalopathy, GoF=gain-of-function, PRIME= Priority Medicines

The EMBRAVE program: clinical development path for elsunersen in SCN2A GoF DEE

EMBRAVE Part 1

- Early open-label study (n=4)
- Demonstrated seizure reduction and increased seizure-free days
- No treatment-related adverse events

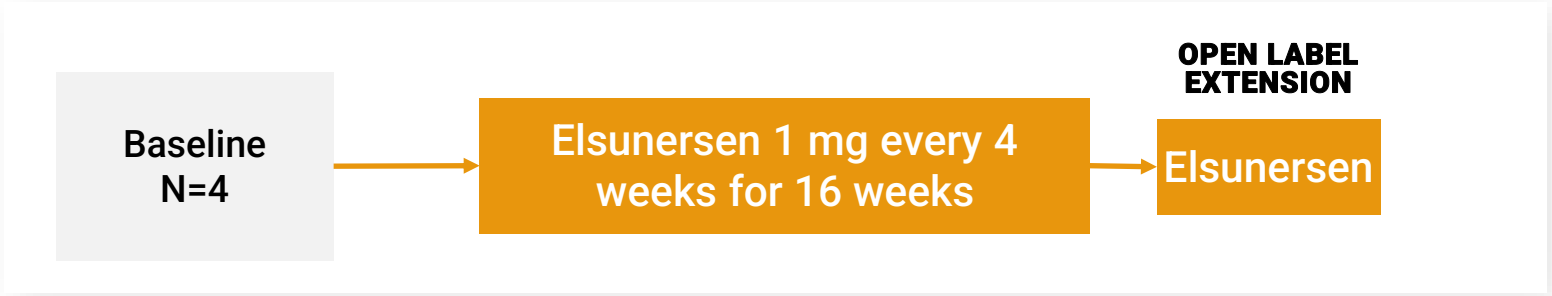
EMBRAVE Part A

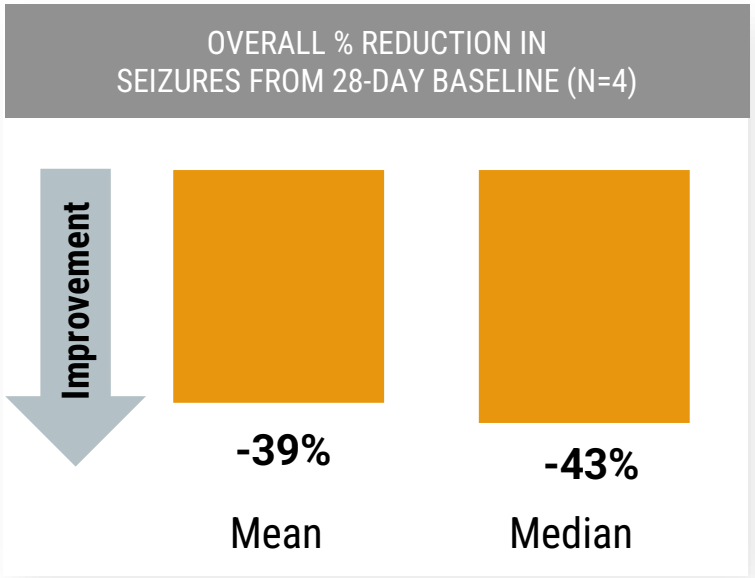
- Ongoing dose-escalation study (n=8-16, ages >2–18)
- 3:1 randomization to active vs. sham
- Evaluates safety and tolerability up to 8 mg
- Supports registration

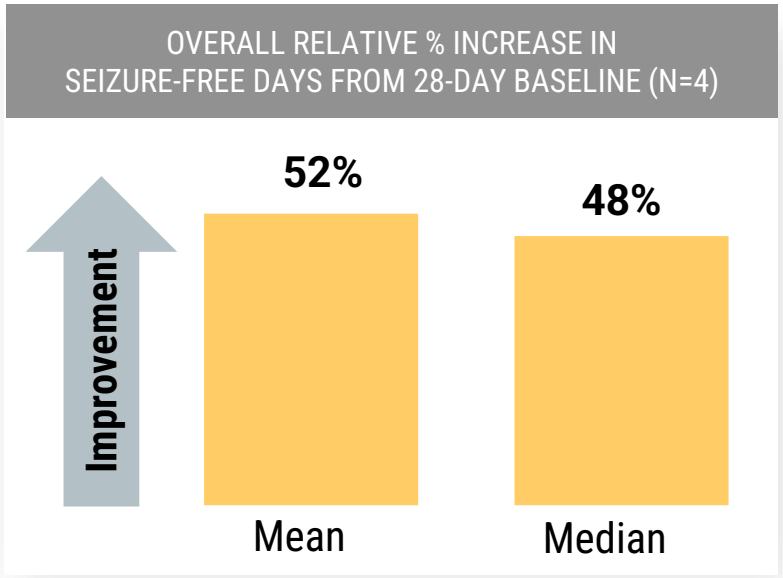
EMBRAVE3 *(registrational trial)*

- Cohort 1: Ages >2–18, randomized and sham-controlled
- Cohorts 2 & 3: Ages 1–2 and 0–1, open-label
- Primary endpoint: Change in motor seizure frequency
- Cohort 1 supports registration and cohorts 2 & 3 support label expansion from birth

EMBRAVE Part 1 showed clinically meaningful seizure reduction in SCN2A GoF patients







KEY ENDPOINTS:

- Incidence and severity of treatment-emergent adverse events
- Change from baseline in monthly motor seizure frequency

SAFETY:

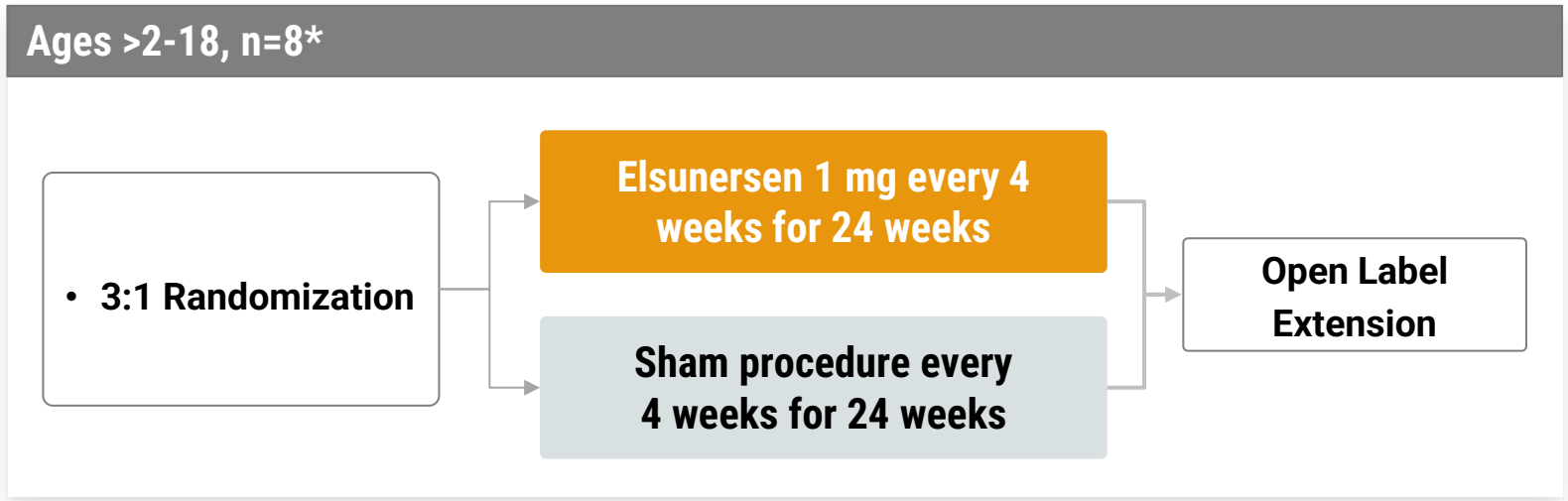
- No TEAEs or SAEs considered related to study drug
- All TEAEs recovered/resolved

EMBRAVE

Frizzo S, et al. EEC 2024, Praxis data on file. , U.S. National Library of Medicine. Study of PRAX-222 in Pediatric Participants With SCN2A Developmental and Epileptic Encephalopathy (EMBRAVE). ClinicalTrials.gov Identifier: NCT05127564.

GoF=gain-of-function, SAE=serious adverse event

Ongoing EMBRAVE Part A supports registrational package



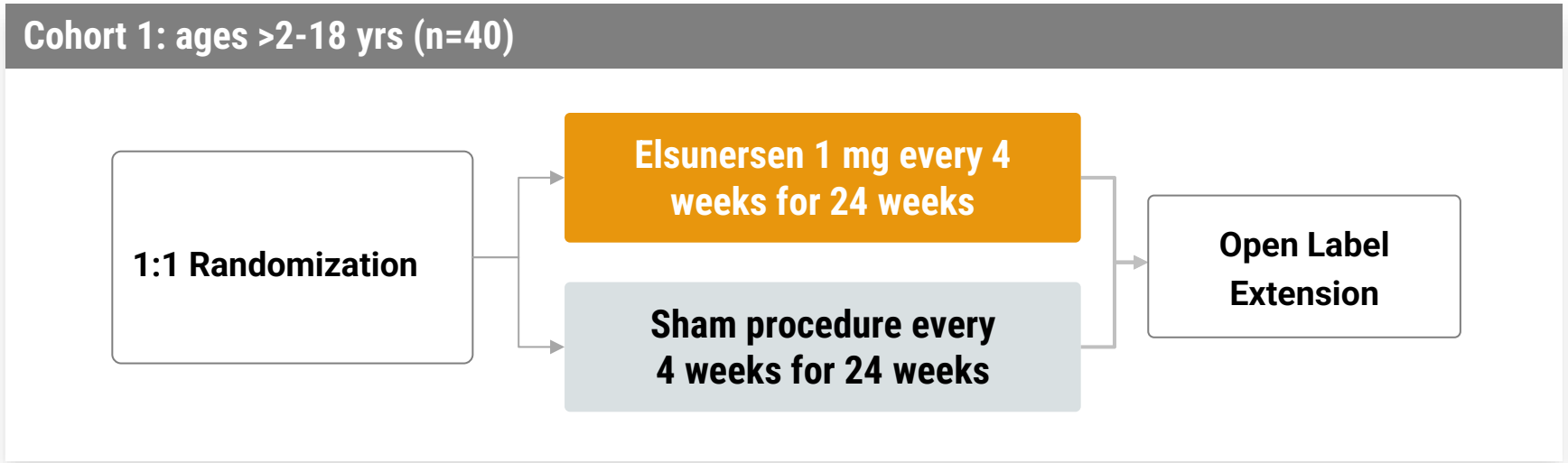
- **Starting dose of 1 mg with optional dose escalation up to 8 mg based on individual tolerability at each dose**
- **Enrollment expected to complete by mid-year**

Key Inclusion criteria
• Documented SCN2A GoF variant with seizures prior to 3 months of age • Between the ages of 2 to ≤18 years at Screening • Seizure frequency of 8 or more countable motor seizures per 28-day during Baseline
Primary Endpoint
• Median percent change in monthly motor seizure frequency from baseline

EMBRAVE

*option to increase to n=16

EMBRAVE3 registrational trial

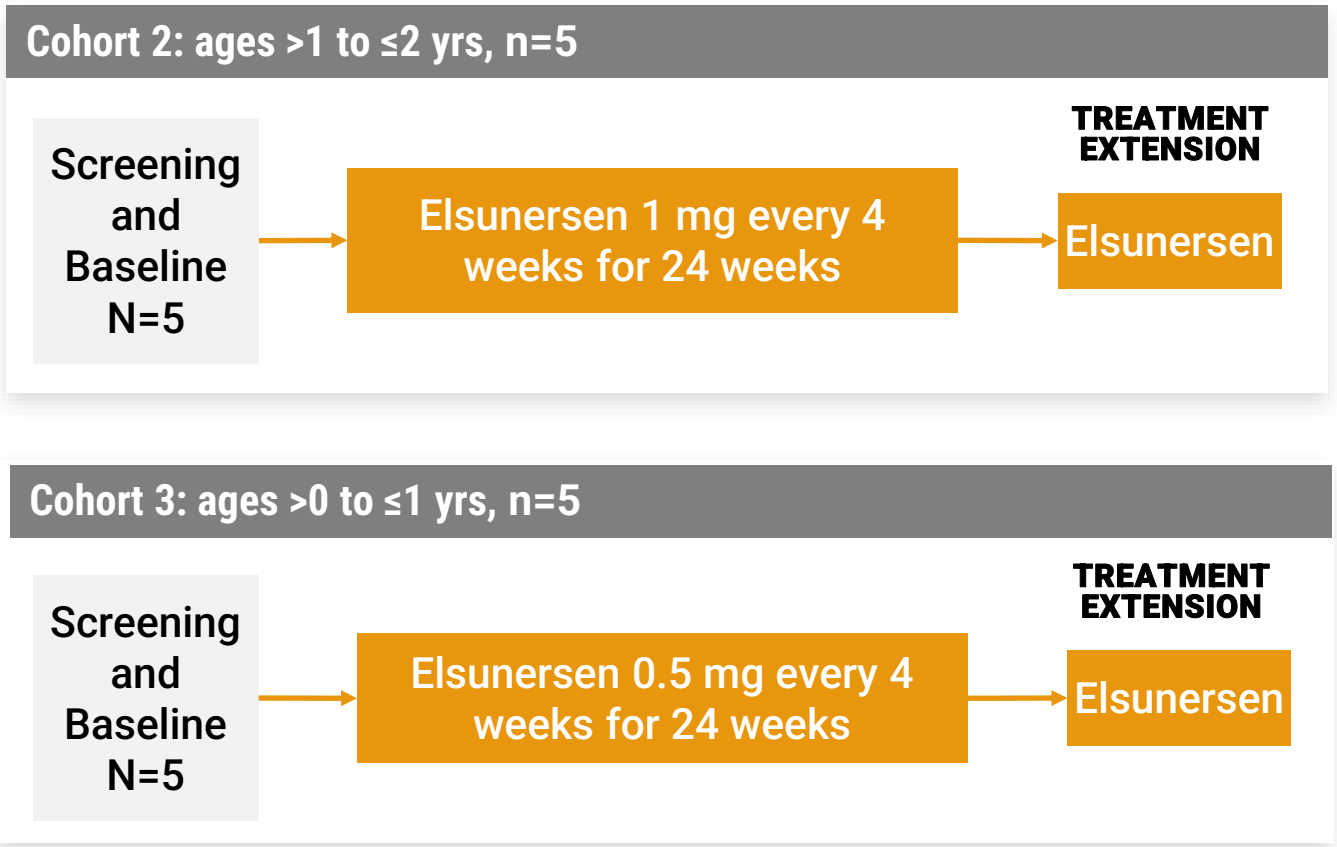


Key Inclusion Criteria
• Documented SCN2A GoF variant with seizures prior to 3 months of age • Between the ages of 0 to ≤18 years at Screening (ages 2-18 go to Cohort 1, 1-2 to Cohort 2, 0-1 to Cohort 3) • Seizure frequency of 4 or more countable motor seizures per 28-day during Baseline
Primary Endpoint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

EMBRAVE③

GoF=gain-of-function

Extending treatment to birth: systematic age-based coverage in EMBRAVE3



- Cohort 1 results will support registration
- Cohort 2 and 3 will allow for label expansion to patients at birth
- Same inclusion criteria and endpoints as Cohort 1

EMBRAVE③

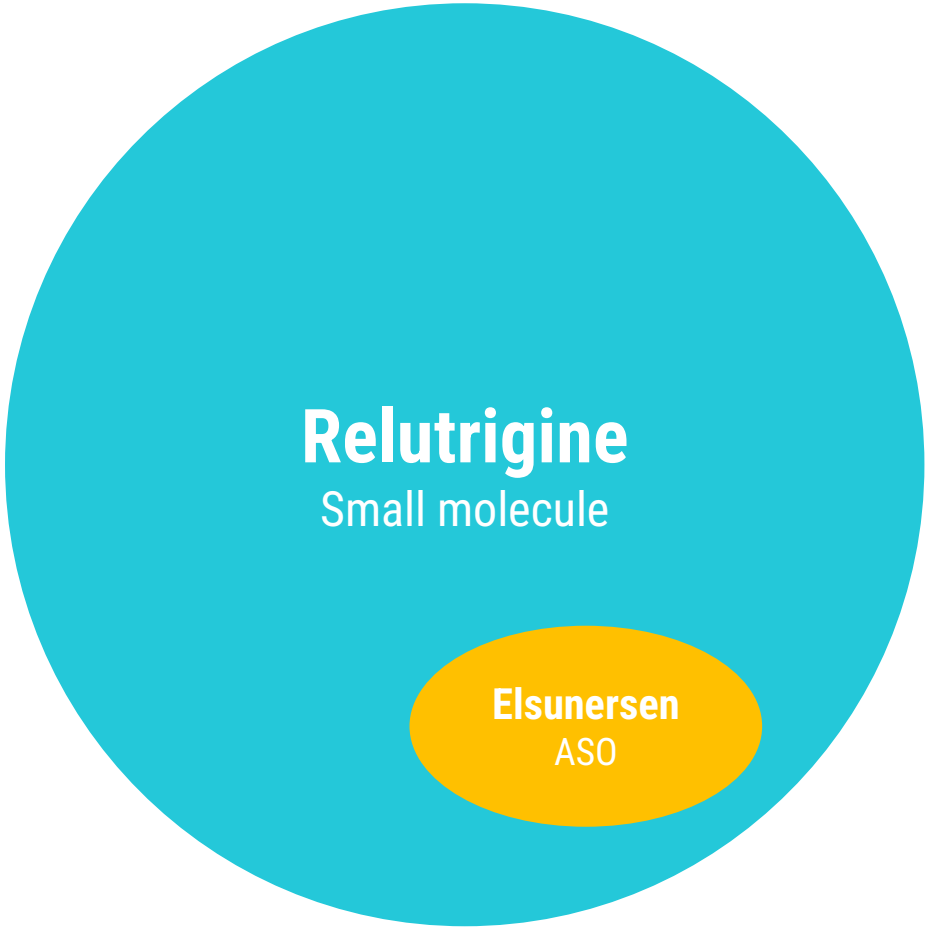
GoF=gain-of-function

Complementary development of elsunersen and relutrigine targeting both the genetic driver and downstream network dysfunction in SCN2A GoF

Elsunersen targets root genetic cause of disease

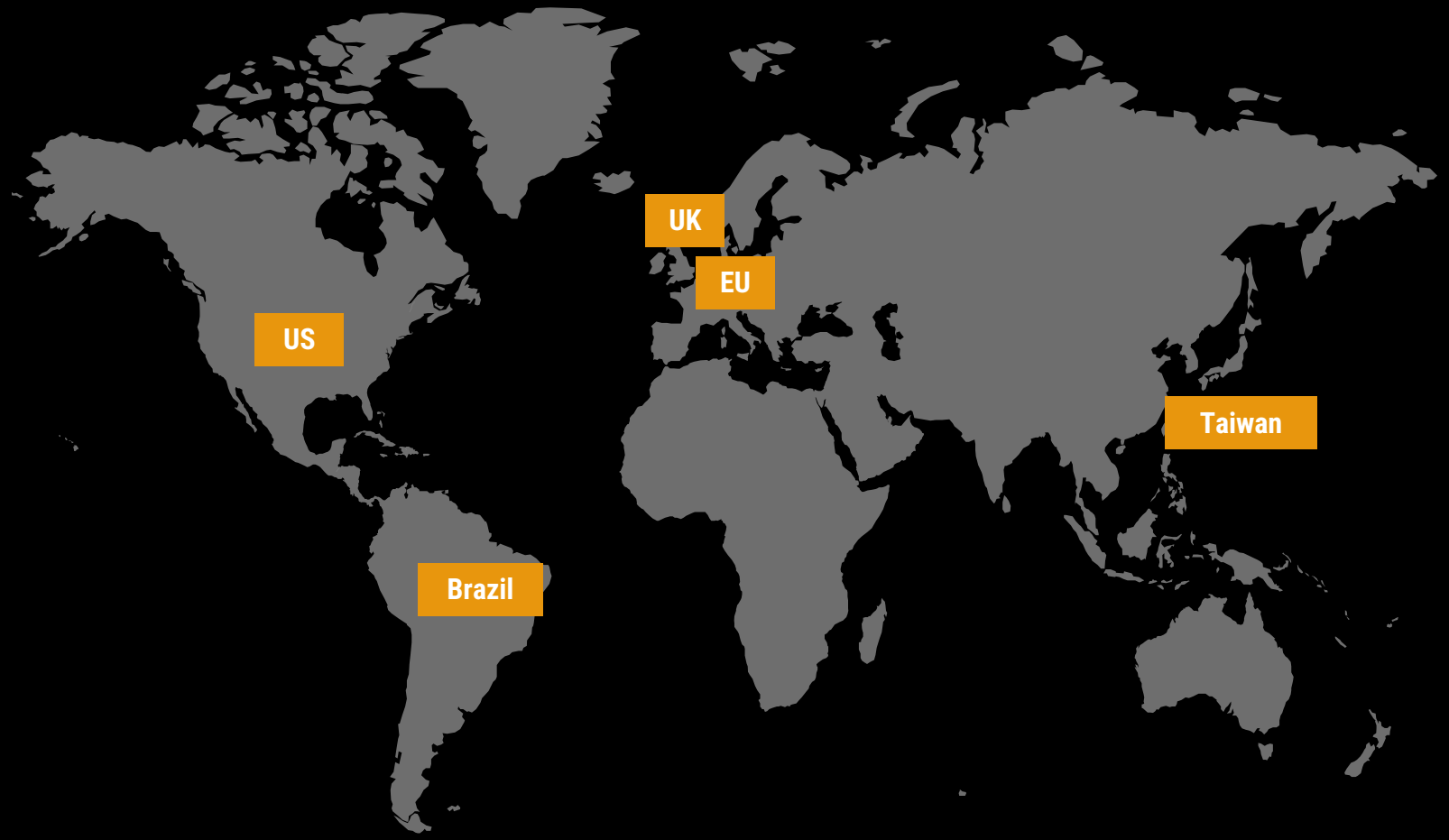
Relutrigine targets residual network hyperexcitability

Relutrigine expected to complement other genetically focused DEE therapies, e.g. PRAX 80, 90

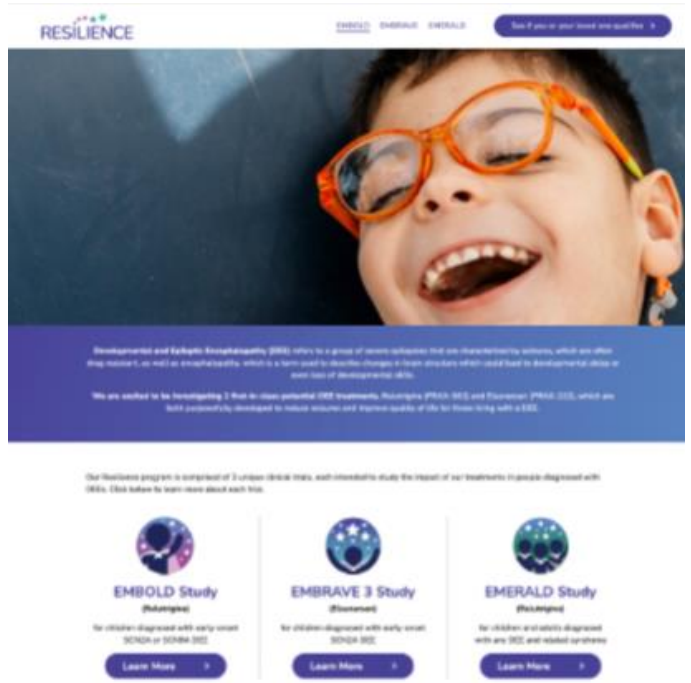


DEE=developmental & epileptic encephalopathy, GoF=gain-of-function

Rapid global expansion ensures efficient execution



A single online portal for all DEE studies



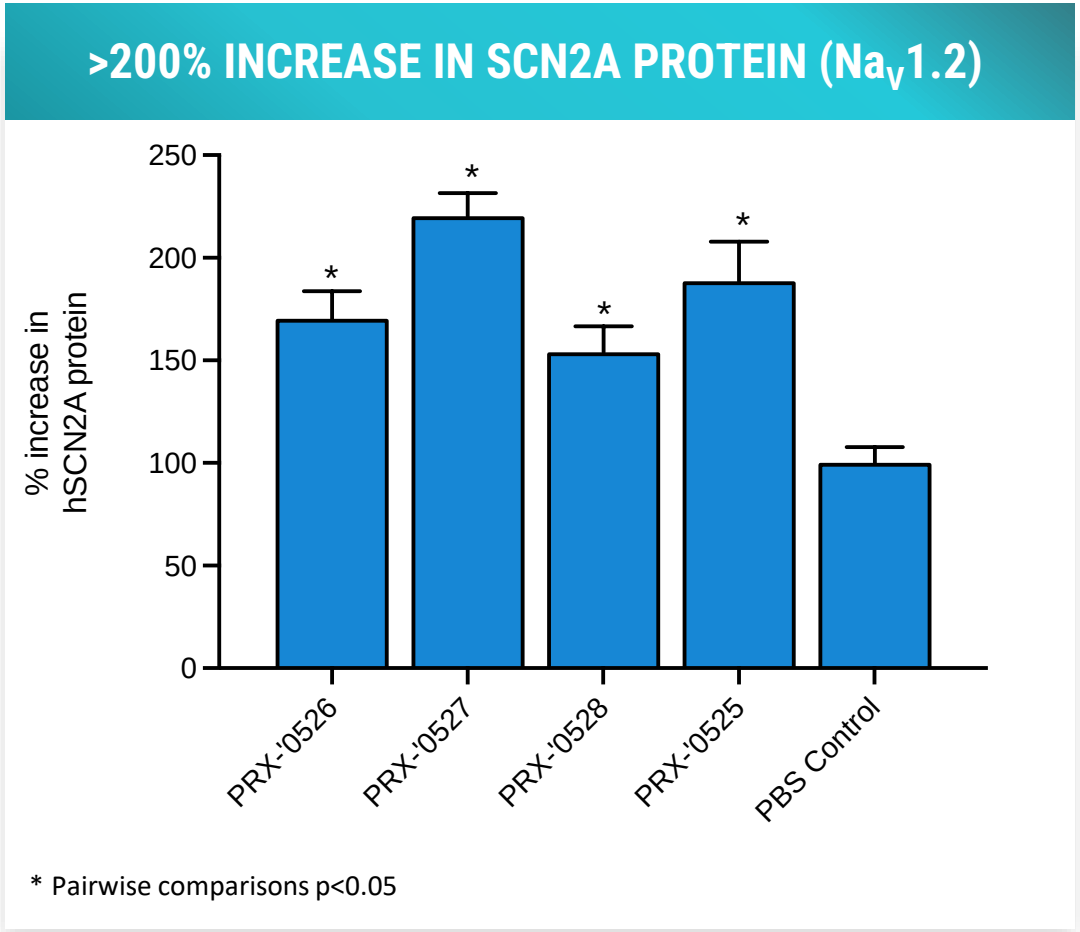
- ASO Pipeline: PRAX 80, 90, 100

Solidus pre-clinical portfolio on-track for clinical trials in 2026

	PRAX-80	PRAX-90	PRAX-100
Indication	*PCDH19* Clustering Epilepsy: X-linked mosaic expression disorder with early-onset clustered seizures and cognitive impairment	*SYNGAP1* DEEs: Leading genetic cause of severe intellectual disability and early-onset epilepsy caused by LoF variants	*SCN2A* Haploinsufficient Autism: A neuro-developmental disorder caused by *SCN2A* LoF variants with early-onset autism
Target	*PCDH19*	*SYNGAP1*	*SCN2A*
Mechanism	Gapmer ASO-mediated *PCDH19* silencing, informed by the benign phenotype of null-expressing carrier males	ASO-mediated upregulation of *SYNGAP1* protein expression	ASO-mediated upregulation of *SCN2A* protein expression
Program Update	Candidate declaration by year end	Candidate declaration by year end	Candidate declaration by mid-year

ASO=antisense oligonucleotide, DEE=developmental and epileptic encephalopathy, LoF=loss-of-function

PRAX-100 achieves >200% $Na_V1.2$ restoration in *SCN2A* humanized model



- **Transgene encoded human SCN2A protein increase at 4 weeks following administration of 4 candidate upregulating ASOs**
- **Mechanism based E_{max} should limit overexpression liability**
- **Candidate ASO to be nominated mid-year based on tolerability, efficacy and durability**

Data are shown for human SCN2A protein in brain from humanized mice at 4 weeks post 500ug ICV dose of ASO. Results were obtained from LC/MS with a unique heavy peptide as an internal standard, and data are expressed relative to PBS injected control animals and normalized to the geometric means of housekeeper proteins and shown as mean and SEM.

ASO=antisense oligonucleotide, ICV=intracebroventricular, LC/MS=liquid chromatography–mass spectrometry, LoF=loss-of-function, PBS=phosphate-buffered solution

- Conclusion and Q&A

An exciting period for the DEE community & Praxis

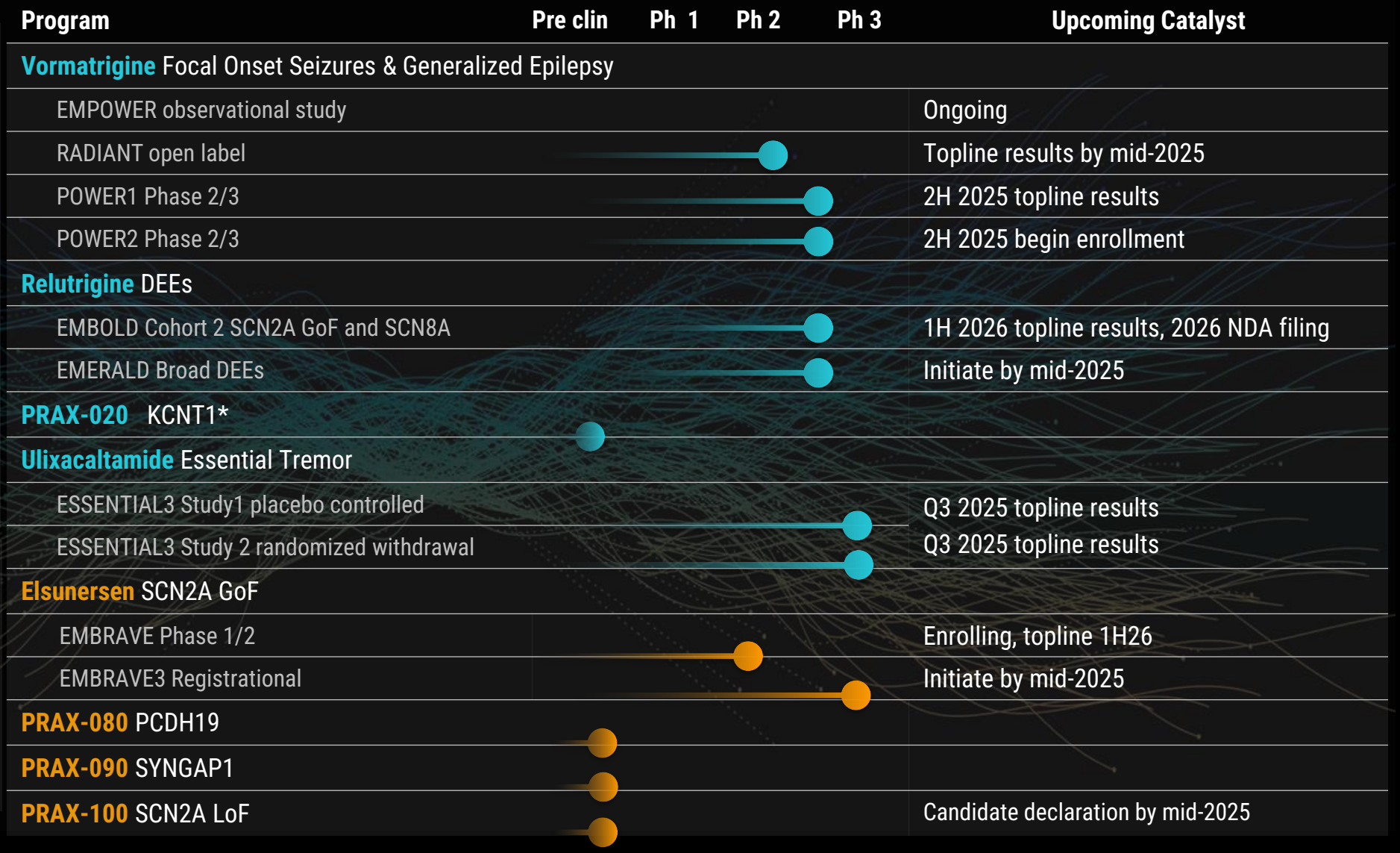
- **Praxis DEE portfolio aims to revolutionize the treatment for an underserved and large population**
  - **Relutrigine's EMERALD study targets the entire DEE population with an improved sodium channel approach to reduce seizures**
  - **Elsunersen and EMBRAVE3 target disease modifying impact for SCN2A GoF patients**
  - **Multi-billion peak revenue potential**
- **Long IP protection across the portfolio**
- **Numerous significant catalysts in the Praxis portfolio**

DEE=developmental & epileptic encephalopathy, GoF=gain-of-function

Praxis pipeline and upcoming catalysts

CEREBRUM™
SMALL MOLECULE PLATFORM

SOLIDUS™
ASO PLATFORM



*PRAX-020 (KCNT1) has been licensed to UCB
DEE=developmental & epileptic encephalopathy, GoF=gain-of-function, LoF=loss-of-function


PRAXIS
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