PRAXIS

PRAXIS

DARE FOR MORE®

Corporate Overview

February 2026

Forward Looking Statements

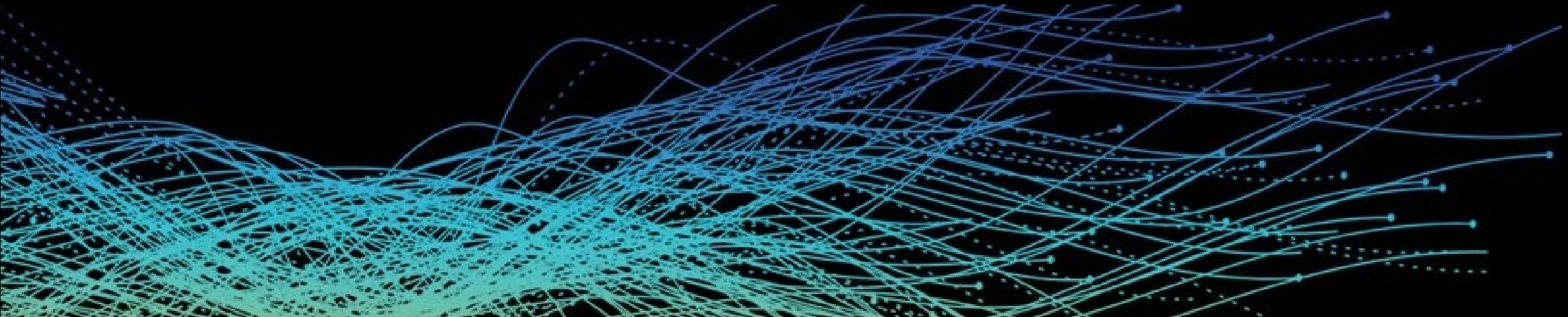
This presentation may contain “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial conditions, including but not limited to express or implied statements regarding the current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, , including 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 and as updated in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2025, as well as other filings made with the Securities and Exchange Commission .

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.



2025 Success is Poised to Continue over the Next 24 Months

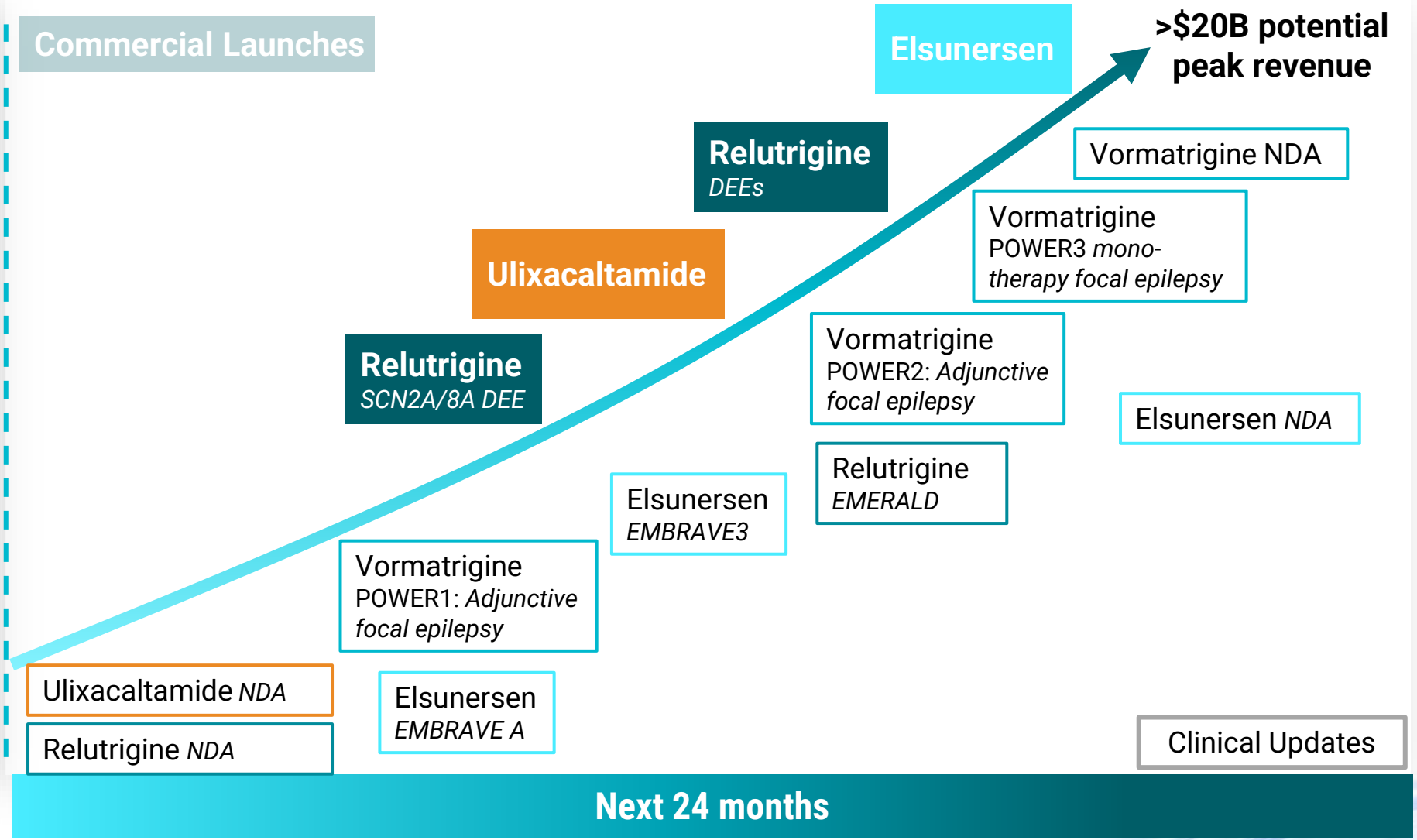
Portfolio Highlights

Ulixacaltamide
- Positive Essential3 Study1 and Study2
- Received Breakthrough Therapy Designation (BTD)

Relutrigine
- Received BTD
- Positive EMBOLD readout

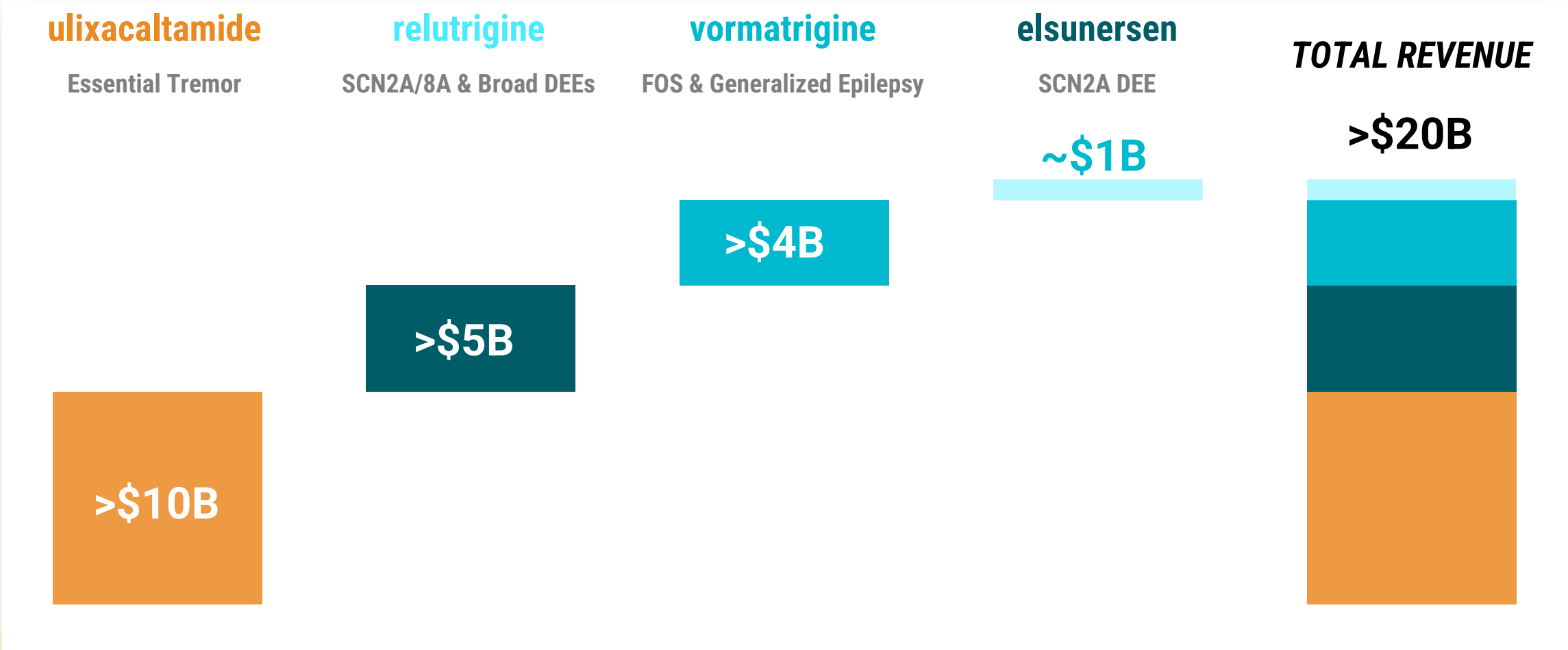
Vormatrigine
- RADIANT positive in 2 cohorts
- Vormatrigine POWER1 recruitment completed

Elsunersen
- FDA meeting approved streamlined study design



Praxis is Set to Capitalize on Late-Stage Portfolio

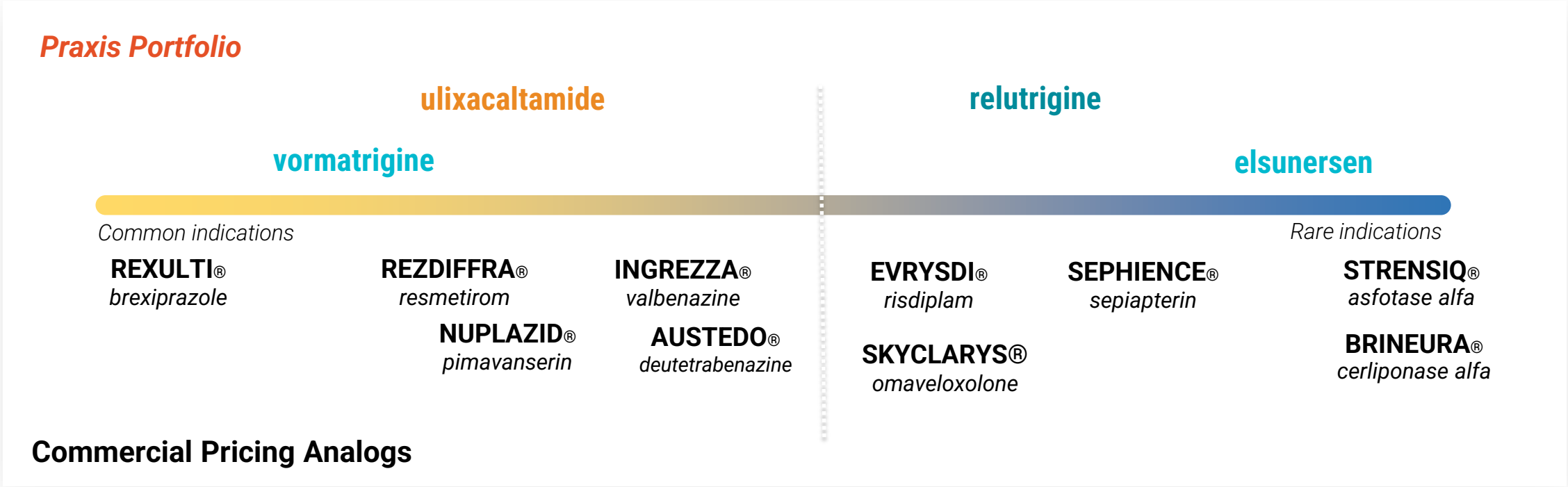
Holding Over $20bn in Commercial Potential



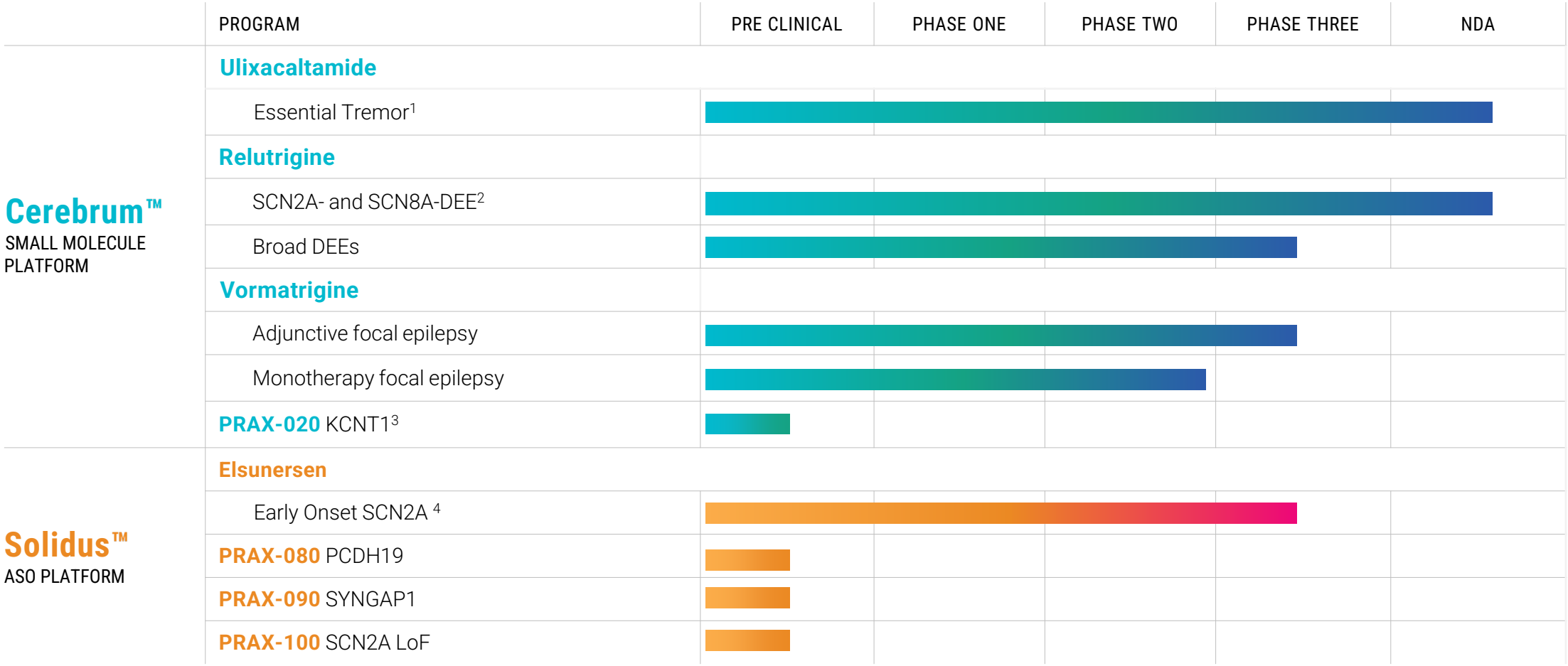
Pricing for recent approvals reflects significant value to patients

Praxis portfolio poised for similar impact

- High unmet-need indications with few, if any, effective treatment modalities
- Significant price potential within current market analogs

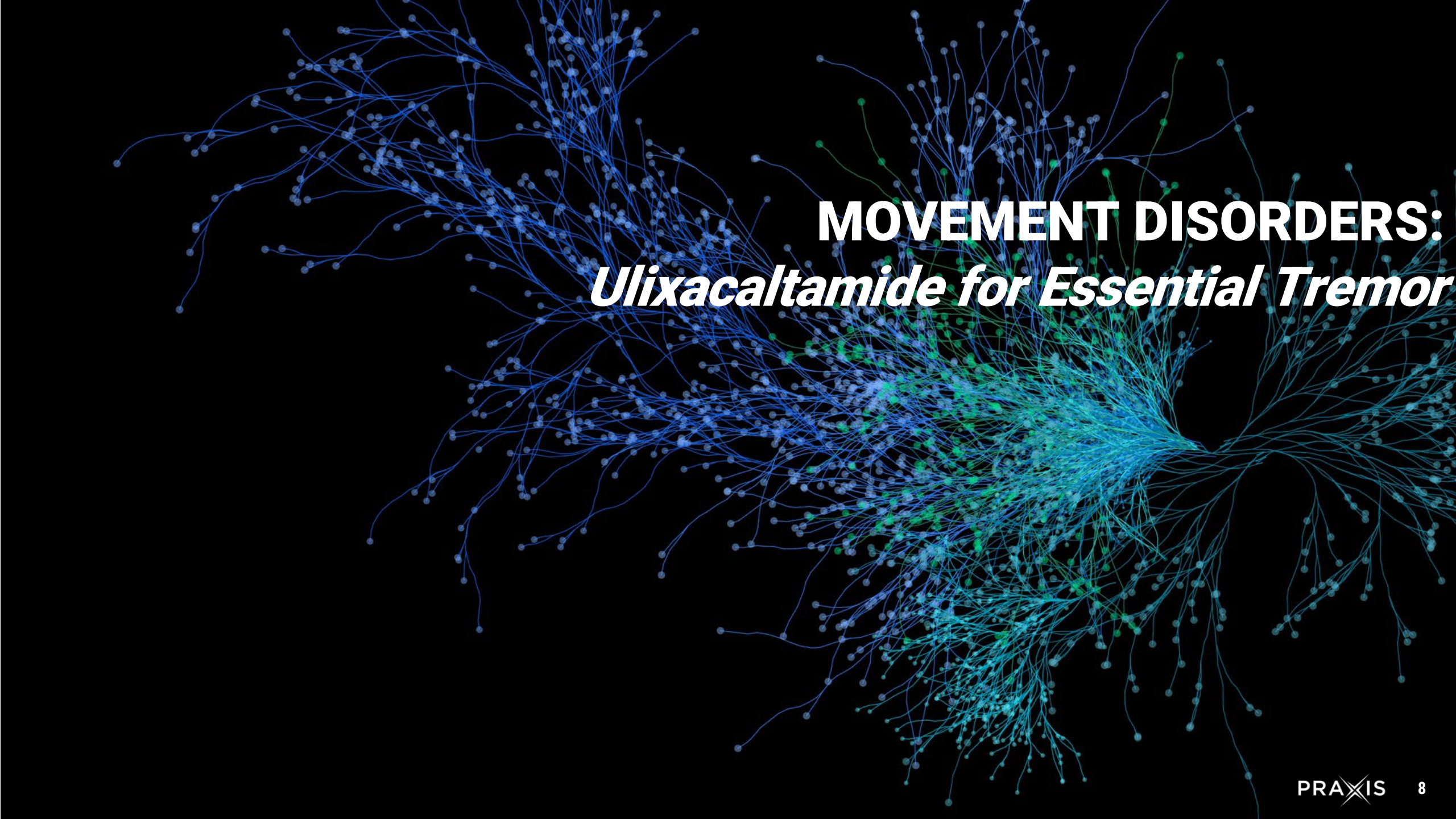


Praxis comprehensive CNS pipeline



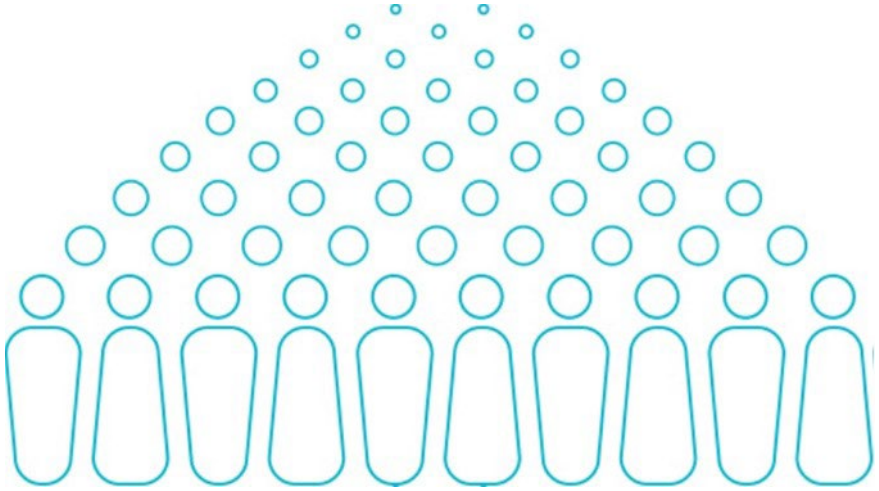
1. Ulixacaltamide has received Breakthrough Therapy Designation
2. Relutrigine has received Breakthrough Therapy Designation (BTD), Orphan Drug Designation (ODD) and Rare Pediatric Disease (RPD) designation from the FDA, and ODD from the European Medicines Agency (EMA) for the treatment of SCN2A and SCN8A-DEE and RPD designation for Dravet Syndrome
3. PRAX-020 (KCNT1) has been licensed to UCB
4. 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



MOVEMENT DISORDERS:
Ulixacaltamide for Essential Tremor

Essential Tremor: A Major Unmet Need



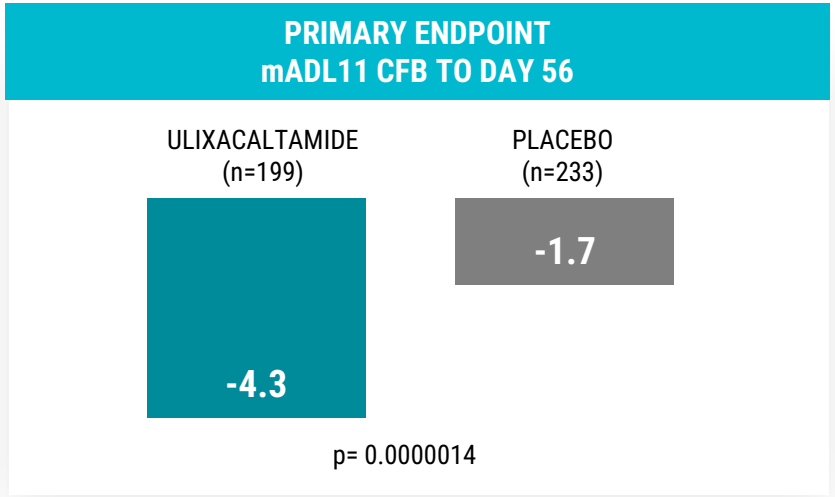
No ET-specific FDA-approved therapies

- An estimated **7 million people** in the U.S. live with ET
- Major functional impacts affecting writing, eating, drinking and social activities
- High psychosocial burden (frustration, anxiety, embarrassment, isolation)
- Significant proportion receive no or inadequate treatment

Essential3: Two Positive Phase 3 Studies Supporting Breakthrough Therapy Designation, NDA submitted

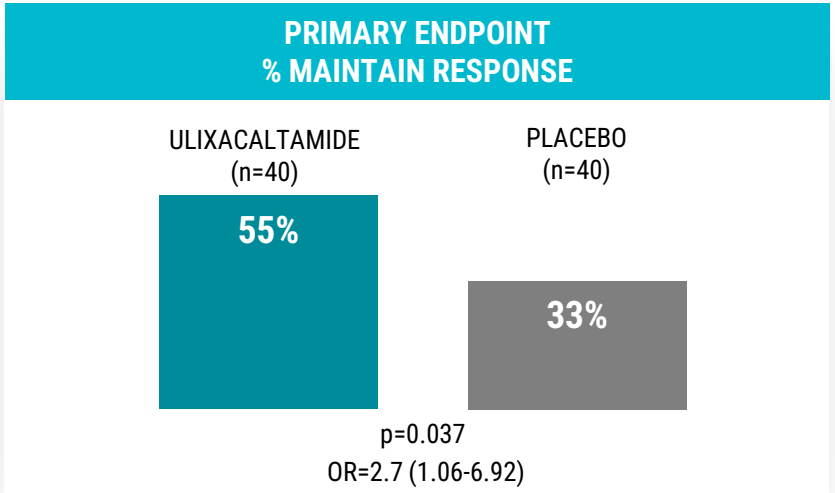
The first successful Phase 3 program for a drug in Essential Tremor

Study 1: 12-week Parallel-group Design (n=432)



- Effect as early as 2 weeks and maintained for 12-weeks
- Improvement in secondary endpoints rate of disease improvement, PGI-C and CGI-S for all timepoints
- Benefit for patients on background propranolol and other ET medications, with or without intention tremor and with or without family history of ET

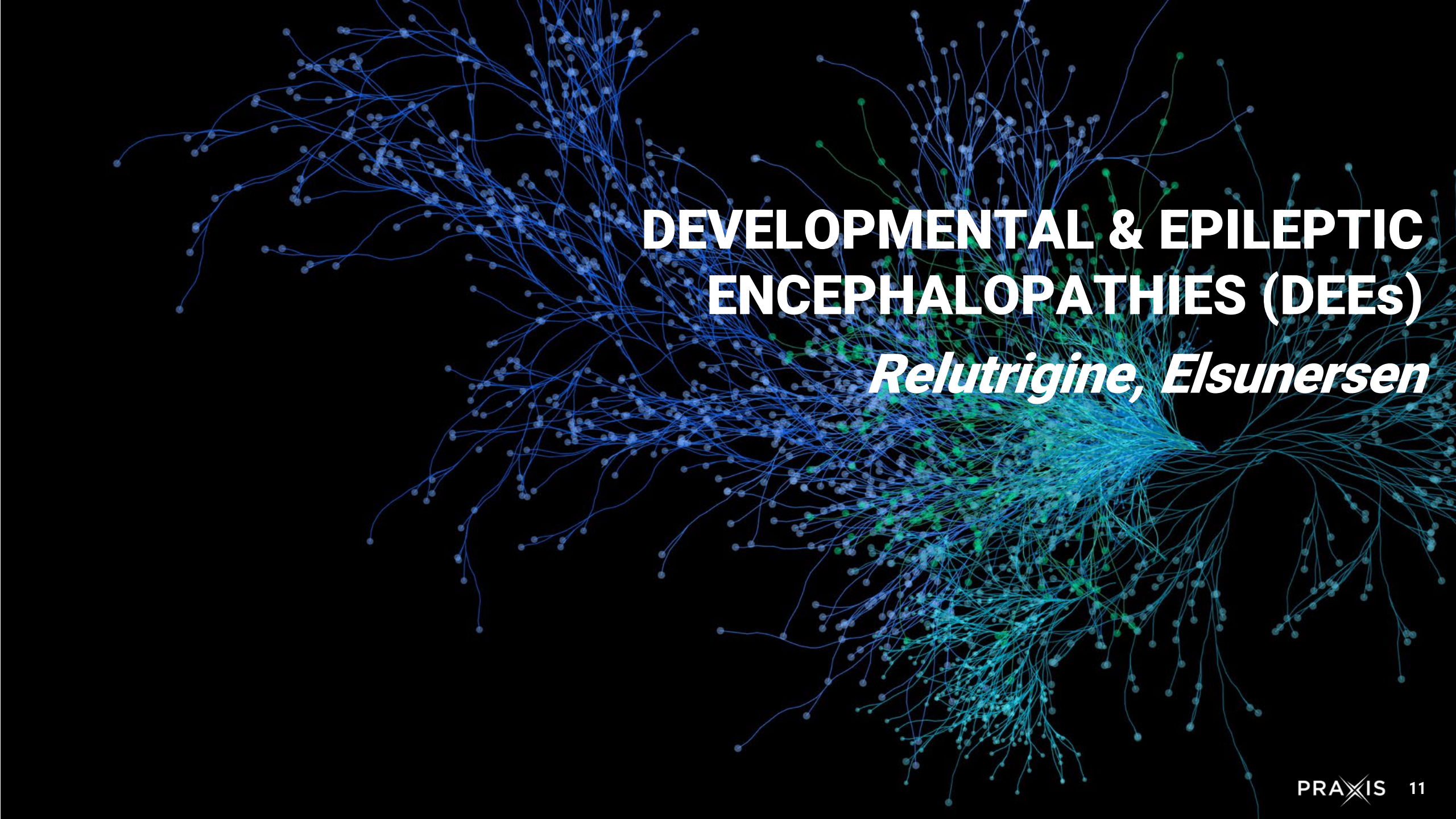
Study 2: Blinded Stable Responder, Randomized Withdrawal Design (n=80)



- Demonstrates maintenance of benefit
- Validates durability and robustness of response
- Reinforces functional benefit observed in Study 1

Favorable tolerability with no drug-related SAEs.
Majority of TEAEs were mild to moderate, occurred within 2 weeks of starting treatment and resolved quickly without intervention.

mADL11: modified score derived from items 1 to 11 of the TETRAS-Activities of Daily Living; **CFB**: Change from Baseline; **OR**: Odds Ratio; **TEAE**: Treatment Emergent Adverse Event



DEVELOPMENTAL & EPILEPTIC ENCEPHALOPATHIES (DEEs)

Relutrigine, Elsunersen

Relutrigine: Potential for class leading efficacy and tolerability

Relutrigine

Small molecule functional state modulator

No titration required

Once daily dosing

Liquid formulation - oral or G/J tube administration

Precision Mechanism:

Superior selectivity for hyperactive Na_V channels, a known driver of seizure activity across DEEs

Clinical Profile:

- Demonstrated robust seizure reduction and unprecedented seizure-free periods over 28-day intervals
- Generally well-tolerated with mostly mild to moderate AEs, no drug-related SAEs and no dose reductions required

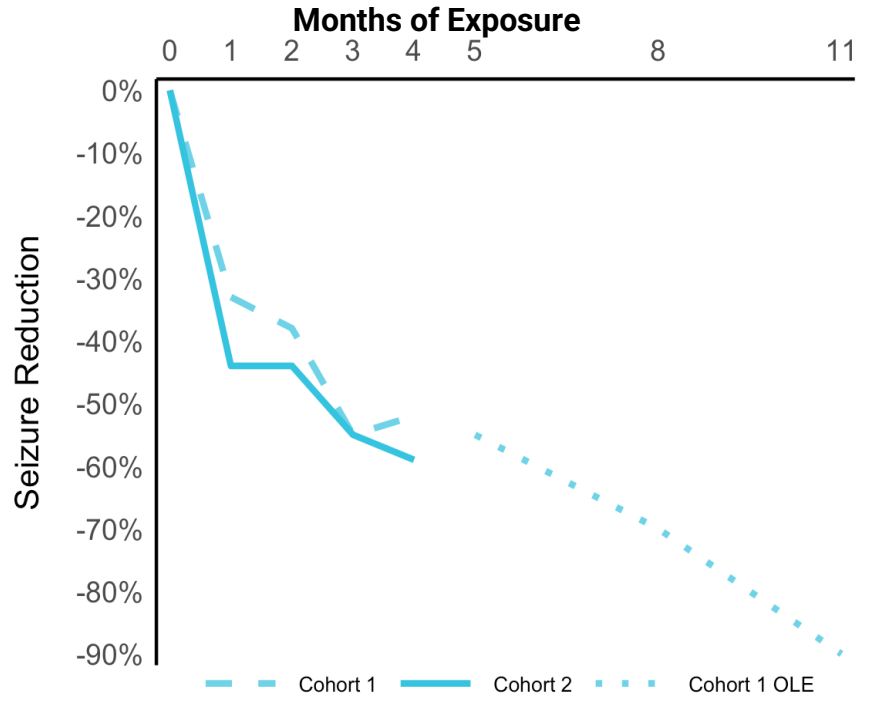
Regulatory Designations:

- FDA: Orphan Drug, Rare Pediatric Disease Designations for SCN2A DEE, SCN8A DEE, and Dravet syndrome, plus Breakthrough Therapy
- EMA: Orphan Drug Designations for SCN2A DEE and SCN8A DEE
- Submitted NDA to FDA

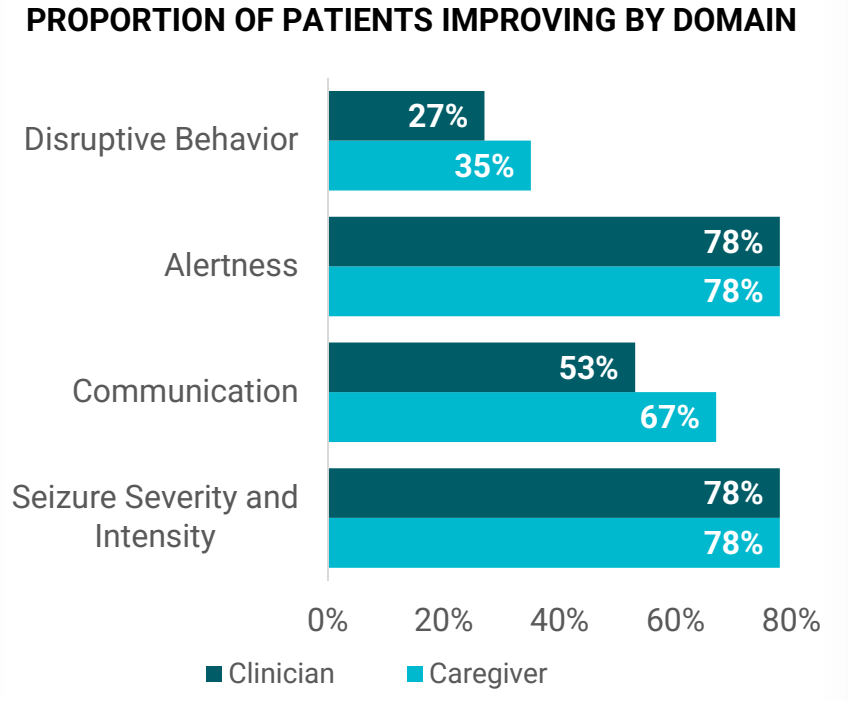
AE: adverse event, DEE: developmental & epileptic encephalopathy, NaV: voltage-gated sodium channel, SAE: serious adverse event

EMBOLD results: Disease modifying results in SCN2A/8A DEEs

SEIZURE REDUCTION OVER TIME ON RELUTRIGINE COHORTS 1 and 2, COHORT 1 OLE



MARKED IMPROVEMENT IN DISEASE MODIFYING DOMAINS



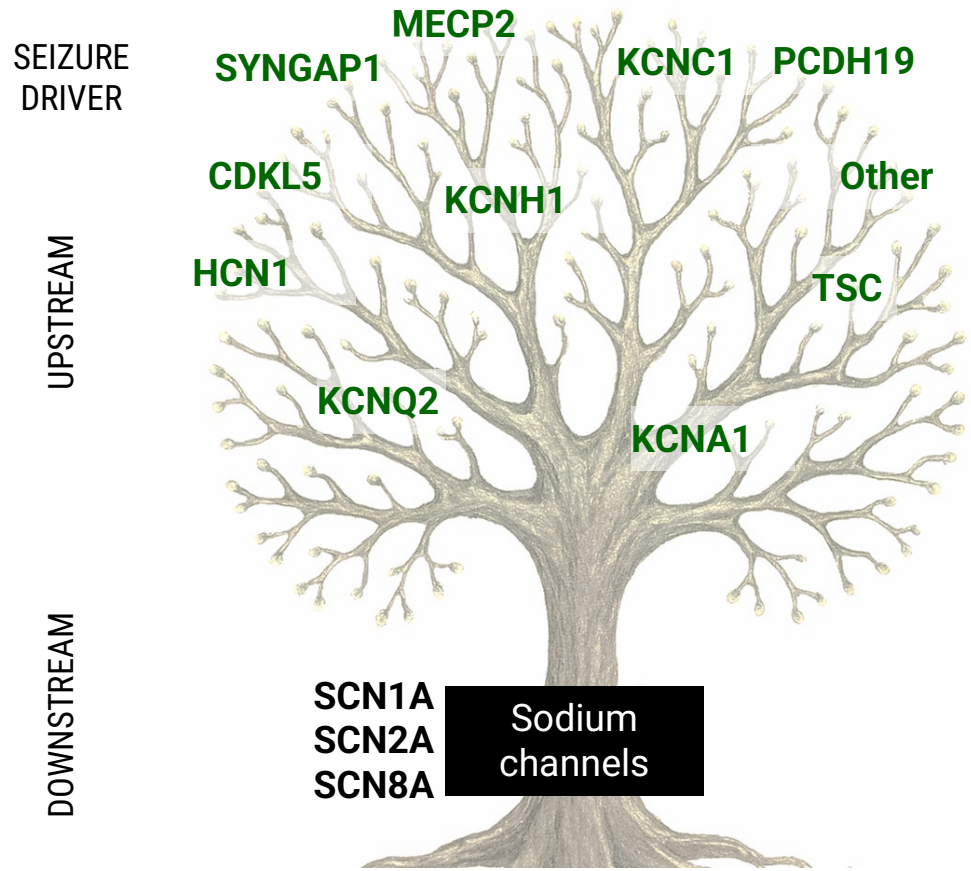
- >80% of patients were on stable doses of Sodium Channel Blockers at baseline
- AEs were mostly mild to moderate
- No drug-related SAEs
- No dose reduction of relutrigine required

Kamireddy et al AES 2025

Relutrigine's potential for broad applicability across multiple etiologies

- All genetically driven DEEs result in hyperactivation of sodium channels, manifesting in epilepsy syndromes
- Relutrigine's mechanism of action targets hyperactive NaV channels addressing the neuronal hyperexcitability driving seizures
- By targeting a common pathway implicated in DEE symptomology, relutrigine has the potential to be applicable across a broad range of DEEs

MOST SEIZURE ETIOLOGIES CONVERGE AT SODIUM CHANNELS*



*Illustrative etiologies, not limited by examples shown

DEE=developmental & epileptic encephalopathy, NaV=voltage-gated sodium channel

Elsunersen: First-in-Class ASO for SCN2A GoF DEE

ELSUNERSEN

Antisense oligonucleotide (ASO)

Intrathecal administration

Once every 4 weeks

Designed for selective SCN2A mRNA reduction

Mechanistic Precision:

- Selective targeting of SCN2A gain-of-function mutations, a key driver of early-onset, severe seizure activity
- ASO-mediated degradation of SCN2A mRNA reduces NaV1.2 hyperactivity, normalizing neuronal excitability

Clinical Profile:

- Significant reduction in seizures achieved in SCN2A GoF patients
- No adverse events were considered treatment-emergent or serious

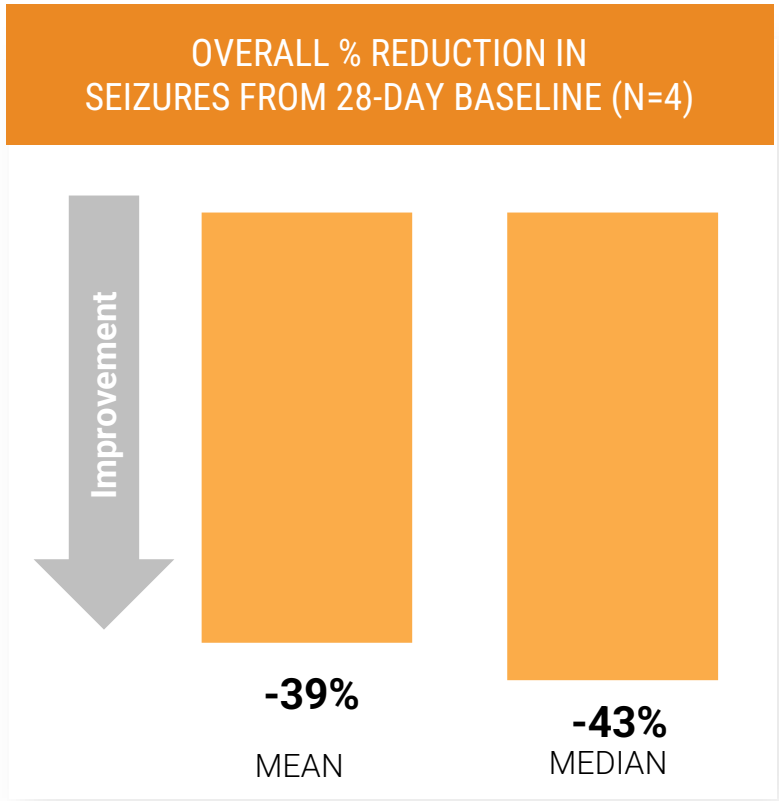
Regulatory Designations:

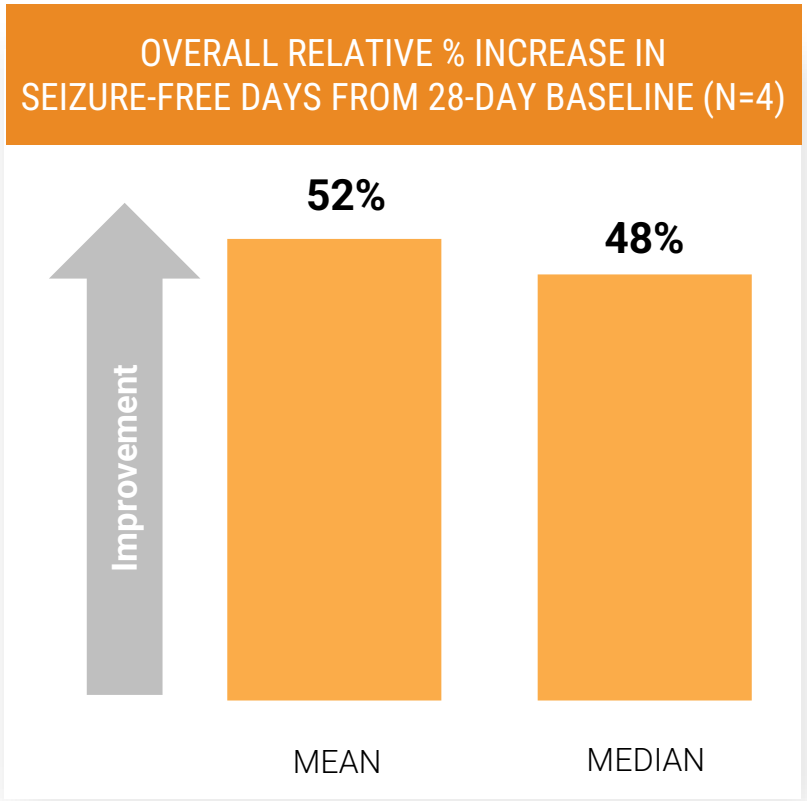
- FDA: ODD and Rare Pediatric Disease designation
- EMA: ODD and PRIME designation

DEE=[illegible] & epileptic [illegible] encephalopathy; GoF=gain-of-function; [illegible]

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

Upcoming EMBRAVE Part A and EMBRAVE3 read outs create a complete, NDA-ready registrational package for elsunersen in SCN2A GoF DEE





Key endpoints:

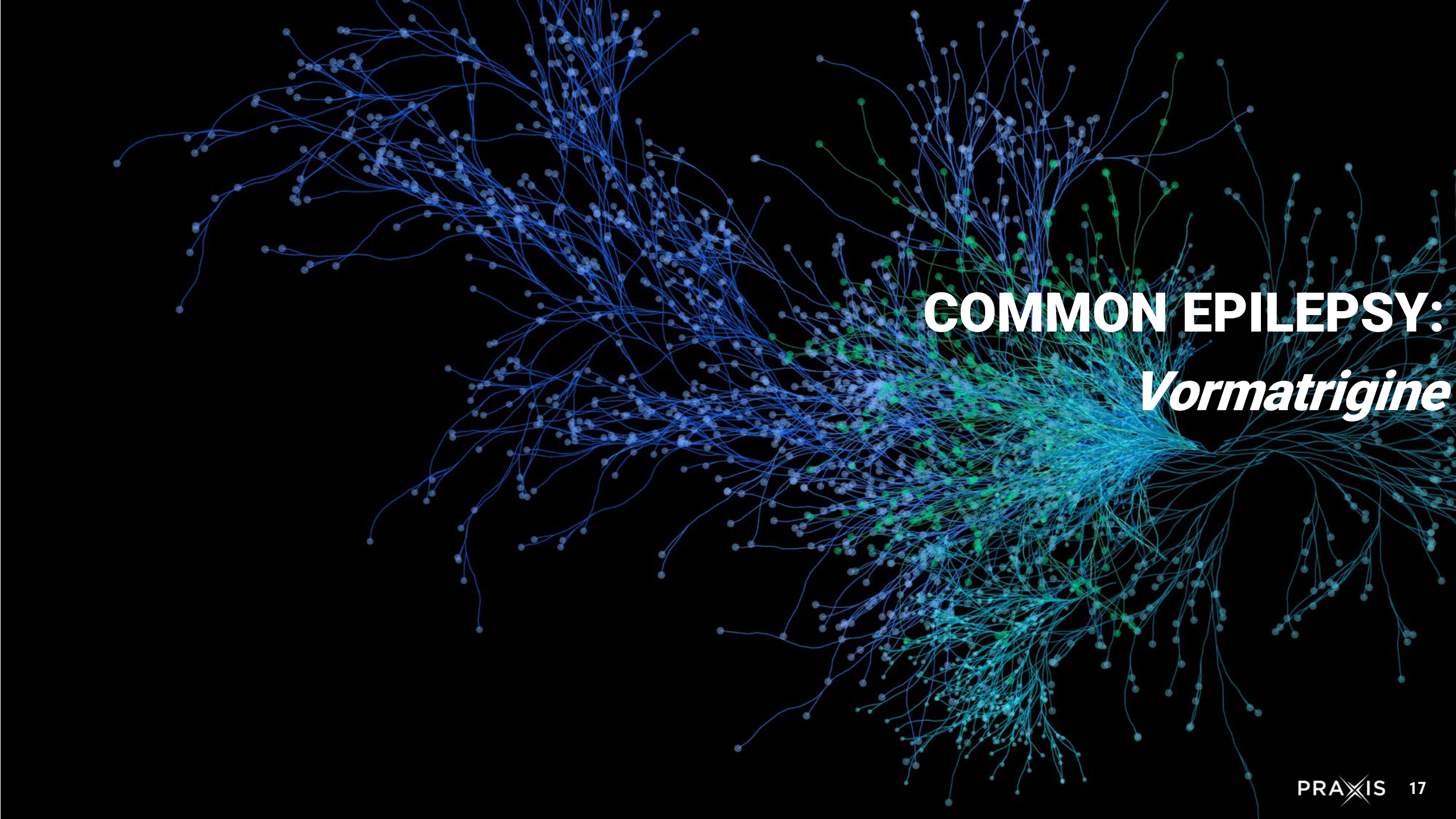
- Incidence and severity of treatment-emergent adverse events (TEAEs)
- Change from baseline in monthly (28-day) motor seizure frequency

Safety:

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

Frizzo S, et al. EEC 2024, Praxis data on file. ClinicalTrials.gov Identifier: NCT05737784. https://clinicaltrials.gov/study/NCT05737784

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



COMMON EPILEPSY:
Vormatrigine

Vormatrigine: Best-in-Disease Sodium Channel Modulator

Epilepsy is a chronic neurological disorder that affects all age groups, causing life-threatening seizures

- An estimated **3 million** patients live with epilepsy
- ~35% of patients change medications annually
- 63% require two or more medications[1]
- Treatments are needed which are:
  - Fast acting
  - Durable
  - Better tolerability
  - Compatible with complex regimens

Vormatrigine poised to rapidly transform the epilepsy landscape

Superior Efficacy

- Best-in-disease efficacy in the RADIANT study
- Broad applicability across focal and generalized epilepsy
- Sustained long-term effect

Ease of Administration

- Once daily dose, fast acting
- No need to be taken with food or require dietary changes

Ideal Tolerability and Limited DDIs

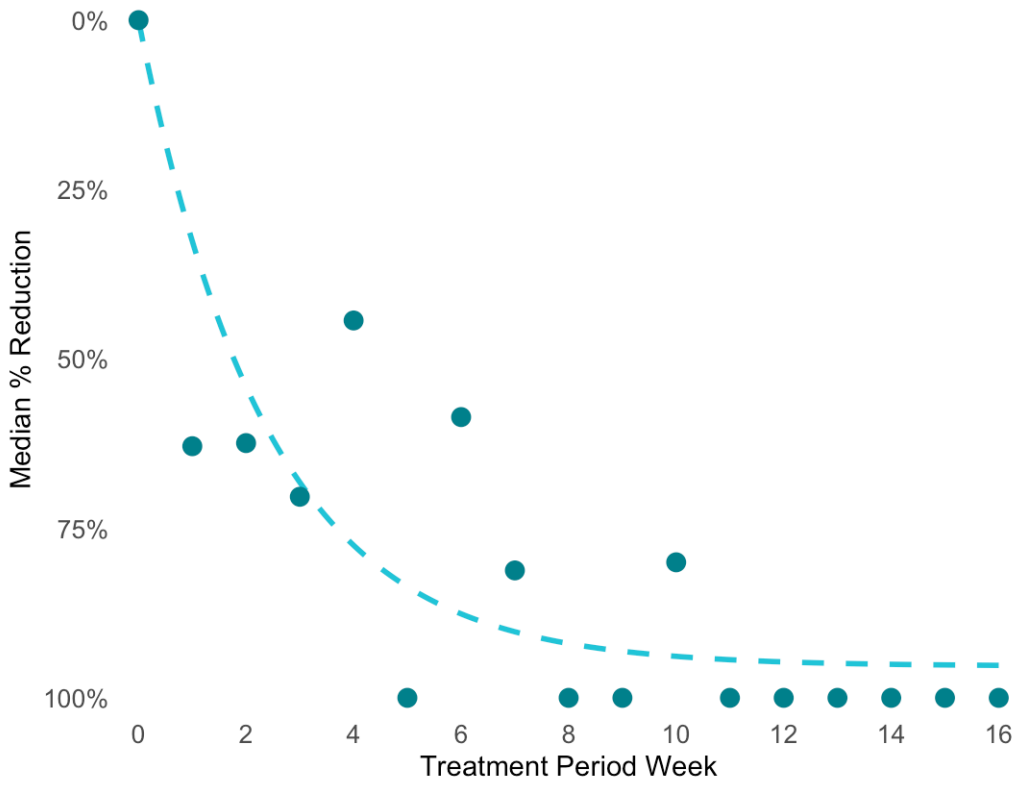
- Favorable safety profile
- Minimal drug-drug interaction risk with common ASMs

Sources:
AAN 2023 Poster - PRAX-628: A Novel Sodium Channel Blocker with Greater Potency and Activity Dependence Compared to Standard of Care; Kahlig, K., Chapman, M., Petrou, S.
AAN 2024 Poster - First-in-human Phase 1 Clinical Trial Evaluating the Safety, Tolerability, Pharmacokinetics and Food Effect of Vormatrigine in Healthy Participants; Hansen, K.; Frizzo, S., Jacotin, H., Patel, D., Epstein, N., Patel, A., Sun, H., Petrou, S., Souza, M.
1. Praxis Claims Analysis on File 2024. FOS patient cohort (n = 440k)
ASM: Anti-Seizure Medication

RADIANT Phase 2 study showed disease-leading efficacy

100% median seizure reduction after 10 weeks

MEDIAN % REDUCTION IN FOCAL SEIZURES (Weeks 1-16)



DISEASE IMPACTING CRITERIA	RADIANT RESULTS
Speed and durability of response	• Rapid response after only 1 week of dosing • By week 10 median reduction was 100% • Generalized epilepsy patients had similar benefit of FOS patients
Efficacy with other ASMs	• Patients were on an average of 2.1 ASMs • >30% of patients on best approved drug (Cenobamate)
Seizure freedom	• 11% of patients were seizure free within the treatment period • Over 30% were seizure free for any 28-day period
Safety & tolerability	• Lowest rate of TEAEs and CNS AEs with modern ASMs • Most AEs were mild to moderate and transient

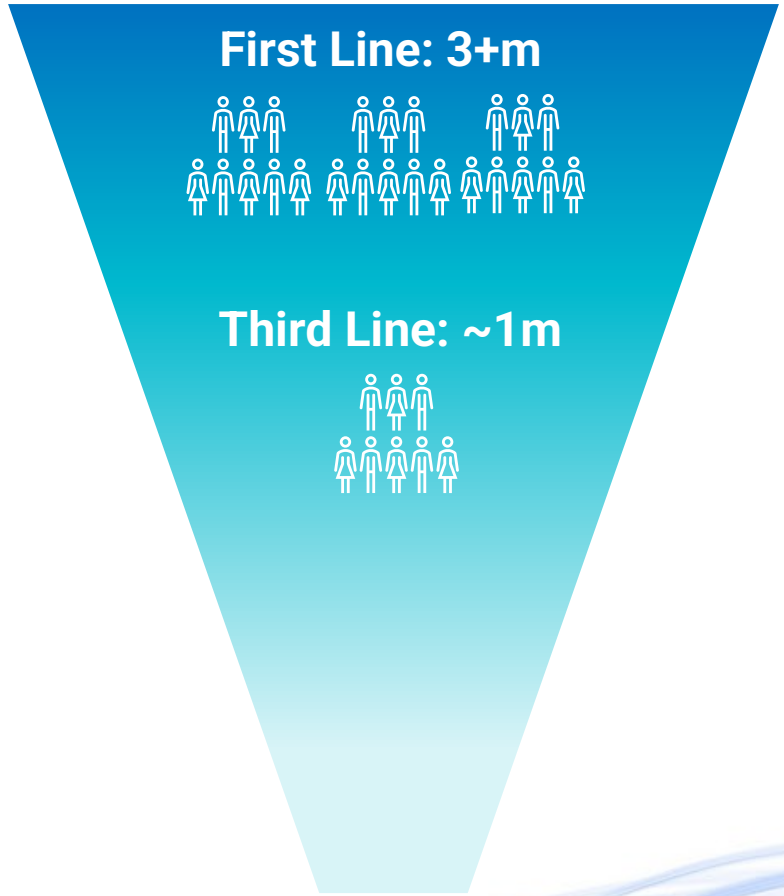
Hansen et al AES 2025

Vormatrigine ENERGY Program: Developing for Broad, Foundational Use

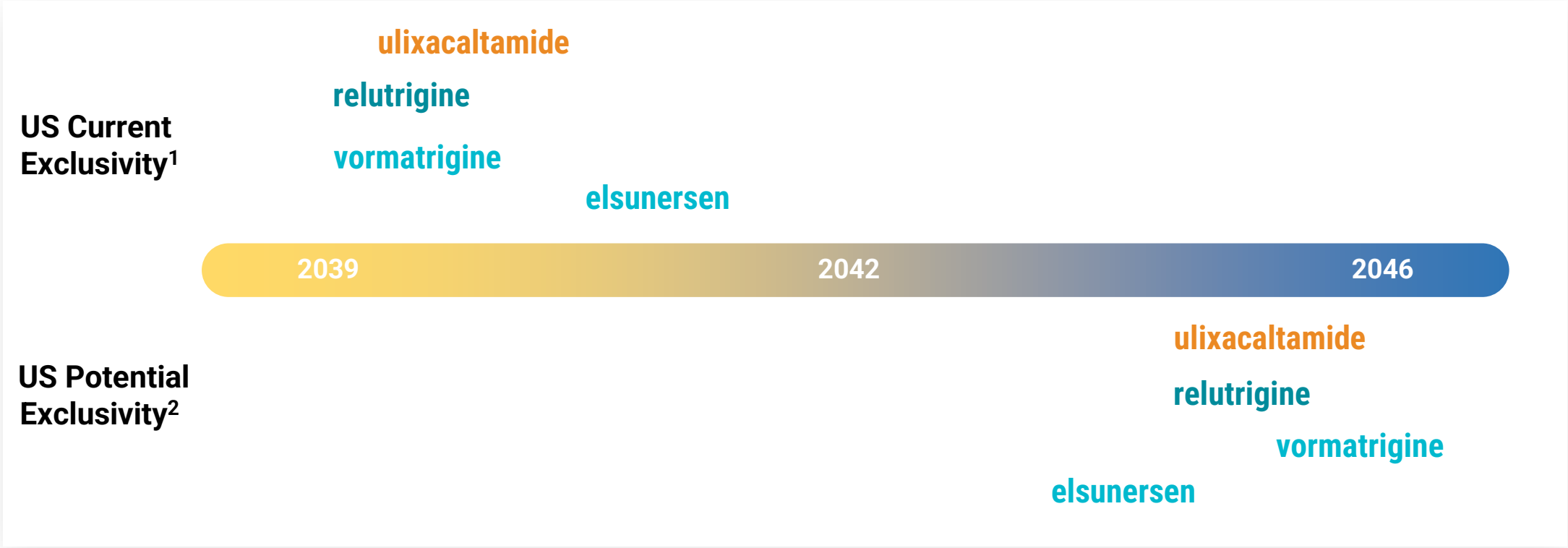
STUDY / OBJECTIVE	*2H 2025*	*1H 2026*	*2H 2026*
Study evaluating Vormatrigine as a single agent		POWER3	
Pivotal Efficacy Studies	POWER1, n=230+		
		POWER2, n=400	
Proof of Concept in Focal and Generalized epilepsy, Safety & tolerability	RADIANT ✓		

- Rapid, durable effect
- Significant impact in seizures after 8 weeks
- 100% median reduction at 10 weeks for OLE
- Over 1/3 patients seizure free for any 28-day period
- Improved efficacy on top of SoC
- TEAEs mostly mild/moderate and transient

Total Addressable Market (patients)



Long, multi-layered and strong IP position across the clinical portfolio



1 based on US Patent Nos. 11,649,207; 11,427,540; 12,077,502; 11,014,931; 12,325,711; 11,866,439; 11,731,976; 11,731,978; and 12,227,746
2 based on issuing of US App Nos. 17/975,457; 18/834,466; 19/312,146; 18,885,261 and others

Appendix

Ulixacaltamide

Relutrigine

Vormatrigine

Elsunersen

Two platforms enabling repeatable CNS innovation

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	Sodium channel functional state modulator for pediatric use
PRAX-020^	KCNT1 Epilepsy	KCNT1 specific inhibitor
PRAX-050	Movement Disorders	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*	Early onset SCN2A DEE	Gapmer ASO
PRAX-080	PCDH19 DEE	Gapmer ASO
PRAX-090	SYNGAP1 DEE	Splice switching ASO
PRAX-100	SCN2A Autism	Undisclosed mechanism ASO

* Relutrigine has received Breakthrough Therapy Designation (BTD), 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

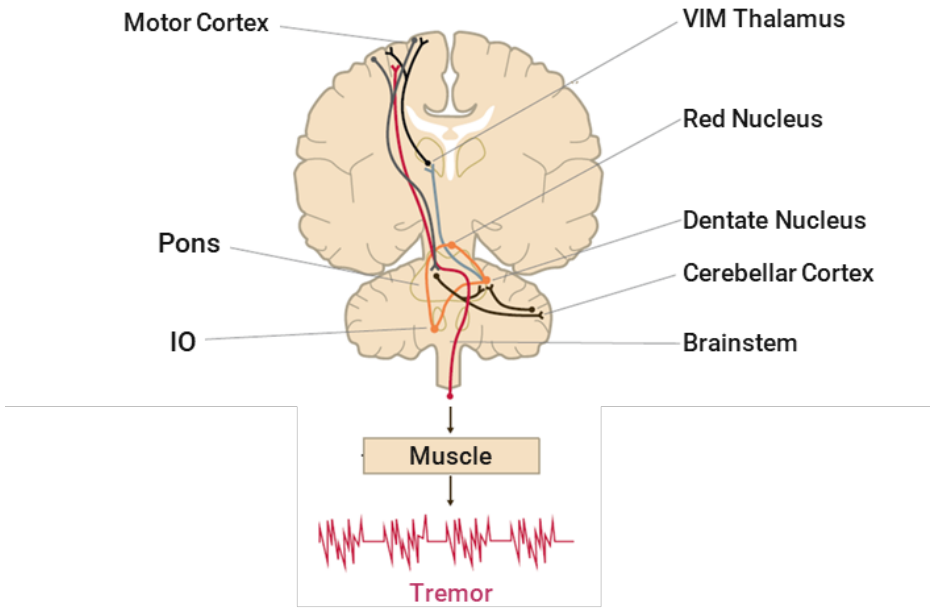
** Elsunersen has received ODD and RPD designation from the FDA, and ODD and PRIME designations from the EMA for the treatment of SCN2A GoF

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

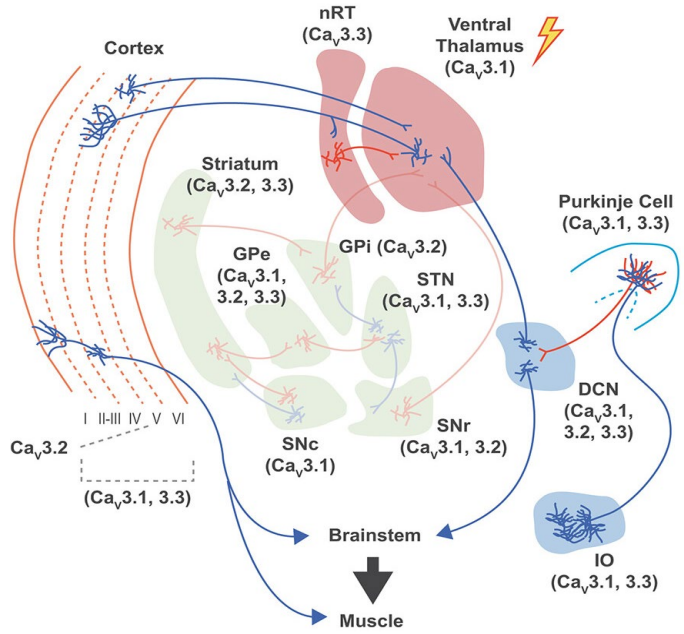
Ulixacaltamide: Precision Modulation of Tremor Circuits

- **Mechanism of Action** selectively modulates T-type calcium channels within the cerebello-thalamo-cortical circuit, normalizing abnormal tremor oscillations.
- **Modified release formulation** blunts Cmax and distributes ~70% of dose over 8-hour period

Aberrant T-type calcium channel activity in the cerebello-thalamo-cortical circuit drives essential tremor



Targeting T-type Ca^{2+} channels offers circuit-level normalization



Images from Matthews et al. Ann Clin Transl Neurol. 2023

Surveys of >400 ET patients across the US highlight ongoing hidden burden of ET and associated challenges in managing everyday life

ET burden has a profound impact on daily activities

UP TO **80%** of patients with ET reported needing to adjust how they complete daily tasks due to their symptoms

TOP CHALLENGES:

- working / attending social events
- writing
- drinking from a glass

Patients with ET experience high psychosocial burden

Nearly all patients with ET experience a level of psychosocial burden, with many reporting feeling:

- hopeless
- ashamed
- worried
- frustrated
- sad

ET is inadequately managed and undertreated

UP TO **77%** of patients do not feel their ET symptoms are manageable with current treatments

UP TO **50%** of patients are not receiving treatment for their ET

Praxis data on file. The Essential Tremor Patient Research was conducted by Fuel Insights (www.fuelinsights.com) from June-July 2024. Two separate surveys were completed online and included 150 US adults living with ET and a further 261 US adults living with ET who were pre-screened, but did not qualify, for the Essential3 study (https://essential3study.com/)

US neurologists emphasize the need for more effective treatments and the importance of patient-physician dialogue in ET

ET burden has a profound impact on daily activities

>90% of neurologists stated their patients' descriptions of their ET symptoms and impact on daily activities influence treatment decisions

Patients with ET experience high psychosocial burden

60% of neurologists reported **mental and emotional challenges** among the top three challenges for their ET patients

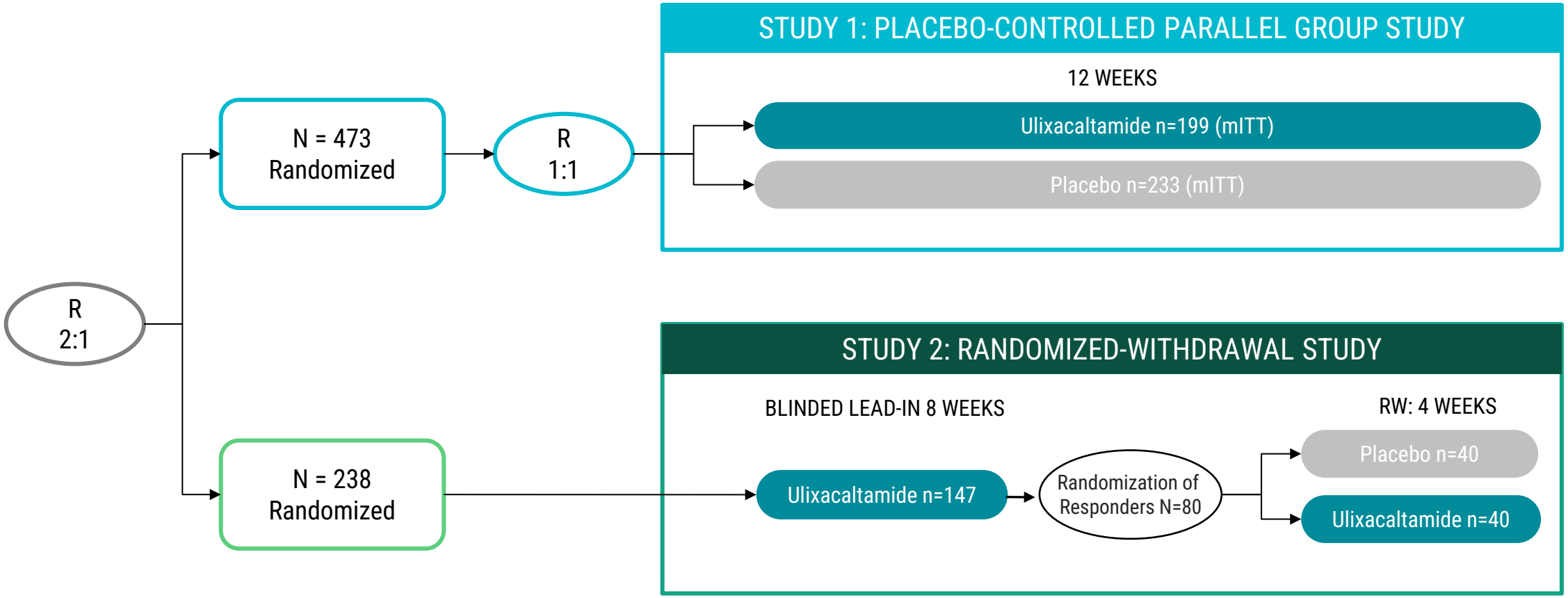
ET is inadequately managed and undertreated

85% of neurologist visits are for patients seeking ET treatment

NEARLY 1/2 of neurologists rarely refer ET patients for specialist management

Praxis data on file. The Essential Tremor Patient Research was conducted by Fuel Insights (www.fuelinsights.com) from June-July 2024. Two separate surveys were completed online and included 150 US adults living with ET and a further 261 US adults living with ET who were pre-screened, but did not qualify, for the Essential3 study (https://essential3study.com/)

Essential3: An ambitious and innovative Phase 3 program



Blinded randomization 2:1 (Study 1: Study 2) occurred following completion of screening

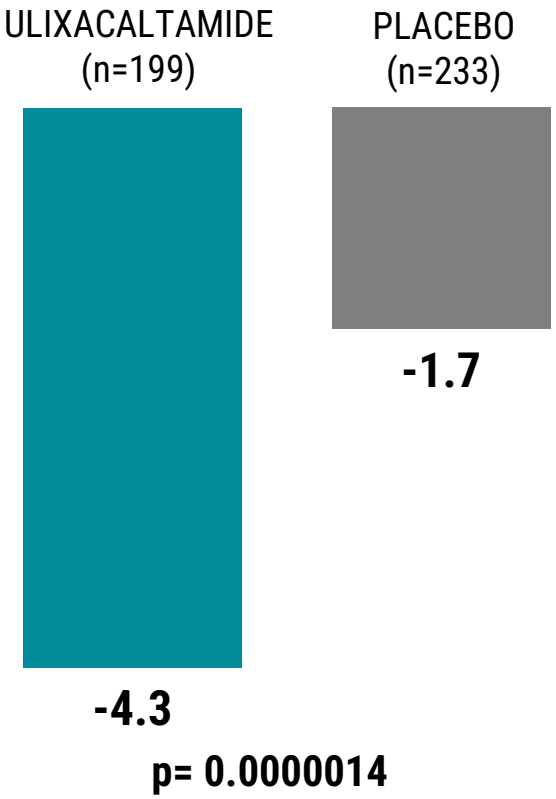
Blinded randomization 1:1 (Ulixacaltamide: Placebo) for treatment arm allocation in Study 1 and for treatment arm allocation of Responders into the randomized withdrawal phase in Study 2

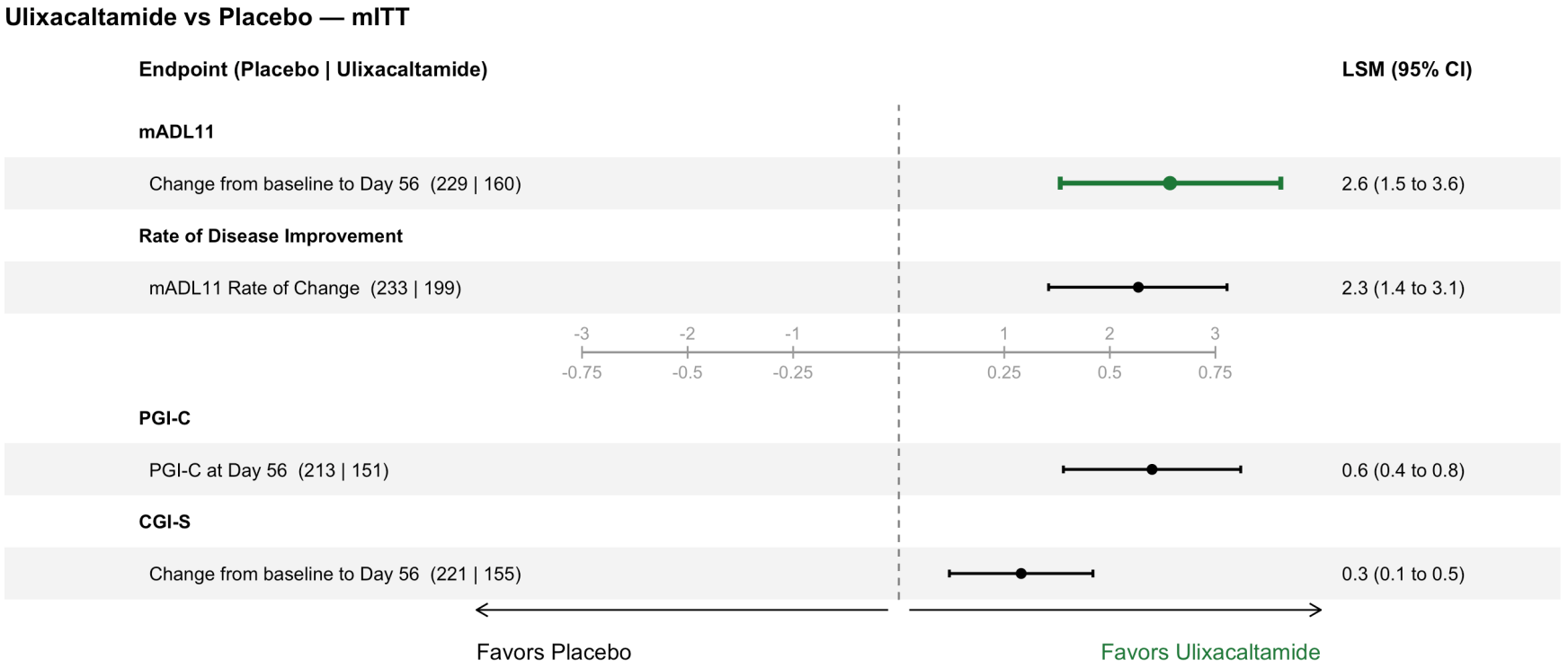
Study 1 Baseline demographics - mITT

	ULIXACALTAMIDE (N = 199)	PLACEBO (N = 233)
Age, Mean (SD)	67.9 (9.1)	68.9 (8.1)
Gender, Male/Female %	57.3% / 42.7%	56.7% / 43.3%
Race, White/Other %	98.5% / 1.5%	95.7% / 4.3%
Years since ET Onset, Mean (Median)	29.8 (26.0)	31.1 (27.0)
ET symptoms worsened over past 3 years, Yes %	188 (94.5%)	216 (92.7%)
Currently on ET Medication, Yes % **Currently on Propranolol,** Yes %	44.2% 35.7%	48.1% 36.5%
Family History of ET, Yes/No/Unknown %	71.9% / 20.6% / 7.5%	72.1% / 19.7% / 8.2%
Presence of Intention Tremor, Yes %	65.3%	66.1%
mADL11, Mean (SD)	18.5 (2.4)	18.4 (2.4)
Patient Global Impression – Severity, Mean (SD)	3.0 (0.7)	2.9 (0.7)
Clinician Global Impression –Severity, Mean (SD)	4.0 (0.6)	4.0 (0.6)

Study 1 - Primary and all key secondary efficacy endpoints met

Primary Endpoint
mADL11 CFB to Day 56

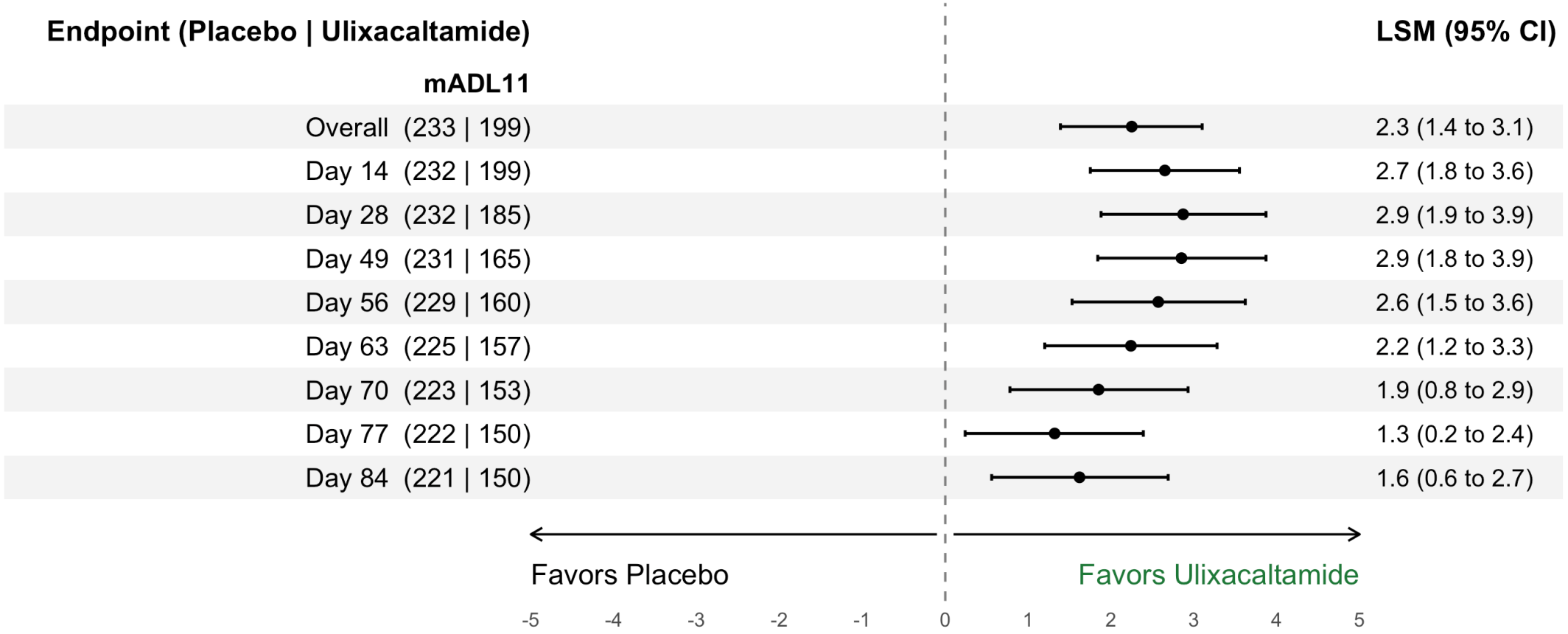




Secondary Endpoint Analyses: Rate of Disease Improvement: $p < 0.0001$; PGI-C: $p < 0.0001$; CGI-S: $p = 0.0007$

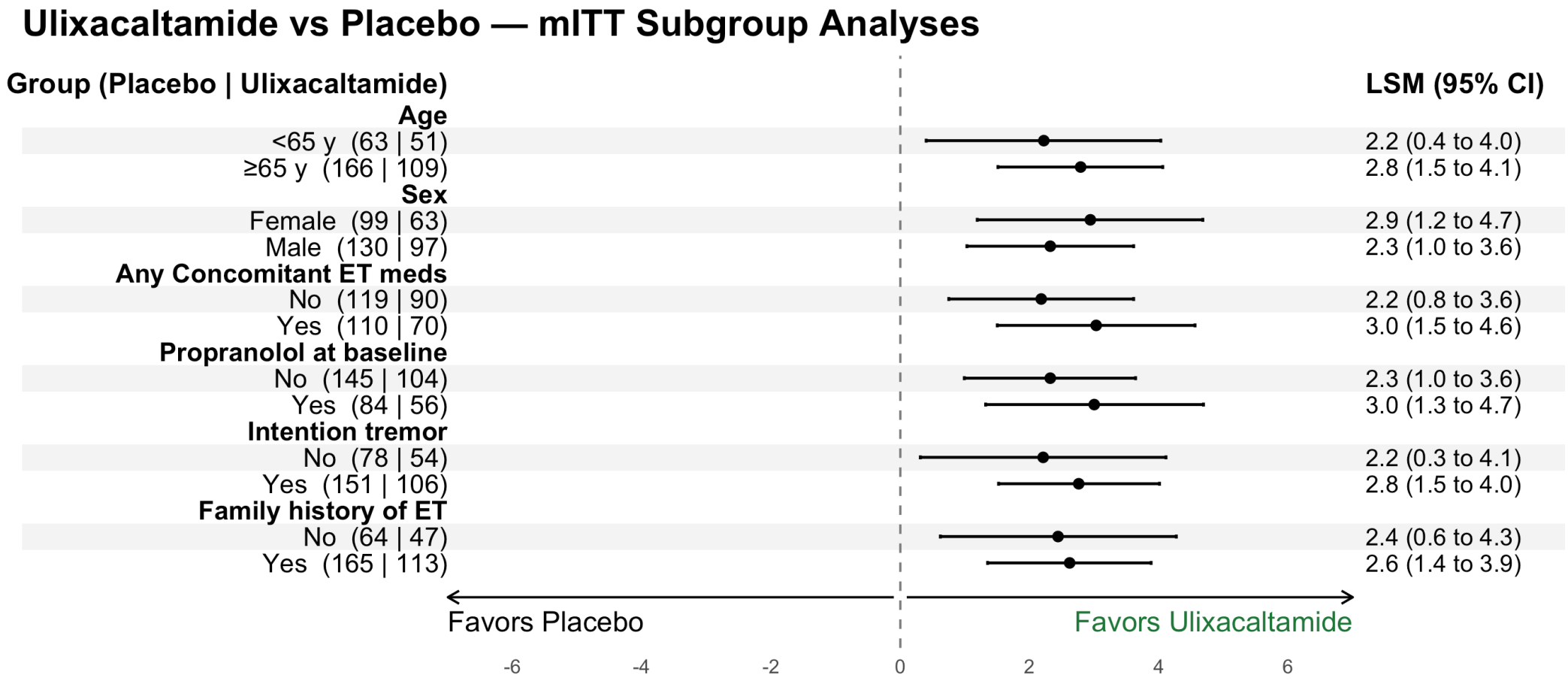
LS means for the mADL11 were estimated using a mixed model for repeated measures with treatment group, visit (categorical), treatment-by-visit interaction, randomization strata (IT status, propranolol use, family history of ET), and baseline mADL11 score as fixed effects; subject was a random effect with an unstructured covariance matrix. Sensitivity to missingness was done with a pre-specified delta-adjusted tipping-point analysis which remained statistically significant at the maximum pre-specified shift ($\Delta = 2.5$; $p = 0.0026$), exceeding the ~½ SD robustness criterion of Ratitch et al. (2013) and confirming strong resilience of the primary endpoint to non-MAR assumptions.

Study 1 - Rapid and consistent response over 12 weeks



All Visits: p-value < 0.017

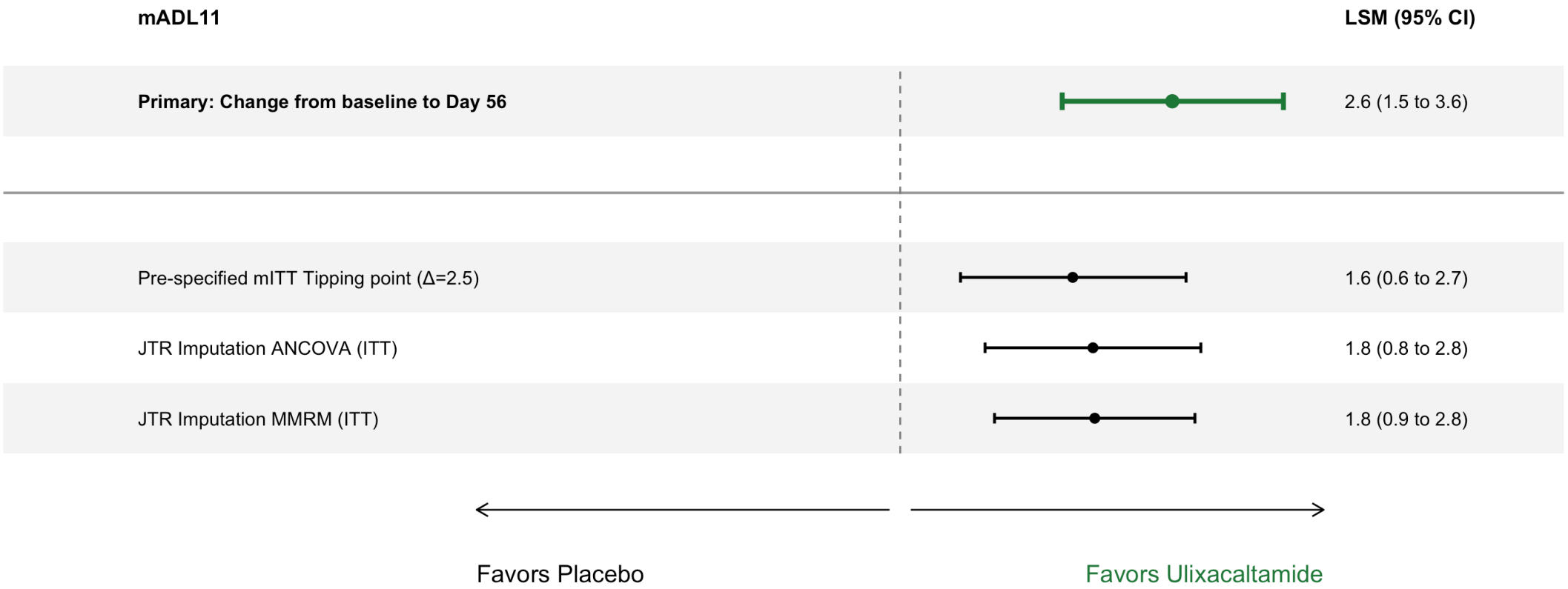
Study 1 efficacy – Robust response across subgroups



All subgroups: p-value < 0.05

Study 1 Efficacy remains significant under extreme scenarios

Ulixacaltamide vs Placebo — (Primary + Sensitivity Analyses)



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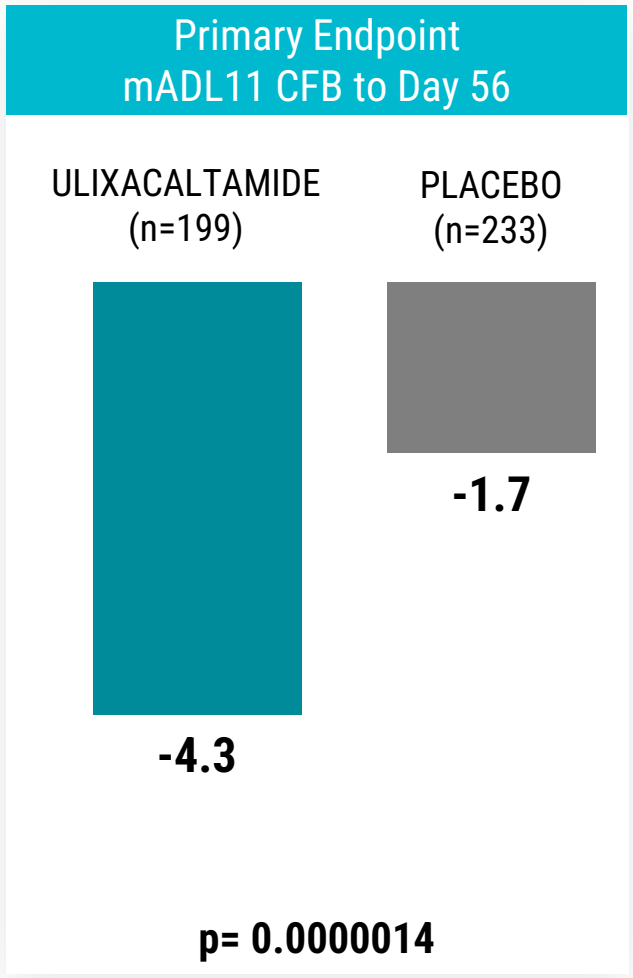
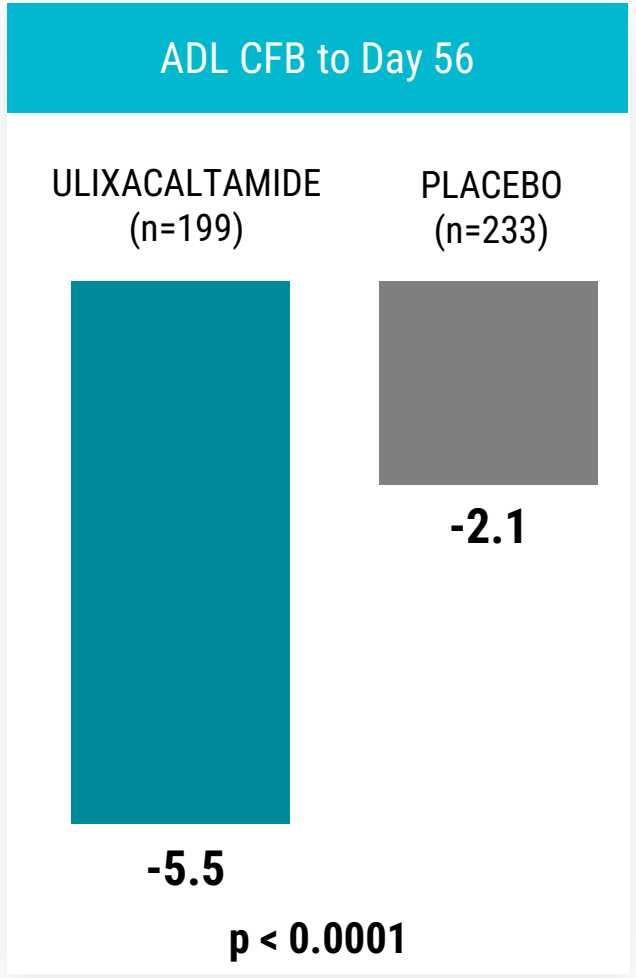
Study 1 – Clinical meaningfulness with mADL11 and ADL





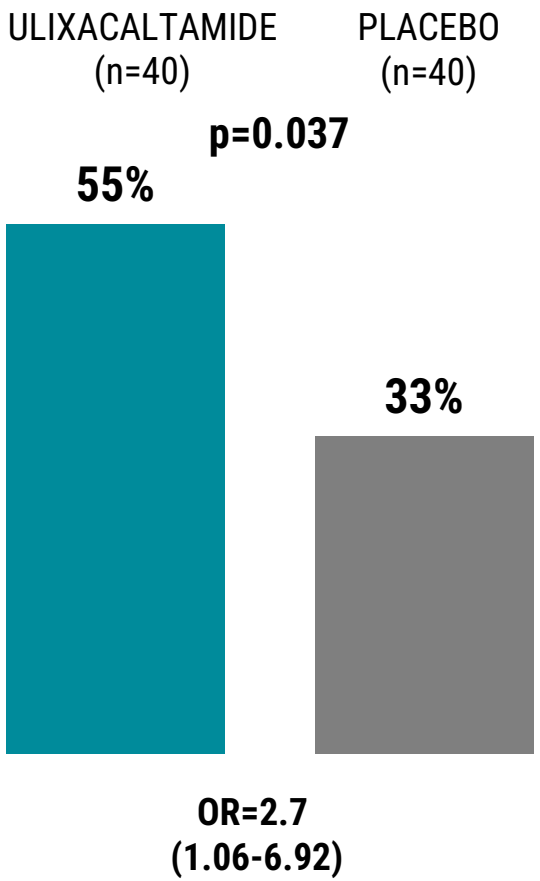
LS means for the mADL11 were estimated using a mixed model for repeated measures with treatment group, visit (categorical), treatment-by-visit interaction, randomization strata (IT status, propranolol use, family history of ET), and baseline mADL11 score as fixed effects; subject was a random effect with an unstructured covariance matrix. Sensitivity to missingness was done with a pre-specified delta-adjusted tipping-point analysis which remained statistically significant at the maximum pre-specified shift (Δ = 2.5; p = 0.0026), exceeding the ~½ SD robustness criterion of Ratitch et al. (2013) and confirming strong resilience of the primary endpoint to non-MAR assumptions.

Study 2 – RW baseline demographics – stable-responders

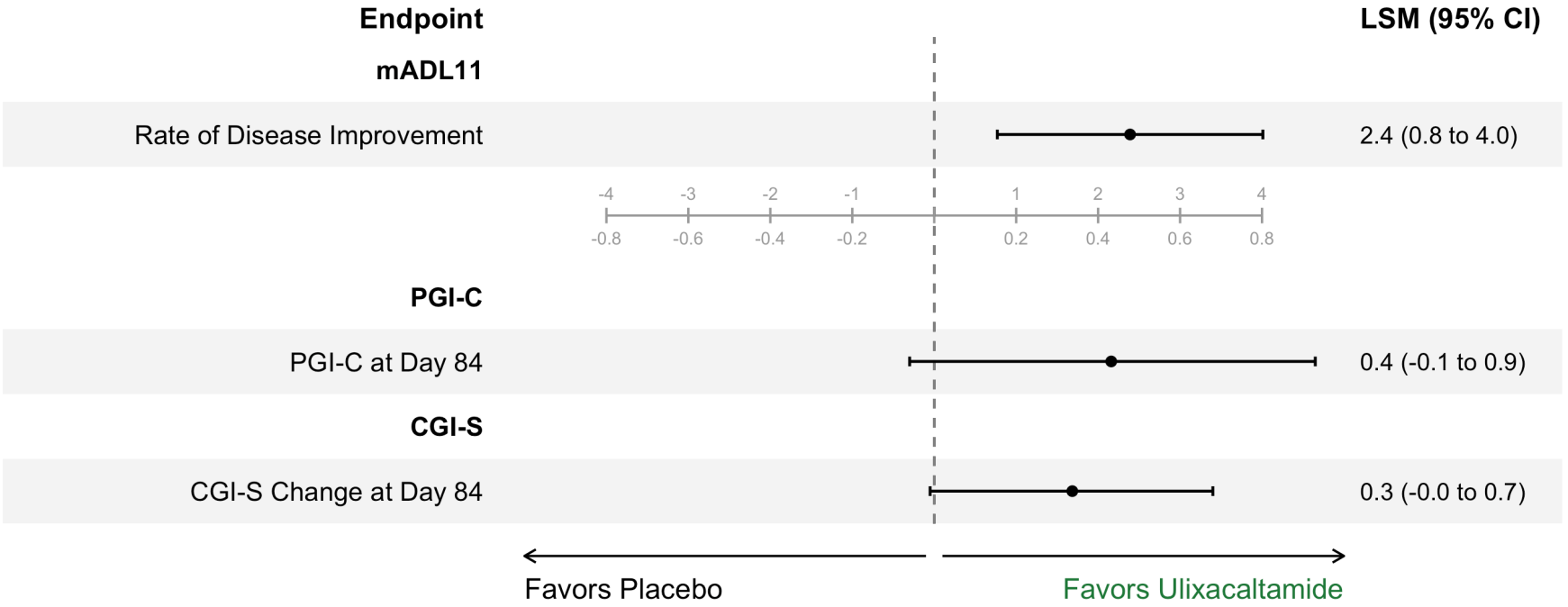
	BLINDED LEAD-IN ULIXACALTAMIDE	ULIXACALTAMIDE STABLE RESPONDERS
Age, Mean (SD)	67.9 (7.9)	67.3 (8.4)
Gender, Male/Female %	51.8% / 48.2%	55.0% / 45.0%
Race, White/Other %	96.3% / 3.7%	95.0% / 5.0%
Years since ET Onset, Mean (Median)	28.7 (25.0)	28.5 (24.5)
ET symptoms worsened over past 3 years, Yes %	95.8%	93.8%
Currently on ET Medications, Yes % **Currently on Propranolol,** Yes %	42.4% 34.6%	41.3% 38.8%
Family History of ET, Yes/No/Unknown %	73.3% / 22.0% / 4.7%	76.3% / 18.8% / 5.0%
Presence of Intention Tremor, Yes %	63.9%	53.75%
mADL11, Mean (SD)	19.0 (2.5)	10.6 (4.8)
Patient Global Impression – Severity, Mean (SD)	3.0 (0.7)	1.2 (0.6)
Clinician Global Impression – Severity, Mean (SD)	4.0 (0.7)	3.1 (0.9)

Study 2 efficacy - Primary and first secondary endpoint met

Primary Endpoint
% Maintain Response



Ulixacaltamide vs Placebo — Key Secondary Endpoints

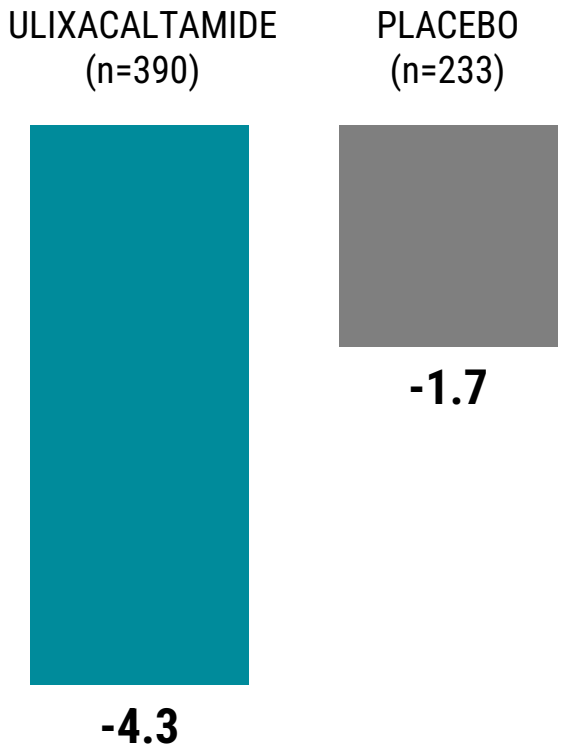


Secondary Endpoint Analyses: Rate of Disease Improvement: p =0.0042 ; PGI-C: p = 0.0871 ; CGI-S: p = 0.0545

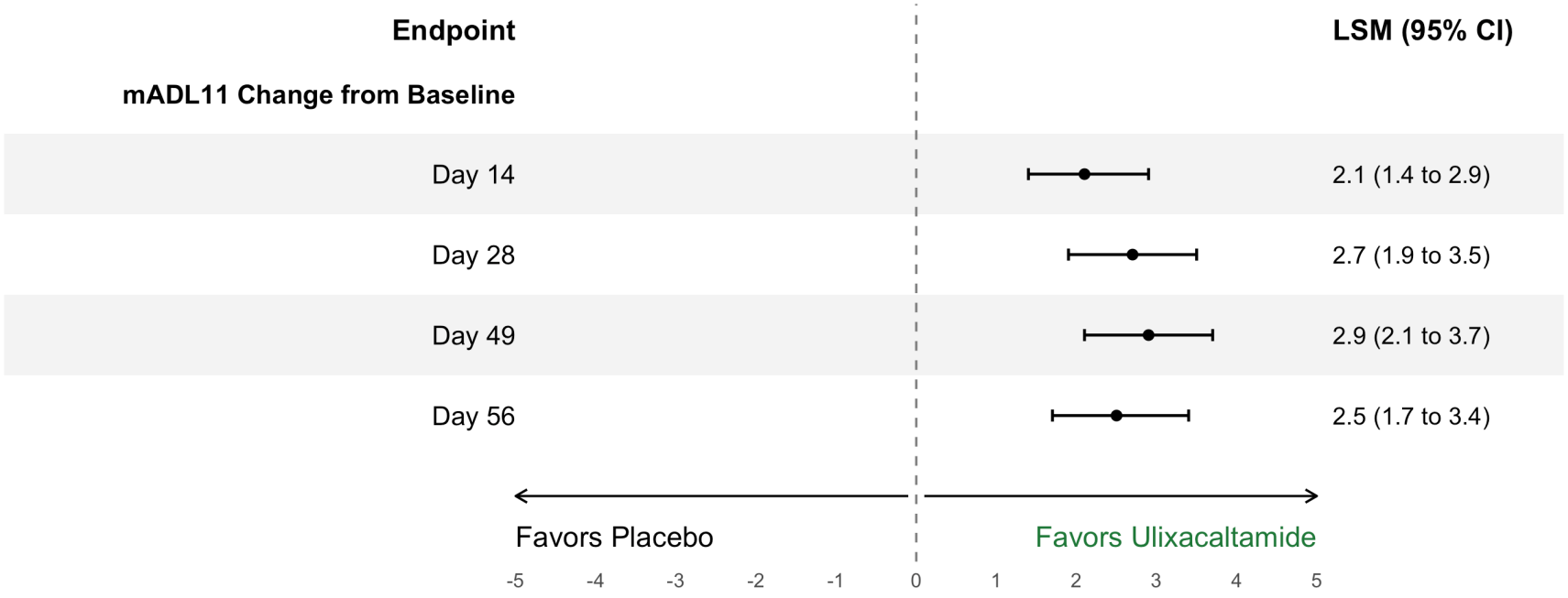
For primary endpoint, odds ratio, 95% confidence interval, and p-value were obtained from a logistic regression model including treatment group as the main effect and randomization strata (IT status, propranolol use, and family history of ET) as fixed effects.

Hypothesis 3– Day 56 Parallel-group combined efficacy analysis

Primary Endpoint
mADL11 CFB to Day 56



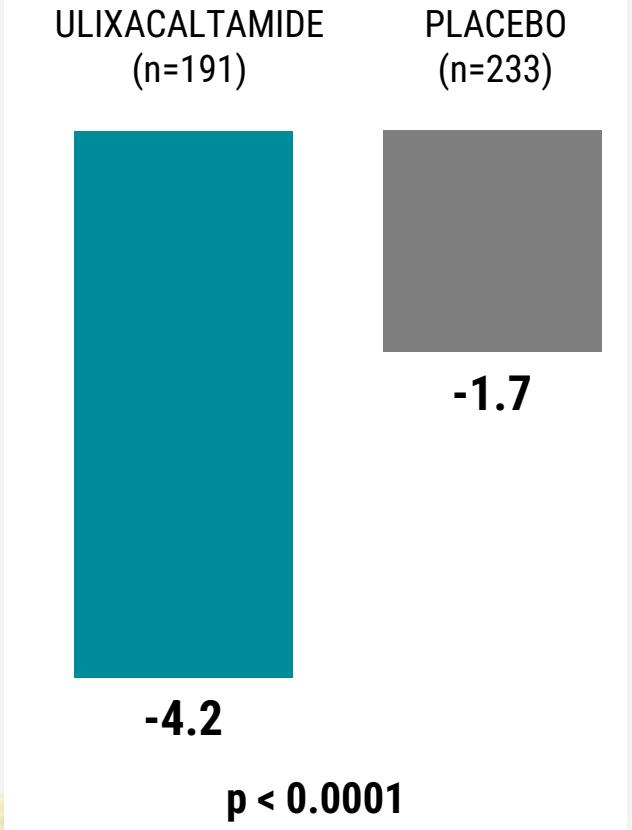
Parallel-group combined analysis - Studies 1+2 / Study 1



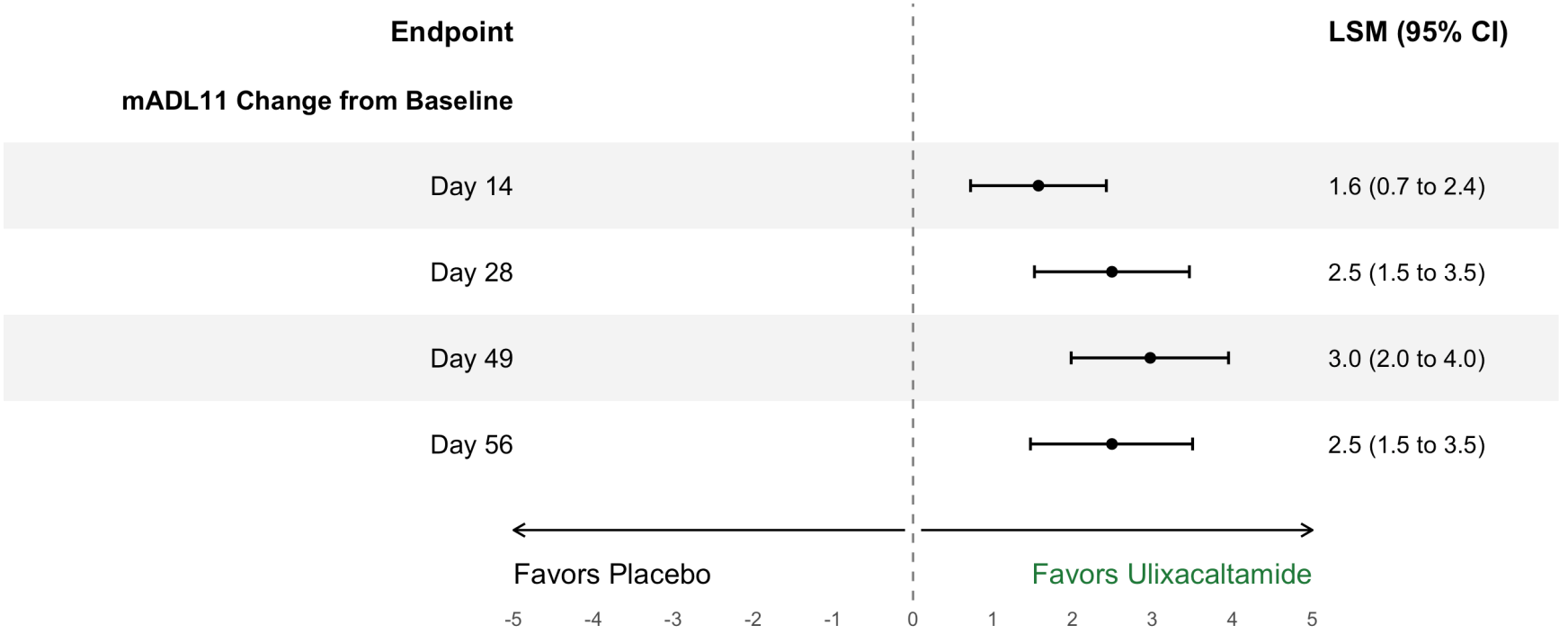
All Visits: p < 0.0001

Hypothesis 4– Day 56 Parallel-group combined efficacy analysis

Primary Endpoint
mADL11 CFB to Day 56



Day 56 Parallel-group placebo versus Study 2 analysis



All Visits: p < 0.0004

Safety across studies remains consistent

- No change in overall safety profile and no new signals identified
- Most common TEAEs (≥10%) in participants treated with ulixacaltamide were constipation, dizziness, euphoric mood, brain fog, headache, paraesthesia and insomnia.
  - Discontinuations were primarily due to AEs, with most common due to dizziness and brain fog
- Majority of TEAEs were mild to moderate in severity
- No SAEs related to ulixacaltamide

Essential3 Program: Study 1 and Study 2 disposition

DISPOSITION STUDY 1

POPULATIONS	ULIXACALTAMIDE	PLACEBO
Enrolled/ITT	236 (100%)	237 (100%)
Safety	233 (98.7%)	234 (98.7%)
mITT	199 (84.3%)	233 (98.3%)

DISPOSITION STUDY 2

POPULATIONS	OVERALL
Enrolled	238 (100%)
Population at Day 56	147 (61.8%)
Stable Responders (mITT)	80 (54.4%)
Non-stable responders	67 (45.6%)

Study 1 Enrolled/ITT: All randomized participants
Study 2 Enrolled: All randomized participants
Safety: All participants who received at least one dose of study drug
Study 1 mITT: All randomized participants who received at least one dose and had at least one post-baseline efficacy assessment
Study 2 mITT/Stable responders: Participants with an average improvement of three or more points in mADL11 at Days 49–56, received at least one dose in RW and one post RW baseline efficacy assessment
Non-stable responders: Participants at Day 56 who did not meet the criteria for Responders

Safety population – Overview of AEs

OVERVIEW OF ADVERSE EVENTS			
	STUDY 1		STUDY 2
	ULIXACALTAMIDE (N = 233)	PLACEBO (N = 234)	ULIXACALTAMIDE (N = 231)
Participants with any TEAE	221 (94.9%)	177 (75.6%)	209 (90.5%)
Participants with:			
Mild TEAEs	98 (42.0%)	89 (38.0%)	87 (37.7%)
Moderate TEAEs	109 (46.8%)	78 (33.3%)	105 (45.5%)
Severe TEAEs	14 (6.0%)	10 (4.3%)	17 (7.4%)
Participants with any SAE*	2 (0.86%)	8 (3.4%)	4 (1.73%)
Participants with drug-related TEAEs leading to discontinuation	63 (27.0%)	4 (1.7%)	65 (28.1%)
Discontinued from the study	83 (35.6%)	13 (5.6%)	88 (38.1%)

*none related to study drug

Safety population - Most common TEAEs

TREATMENT EMERGENT ADVERSE EVENTS ≥10% OF PATIENTS			
	STUDY 1		STUDY 2
Preferred Term	ULIXACALTAMIDE (N = 233)	PLACEBO (N = 234)	ULIXACALTAMIDE (N = 231)
Constipation	57 (24.5%)	16 (6.84%)	68 (29.4%)
Dizziness	56 (24.0%)	27 (11.5%)	59 (25.5%)
Euphoric mood	30 (12.9%)	3 (1.28%)	15 (6.5%)
Brain fog	27 (11.6%)	8 (3.42%)	44 (19.0%)
Paraesthesia	23 (9.87%)	5 (2.14%)	27 (11.7%)
Fatigue	22 (9.44%)	26 (11.1%)	22 (9.52%)
Headache	19 (8.15%)	20 (8.55%)	29 (12.6%)
Insomnia	18 (7.73%)	9 (3.85%)	27 (11.7%)

Appendix

Ulixacaltamide

Relutrigine

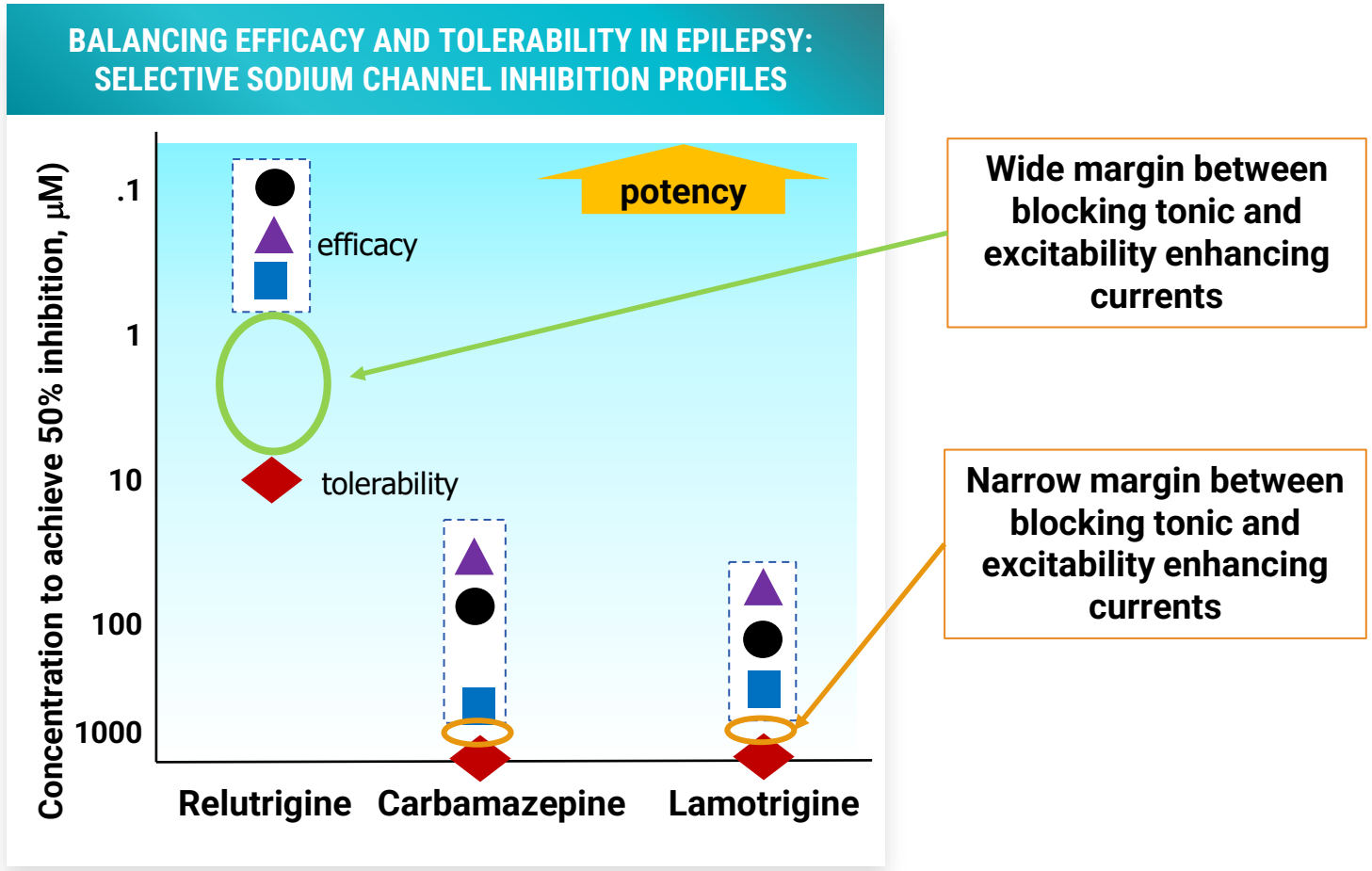
Vormatrigine

Elsunersen

Relutrigine: Mechanistic Differentiation & Superior Selectivity

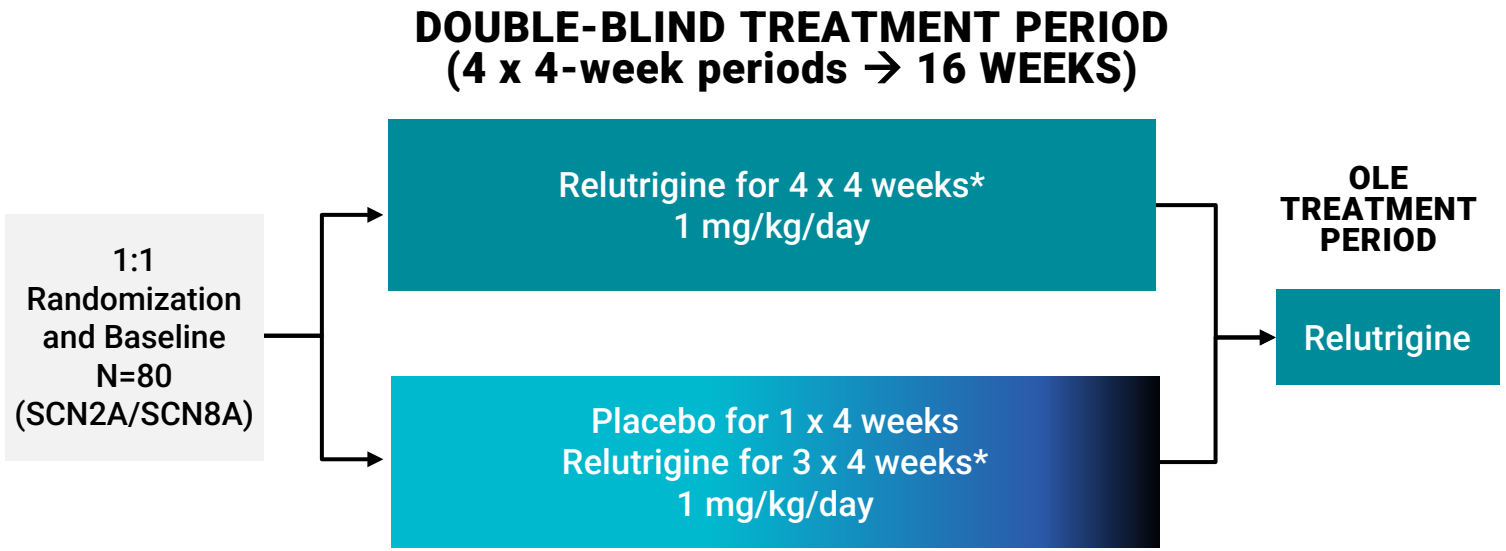
Tolerability-Supporting Current
- Physiological (Tonic) Sodium Current
- Maintains normal neuronal function
- Inhibition leads to side effects

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



Praxis data on file
μM = micromolar

EMBOLD pivotal relutrigine study



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 (TEAEs)
- Clinical and Caregiver Global Impression of Improvement and Severity

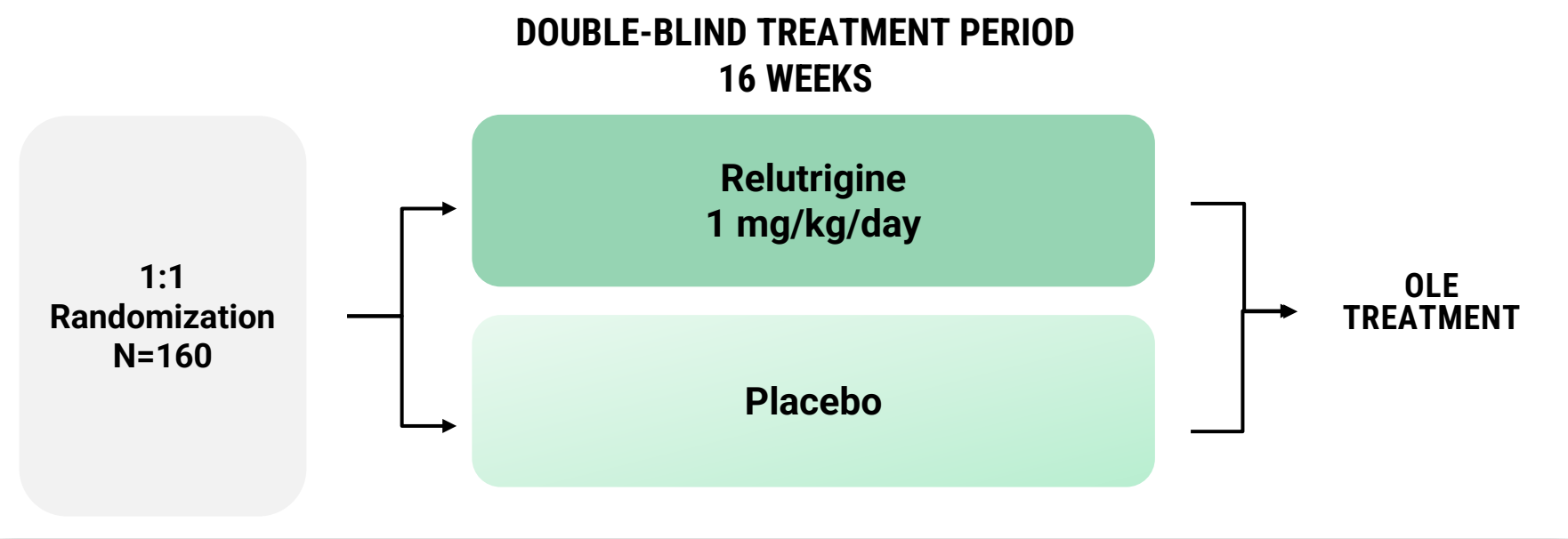
*Participants randomized (1:1) to receive relutrigine QD for 16 weeks, or relutrigine QD for 12 weeks and matching placebo QD for 4 weeks, with timing of placebo administration blinded for both participants and investigator.

ClinicalTrials.gov Identifier: NCT05818553. https://clinicaltrials.gov/ct2/show/NCT05818553

Frizzo et al IEC 2025

EMBOLD

EMERALD targets phenotypic DEEs, regardless of etiology



Primary Endpoint:

Change from baseline in monthly motor seizure frequency

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

ClinicalTrials.gov Identifier: NCT07010471
Kamireddy et al IEC 2025

Appendix

Ulixacaltamide

Relutrigine

Vormatrigine

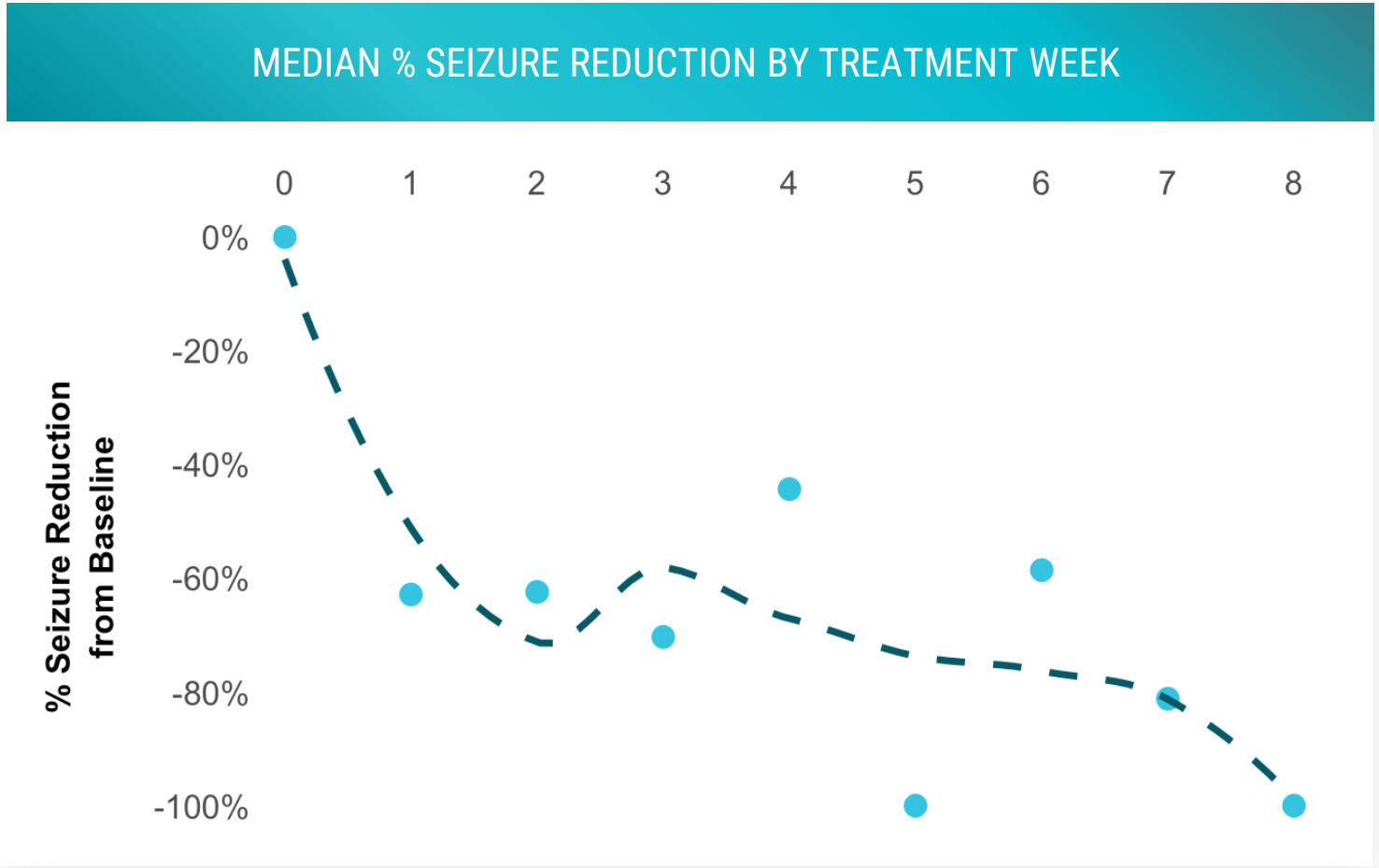
Elsunersen

RADIANT patients represent the real-world refractory group

		N=65
Age (Years)	Mean (SD)	43 (14.45)
Sex	M,F	29,36
# background ASMs	Mean (SD)	2.1 (0.85)
Concomitant ASM	Sodium Channel Blocker SV2A GABA modulators Others	77% 59% 29% 12%
Baseline seizure	Median (IQR)	9 (4,21)

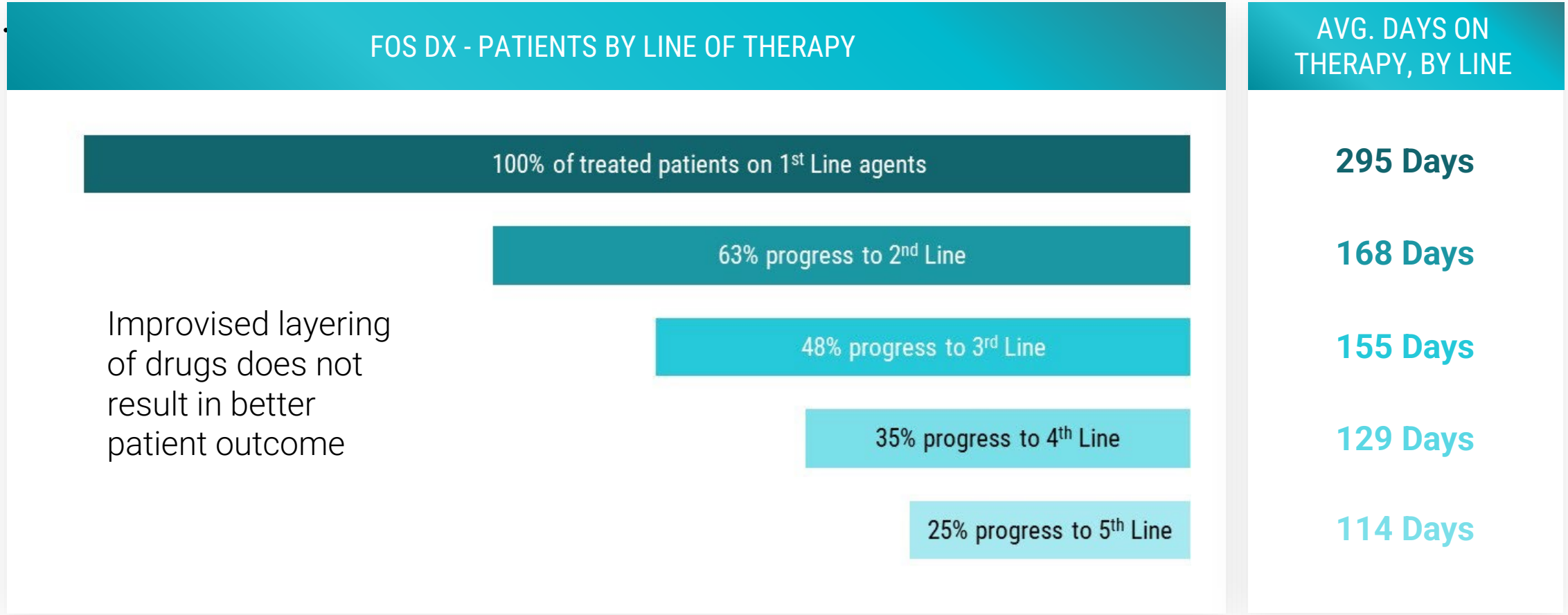
NCT#06908356
QD = Once daily

Vormatrigine Effect in RADIANT: Best-in-Disease Efficacy



Hansen et al AES 2025, Wilcoxon sign test p<0.05 in all weeks and overall; LOESS: Locally weighted plot smoothing

Majority of focal epilepsy patients quickly progress to multiple ASM use by trial and error



Simpler and more rational way to manage patients is needed

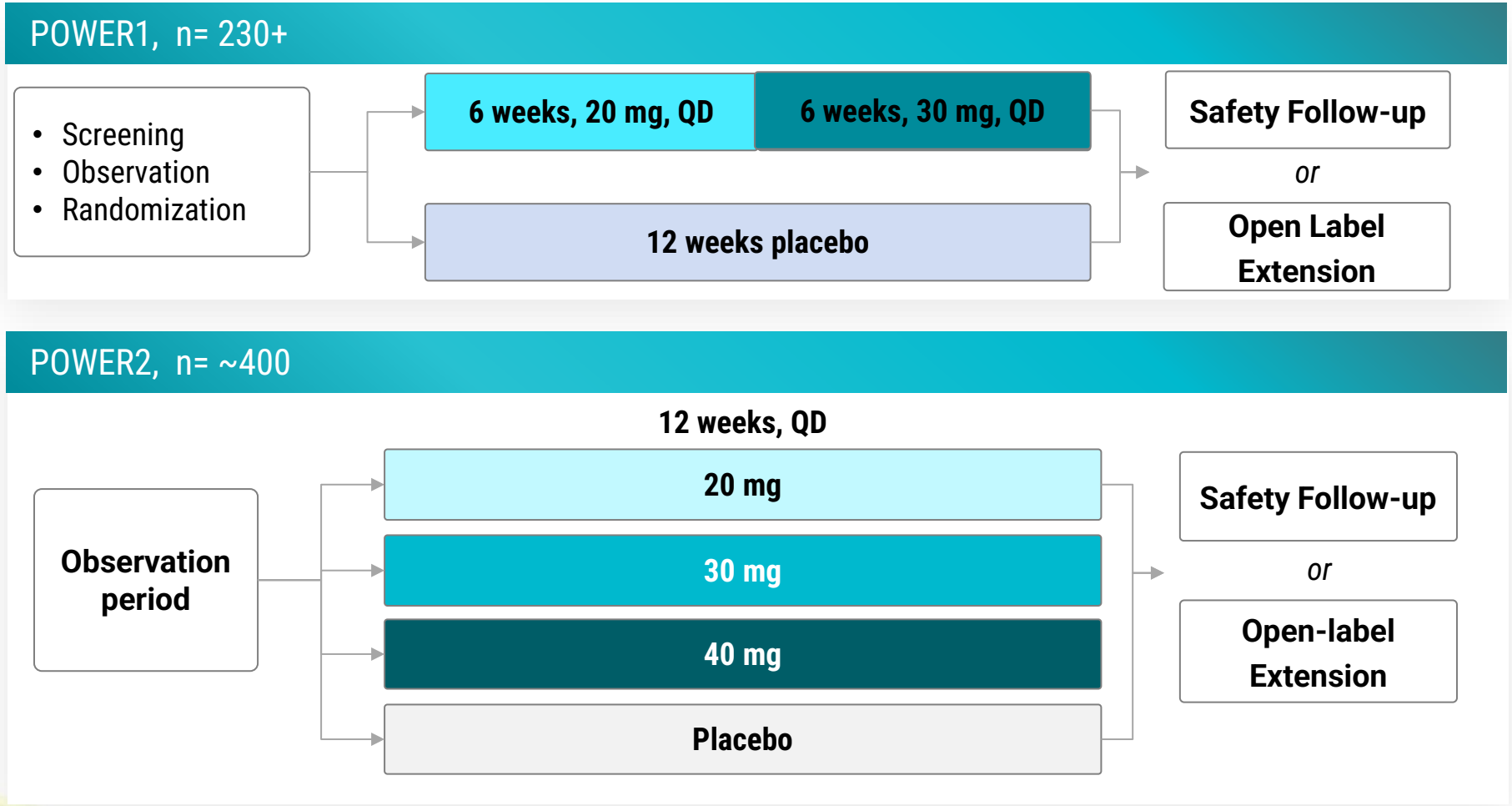
Vormatrigine safety profile positioned to be best-in-disease ASM

	Vormatrigine 30 mg (N = 65)	Cenobamate 400 mg (N = 111)	XEN1101 25 mg (N = 114)
Study	RADIANT	Study C017[1]	X-TOLE[2]
Discontinuation	16 (25 %)	30 (27 %)	26 (23 %)
Patients with ≥ 1 TEAE	44 (68 %)	100 (90 %)	97 (85 %)
Patients with severe AEs	4 (6.2 %)	18 (16 %)	Not reported
Serious AEs (SAEs)	4 (6.2 %)	8 (7 %)	3 (2.6 %)
Related SAE	1 (1.5 %)[3]	–	Not reported
CNS-related AEs (≥ 10%)	39 (60%)	80 (72.1 %)	83 (72.8 %)
Dizziness	21 (32 %)	37 (33 %)	36 (31.6 %)
Somnolence	8 (12 %)	41 (37 %)	17 (14.9 %)
Headache	9 (14 %)	12 (11 %)	9 (7.9 %)
Titration	None	12-weeks	None
Food Effect	None; Any time of day, with or without food	None; Any time of day, with or without food	Yes; Evening dosing with food
Significant DDIs	N/A	Multiple	CYP3A

1. Cenobamate Krauss, G. L., et al. *The Lancet Neurology*,. 2020;19(1), 38–48. https://doi.org/10.1016/S1474-4422(19)30399-0; https://www.ema.europa.eu/en/documents/assessment-report/ontozry-epar-public-assessment-report_en.pdf,
2. XEN1101: French JA, et al; *JAMA Neurology*. 2023;80(11):1145–1154. doi:10.1001/jamaneurol.2023.3542
3. Episode of diplopia, resolved after reduction of lamotrigine dose

Not a head-to-head comparison

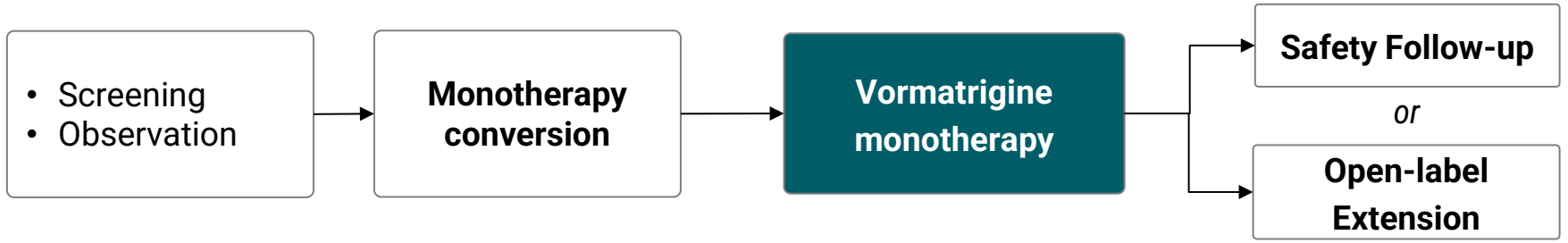
Pivotal POWER1 study topline results Q2 2026, POWER2 topline results in 2027



- Both studies expected to support NDA submission
- Range of doses in POWER2 based off PK/PD analysis to optimize efficacy opportunity

QD: Once-daily dosing

POWER3 designed to demonstrate the potential of vormatrigine as a stand-alone agent



- Key study aspects:
- Refractory epilepsy with 1-2 current ASMs
- Initiate vormatrigine while titrating off current regimen over 4 weeks
- Details to follow after protocol finalization

Expected to initiate 1H 2026

Appendix

Ulixacaltamide

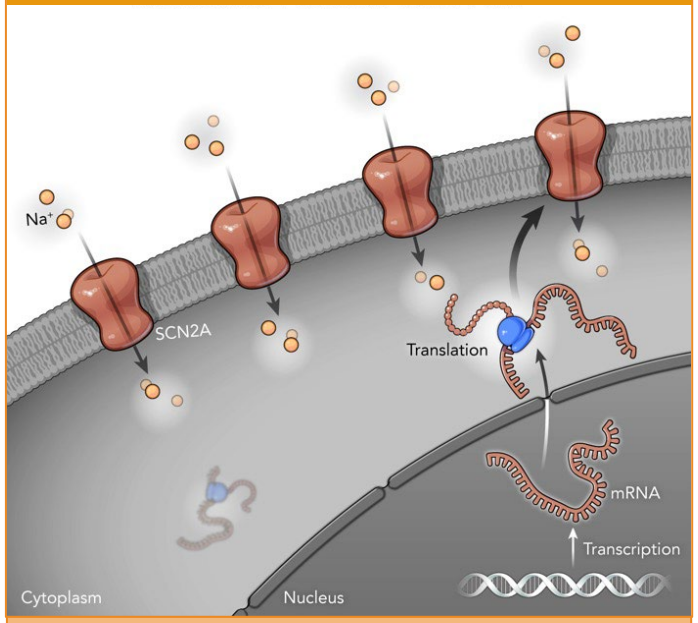
Relutrigine

Vormatrigine

Elsunersen

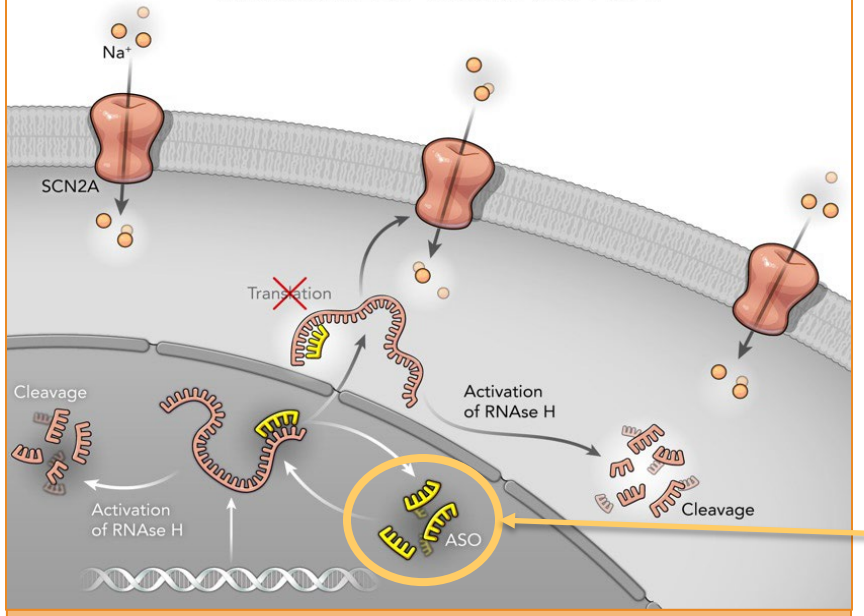
Precision targeting of SCN2A GoF patients positions elsunersen as a potential disease-modifying therapy

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

Ongoing EMBRAVE Part A supports registrational package

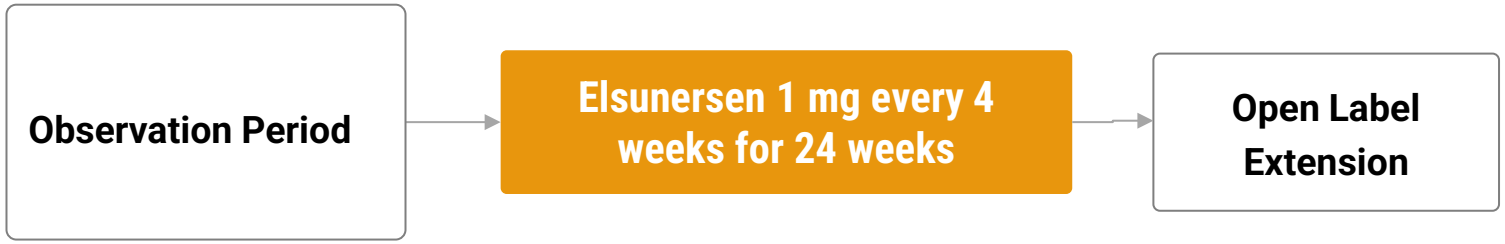
- Starting dose of 1 mg with optional dose escalation up to 8 mg based on individual tolerability at each dose
- Topline results expected 1H 2026

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

EMBRAVE3 registrational trial

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

ClinicalTrials.gov Identifier: NCT07019922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