UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): October 20, 2025

PRAXIS PRECISION MEDICINES, INC.
(Exact name of registrant as specified in its charter)

Delaware	001-39620	47-5195942
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

Praxis Precision Medicines, Inc.
99 High Street, 30th Floor
Boston, Massachusetts 02110
(Address of principal executive offices, including zip code)

(617) 300-8460
(Registrant's telephone number, including area code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trade Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	**PRAX**	**The Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

On October 21, 2025, Praxis Precision Medicines, Inc. (the "Company") updated its corporate presentation for use in meetings with investors, analysts and others. The presentation is available in the "Investors + Media" portion of the Company's website at investors.praxismedicines.com and a copy is furnished as Exhibit 99.1 to this Current Report on Form 8-K (the "Current Report").

The information in this Current Report under Item 7.01, including Exhibit 99.1 attached hereto, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01. Other Events.

As previously disclosed, the Company submitted a pre-NDA meeting request to the U.S. Food and Drug Administration (the "FDA") for ulixacaltamide. On October 20, 2025, the Company was informed by the FDA that, following its review of the Essential3 topline results, the FDA granted a Type B meeting to take place in the fourth quarter of 2025.

Forward-Looking Statements

This Current Report contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws, including statements regarding the anticipated timing of regulatory interactions for ulixacaltamide. The forward-looking statements included in this Current Report are subject to a number of risks, uncertainties and assumptions, including, without limitation, uncertainties inherent in clinical trials, the expected timing of submission for regulatory approval or review by governmental authorities and other risks as described in the Company's Annual Report on Form 10-K for the year ended December 31, 2024, its Quarterly Report on Form 10-Q for the quarter ended June 30, 2025 and its other filings with the Securities and Exchange Commission. These statements are based only on facts currently known by the Company and speak only as of the date of this Current Report. As a result, you are cautioned not to rely on these forward-looking statements and the Company undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future developments or otherwise.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Praxis Precision Medicines, Inc. October 2025 Corporate Presentation
104	Cover Page Interactive Data File (embedded within the inline XBRL document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

PRAXIS PRECISION MEDICINES, INC.

Date: October 21, 2025

By: /s/ Marcio Souza
Marcio Souza
Chief Executive Officer

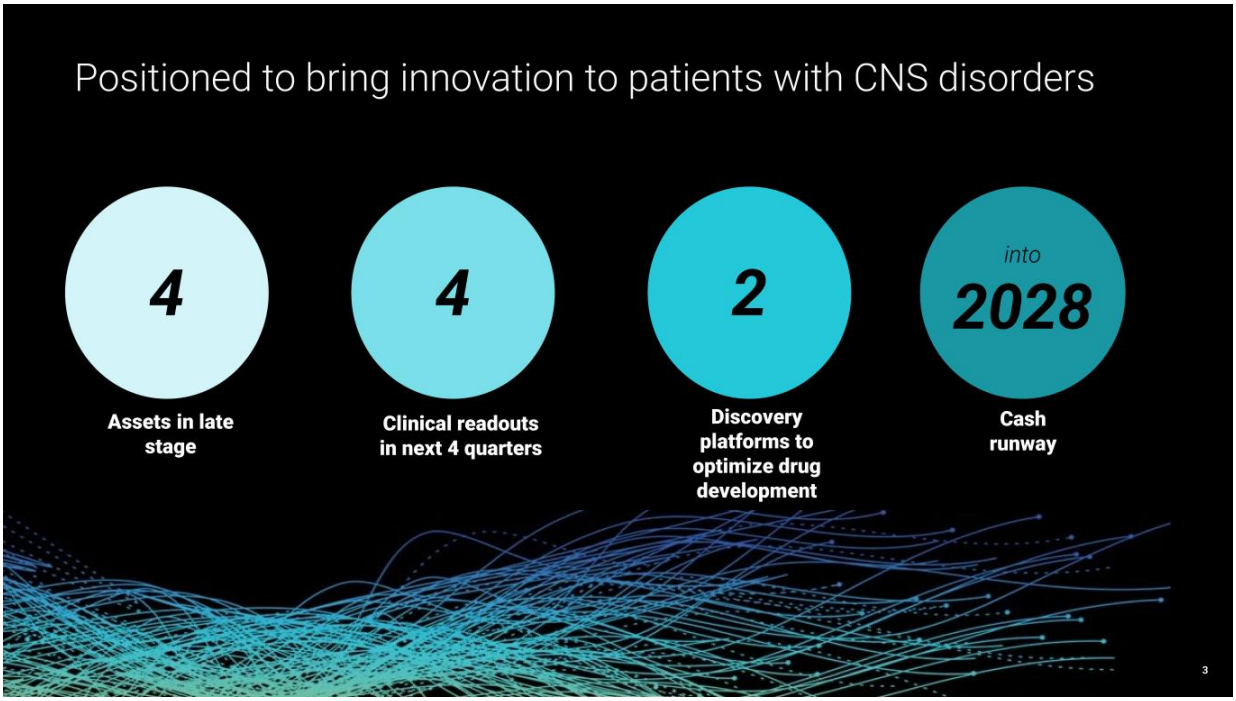

PRAXIS
DARE FOR MORE®
CORPORATE OVERVIEW
October, 2025

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, , 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, our Quarterly Report on Form 10-Q for the quarter ended June 30, 2025 and our other filings 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.


Positioned to bring innovation to patients with CNS disorders
4
Assets in late stage
4
Clinical readouts in next 4 quarters
2
Discovery platforms to optimize drug development
into
2028
Cash runway
3

Four pillars guide how we develop medicines

GENETICS

Focus on therapeutic targets identified through human genetics

TRANSLATIONAL TOOLS

Translational tools validate potential of target and product candidate and can provide early proof of biology

EFFICIENT & RIGOROUS

Efficient, rigorous clinical development paths to proof-of-concept in humans applying an agile way of working

PATIENT-GUIDED

Patient-guided development strategies to deliver on what patients actually need

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	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*	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

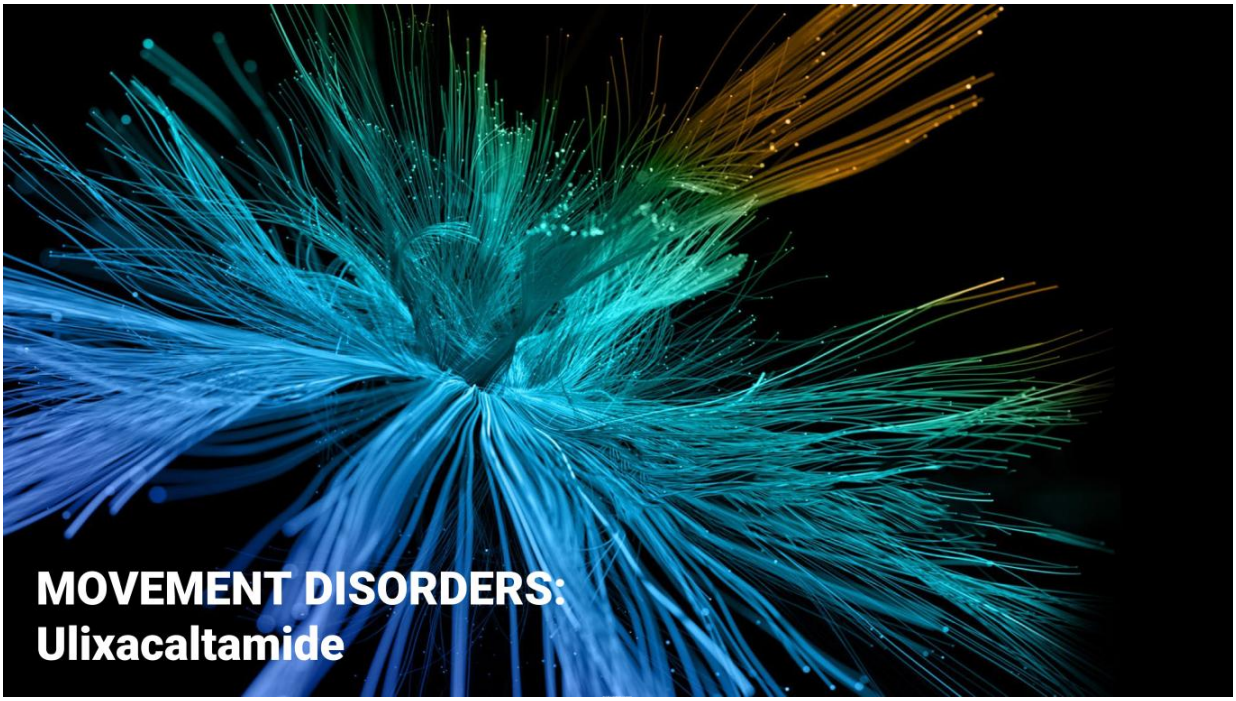
** Elsunersen has received ODD and RPD designation from the FDA, and ODD and PRIME designations from the EMA for the treatment of SCN2A GoF

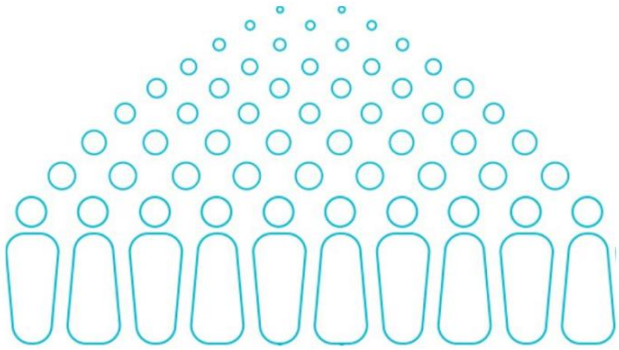
DEE=developmental & epileptic encephalopathy, GoF=gain-of-function, LoF=loss-of-function, PRIME=Priority Medicines

Praxis pipeline and upcoming catalysts

	PROGRAM	PRE CLINICAL	PHASE ONE	PHASE TWO	PHASE THREE	UPCOMING CATALYST
Cerebrum™ SMALL MOLECULE PLATFORM	**Vormatrigine Focal Onset Seizures & Generalized Epilepsy**					
	EMPOWER observational study					Ongoing
	RADIANT Phase 2					Full cohort topline results Q4 2025
	POWER1 Phase 2/3					Finalize study in Q4 2025
	POWER2 Phase 2/3					Complete enrollment 2026
	POWER3 Monotherapy					Initiate 1H 2026
	Relutrigine DEEs					
	EMBOLD Cohort 2 SCN2A GoF and SCN8A					1H 2026 topline results, 2026 NDA filing
	EMERALD Broad DEEs					Complete enrollment in 2026
	PRAX-020 KCNT1*					
	Ulixacaltamide Essential Tremor					
	ESSENTIAL3 Study 1 placebo controlled					Pre-NDA meeting with FDA
	ESSENTIAL3 Study 2 randomized withdrawal					
Solidus™ ASO PLATFORM	**Elsunersen SCN2A GoF**					
	EMBRAVE Phase 1/2					Topline results in 1H26
	EMBRAVE3 Registrational					Complete enrollment in 2026
	PRAX-080 PCDH19					Candidate declaration by year-end 2025
	PRAX-090 SYNGAP1					Candidate declaration by year-end 2025
	PRAX-100 SCN2A LoF					Candidate declaration by mid-2025

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


MOVEMENT DISORDERS:
Ulixacaltamide



An estimated **7 million people** in the U.S. live with ET

No specific drugs developed for ET currently approved

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

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

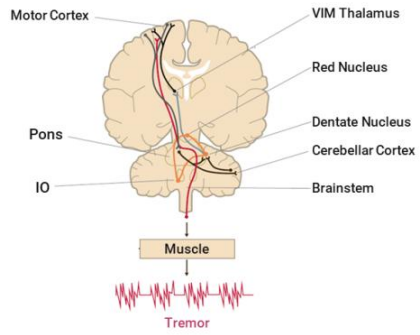
40% of patients seen by neurologists are not receiving treatment

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

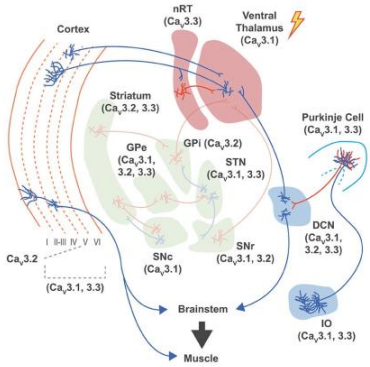
Praxis data on file. The Essential Tremor HCP Research was conducted by Fuel Insights (www.fuelinsights.com) in April 2024. The survey was fielded at the American Academy of Neurology meeting and included 152 neurologists who treat ET in the US, and who were primarily affiliated with academic centers.

Precision modulation of tremor circuits through T-type calcium channel modulation

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



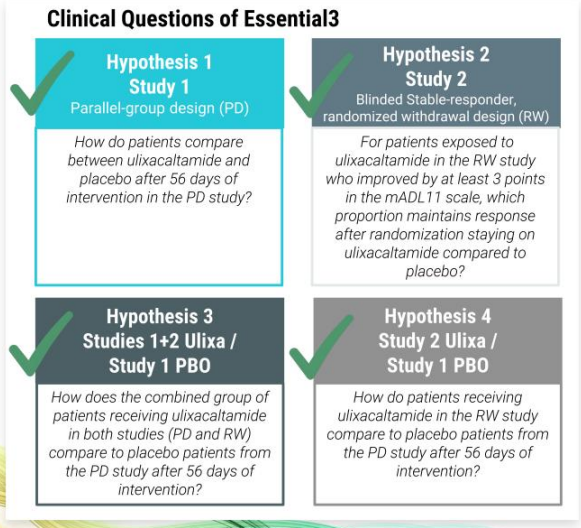
Targeting T-type Ca^{2+} channels offers circuit-level normalization



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

Essential3 is the First Successful Program in Essential Tremor

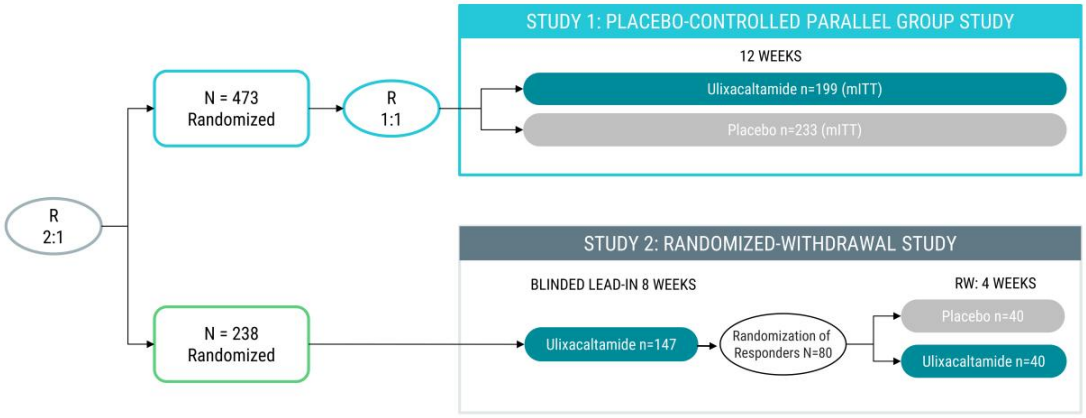
Several important clinical questions answered successfully and support NDA filing



Study Outcomes

- First positive Phase 3 program for a drug in Essential Tremor
- Both studies in the Essential3 Program met their primary endpoints
- Generally well tolerated, with no drug-related SAEs
- Pre-NDA meeting with the FDA in Q4 2015

Essential3: An ambitious and innovative Phase 3 program

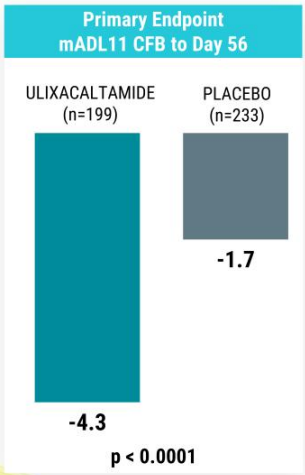


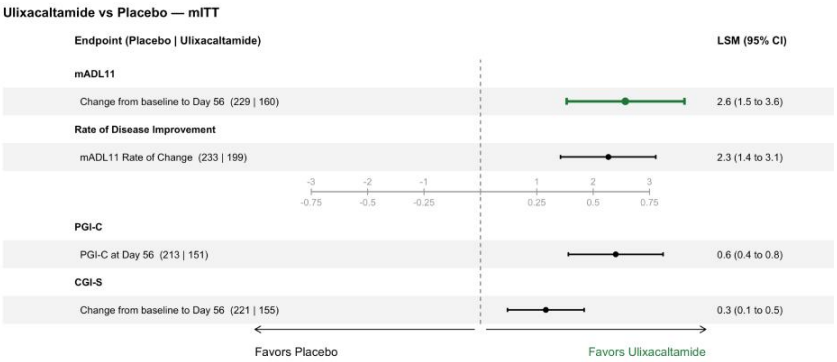
Blinded randomization 2:1 (Study 1: Study 2) occurred following completion of screening
Blinded randomization 1:1 (Ulixacaltamide: Placebo) for treatment arm allocation in Study 1 and for treatment arm allocation of Responders into the randomized withdrawal phase in Study 2

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)

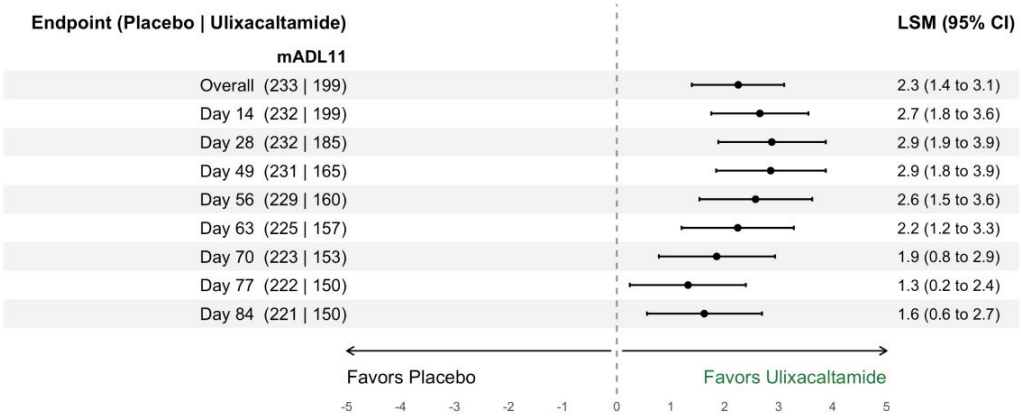
Study 1 - Primary and all key secondary efficacy endpoints met



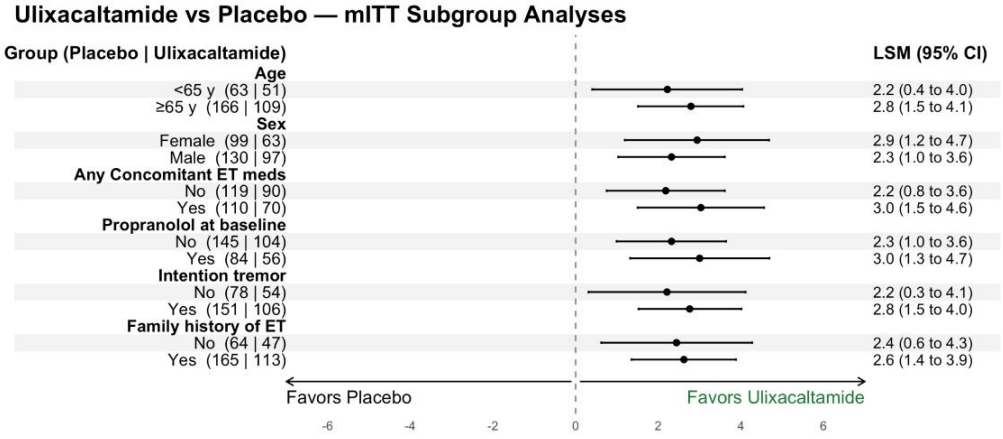


LS means for the mADL11 were estimated using a mixed model for repeated measures with treatment group, visit (categorical), treatment-by-visit interaction, randomization strata (IT status, propranolol use, family history of ET), and baseline mADL11 score as fixed effects; subject was a random effect 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

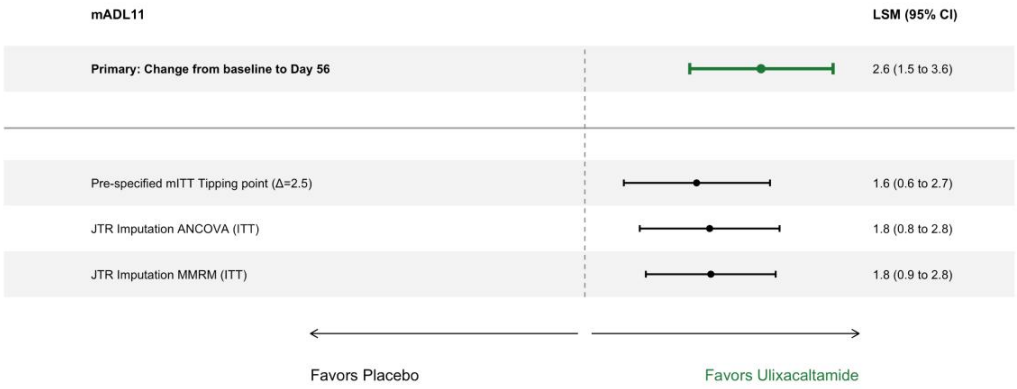


Study 1 efficacy – Robust response across subgroups



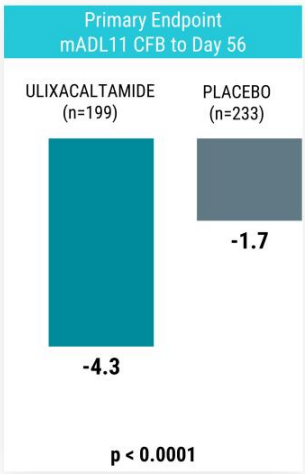
Study 1 Efficacy remains significant under extreme scenarios

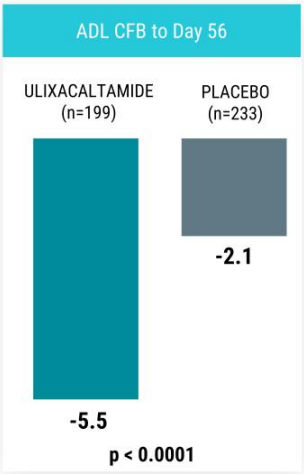
Ulixacaltamide vs Placebo — (Primary + Sensitivity Analyses)



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. Jump to reference (JTR) sensitivity conducted using the ITT population with both the MMRM and ANCOVA models.

Study 1 –Clinical meaningfulness with mADL11 and ADL



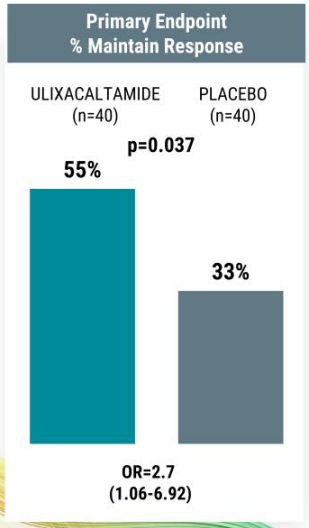


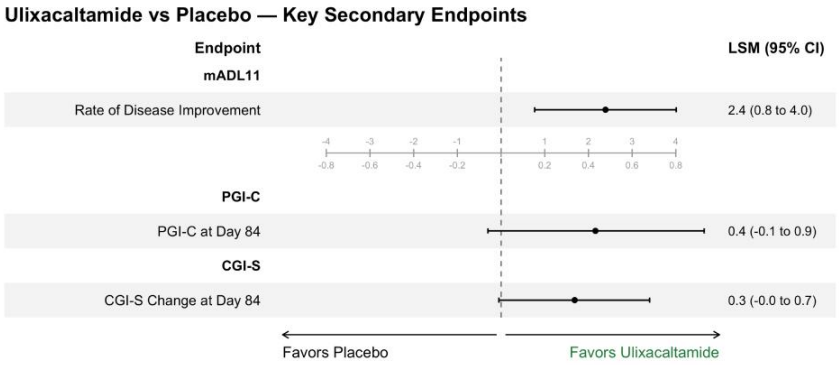
LS means for the mADL11 were estimated using a mixed model for repeated measures with treatment group, visit (categorical), treatment-by-visit interaction, randomization strata (IT status, propranolol use, family history of ET), and baseline mADL11 score as fixed effects; subject was a random effect 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 ($\Delta = 2.5$; $p = 0.0026$), exceeding the ~½ SD robustness criterion of Ratitch et al. (2013) and confirming strong resilience of the primary endpoint to non-MAR assumptions.

Study 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)

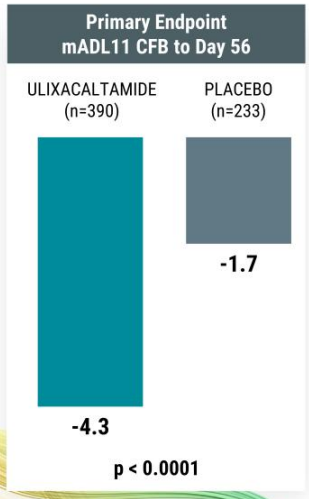
Study 2 efficacy - Primary and first secondary endpoint met

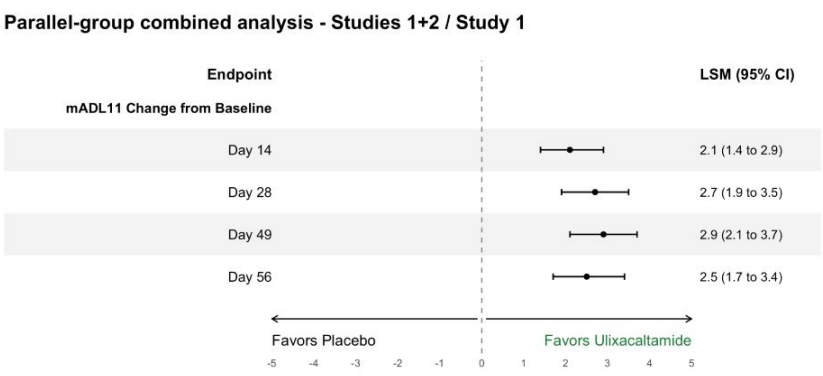




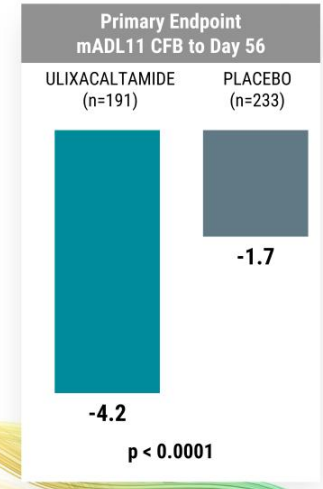
For primary endpoint, odds ratio, 95% confidence interval, and p-value were obtained from a logistic regression model including treatment group as the main effect and randomization strata (IT status, propranolol use, and family history of ET) as fixed effects.

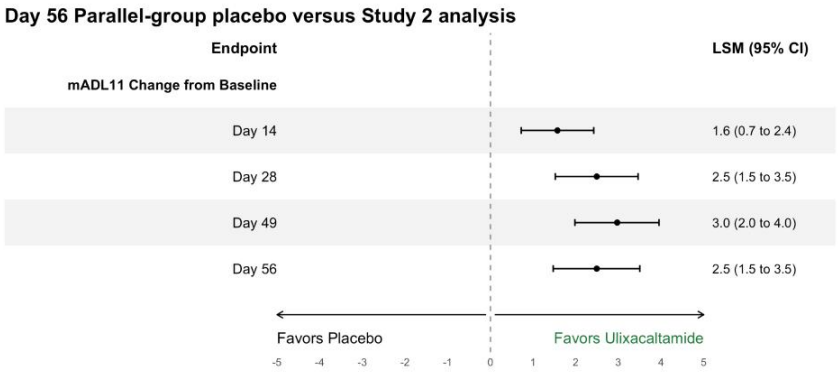
Hypothesis 3– Day 56 Parallel-group combined efficacy analysis





Hypothesis 4– Day 56 Parallel-group combined efficacy analysis





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

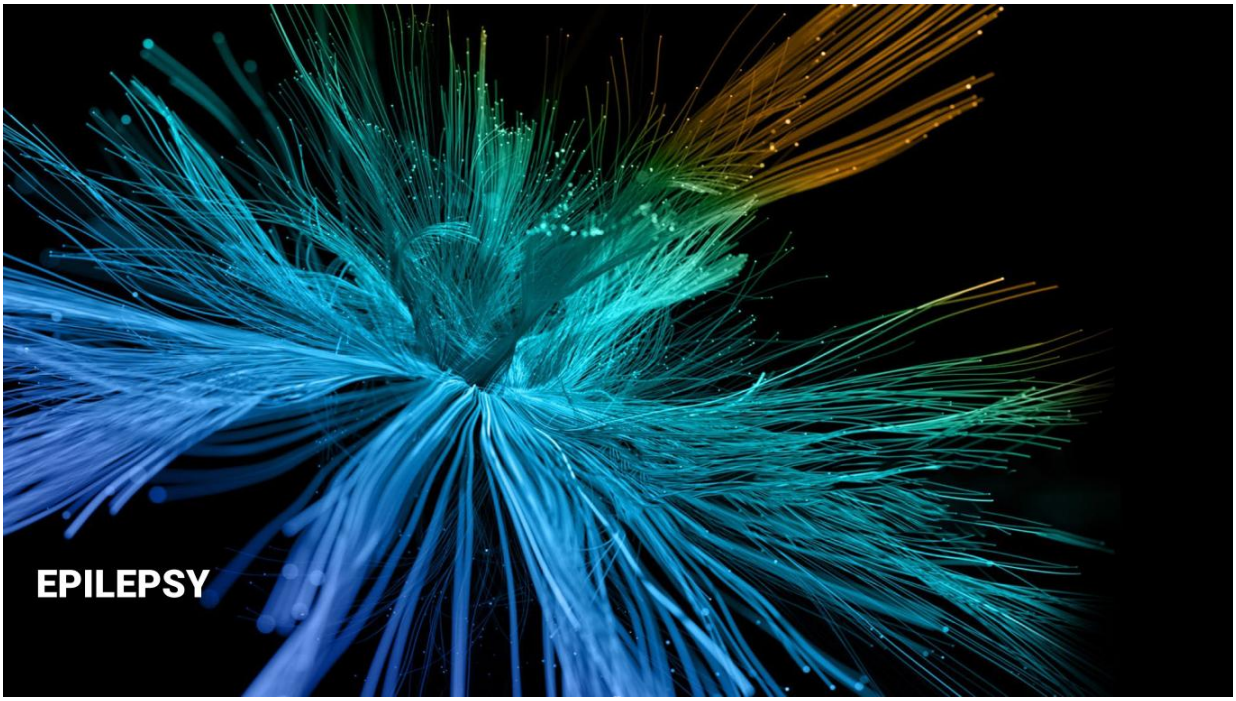
OVERVIEW OF ADVERSE EVENTS			
	STUDY 1		STUDY 2
	ULIXACALTAMIDE (N = 233)	PLACEBO (N = 234)	ULIXACALTAMIDE (N = 231)
Participants with any TEAE	221 (94.9%)	177 (75.6%)	209 (90.5%)
Participants with: Mild TEAEs	98 (42.0%)	89 (38.0%)	87 (37.7%)
Moderate TEAEs	109 (46.8%)	78 (33.3%)	105 (45.5%)
Severe TEAEs	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%)


EPILEPSY

The Praxis Epilepsy portfolio targets significant unmet need and market opportunity in the common and rare epilepsy markets

Program	US Prevalence	US Market Opportunity
Vormatrigine Sodium channel modulator	**3.5M** Common Epilepsy	**>$2.5B**
Relutrigine Sodium channel modulator	**>200k** Developmental Epilepsies with high seizure burden using sodium channel blockers*	**>$3B**
Elsunersen Gapmer ASO	**~2K SCN2A** Genetically typified Developmental Epilepsies	**>$500M**

* Poke G, Stanley J, Scheffer IE, Sadleir LG. Epidemiology of Developmental and Epileptic Encephalopathy and of Intellectual Disability and Epilepsy in Children

Focal epilepsy is a serious medical condition with inadequate therapeutic options impacting approximately 3M patients in the US

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

63% of patients require multiple ASMs[1]

Patients need a new therapy:

- That is tolerable so they adhere and can maintain Quality of Life
- That is fast acting, simple to take and durable
- That stops ASM cycling

1. Praxis Claims Analysis on File 2024. FOS patient cohort (n = 440k)
ASM: Anti-Seizure Medication

Vormatrigine is poised to quickly transform the epilepsy landscape

Superior Efficacy

Best-in-disease efficacy in the RADIANT study

Ease of Administration

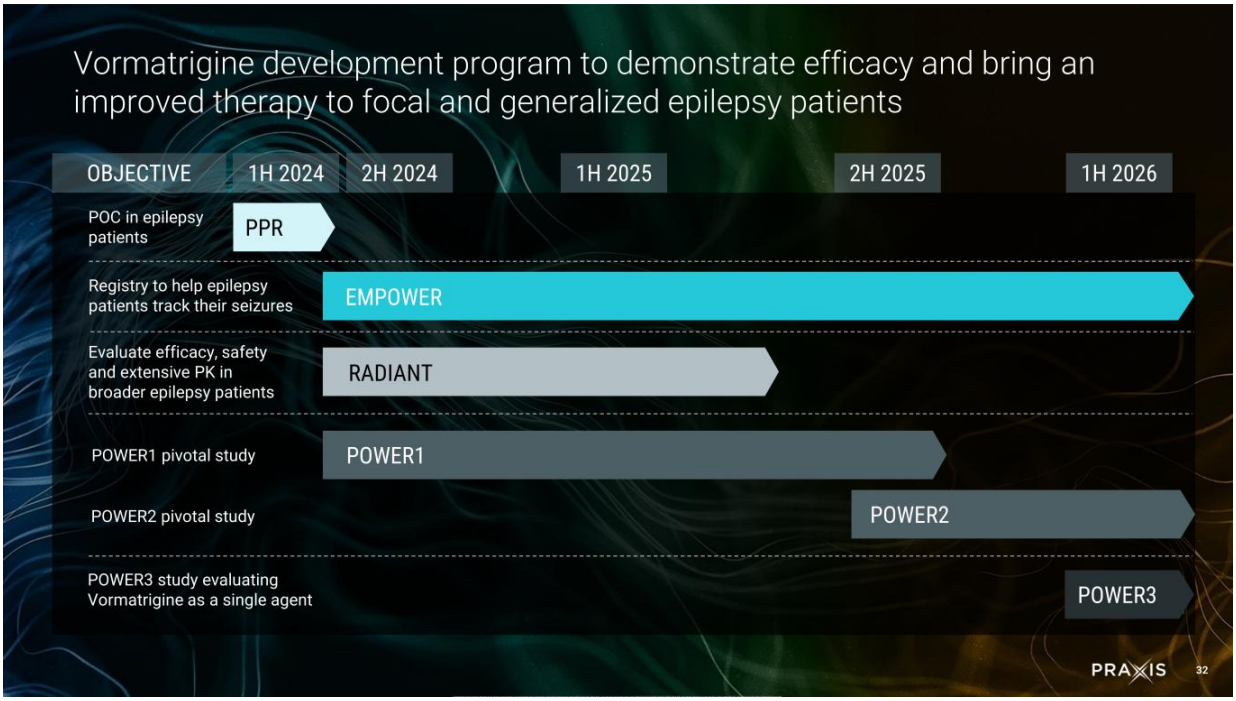
Once daily dose, fast acting

No need to be taken with food or require dietary changes

Ideal Tolerability and Limited DDIs

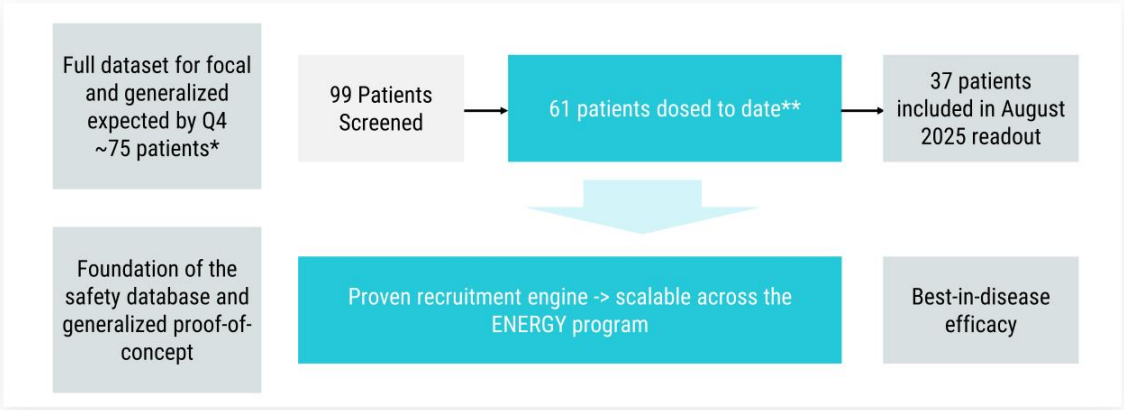
No expected restrictions with co-administration with other ASMs or common contraceptive agents

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.


Vormatrigine development program to demonstrate efficacy and bring an improved therapy to focal and generalized epilepsy patients
OBJECTIVE
1H 2024
2H 2024
1H 2025
2H 2025
1H 2026
POC in epilepsy patients
PPR
Registry to help epilepsy patients track their seizures
EMPOWER
Evaluate efficacy, safety and extensive PK in broader epilepsy patients
RADIANT
POWER1 pivotal study
POWER1
POWER2 pivotal study
POWER2
POWER3 study evaluating Vormatrigine as a single agent
POWER3
PRAXIS
32

RADIANT study: Best-in-class execution in epilepsy

First cohort data shared in August 2025



* Includes patients currently in screening
** First cohort ss of July 25, 2025 cut-off

RADIANT Phase 2 study showed disease-leading efficacy

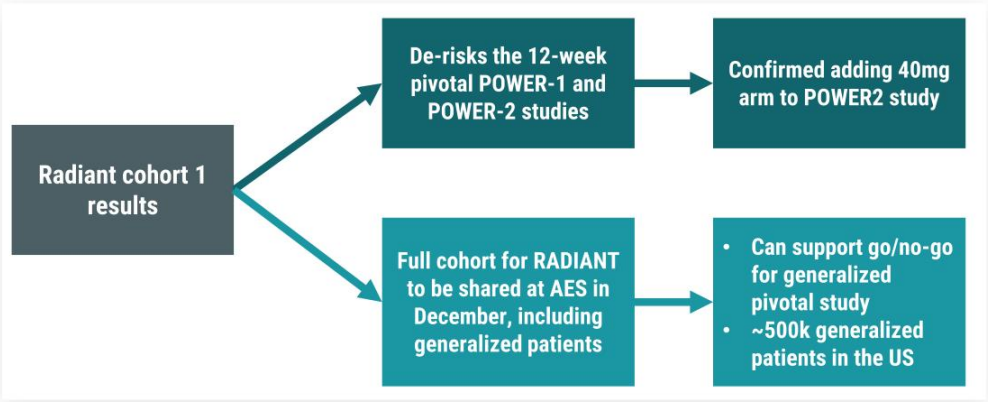
8-week study with focal patients showed a 56% median seizure reduction from baseline

Criteria	RADIANT Cohort 1 Results[1]
Speed and durability of response	54% of patients had >50% seizure (response) in the first week and 67% of patients had response by week 8
Efficacy with other ASMs	Patients were on an average of 2.2 ASMs 55% of patients on best approved drug (Cenobamate) had response
Seizure freedom	14% of patients were seizure free for entire 8 weeks and 22% were seizure free over the last 4 weeks
Safety & tolerability	52% with AEs, mostly mild/moderate and resolved 6 patients down-titrated background ASMs

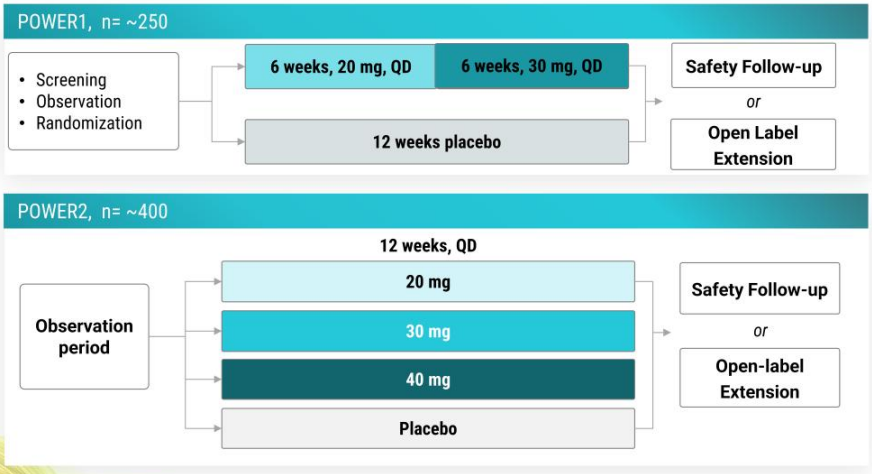
- **8-week RADIANT results de-risks efficacy for POWER1 and POWER2 12-week studies**
- **Full cohort for RADIANT, including generalized patients, to be shared at 2025 AES**

1. Results from Radiant cohort1 study results shared August 4, 2025

First cohort of RADIANT provides confidence and opportunity for ENERGY program

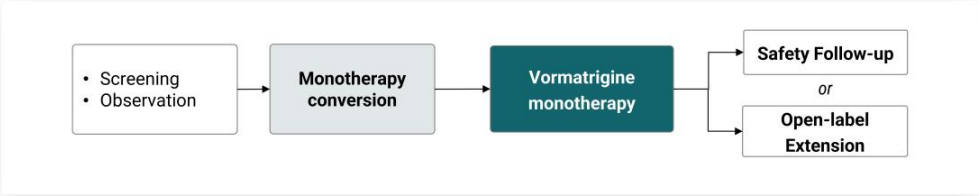


Pivotal POWER1 study completing end of 2025, POWER2 enrollment complete 2H 2026



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

POWER3 designed to demonstrate the potential of vormatrigine as a stand-alone agent, expect to initiate 1H 2026



- 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

Relutrigine: Potential for class leading efficacy and tolerability

Relutrigine

- **Oral suspension, no titration, once daily administration**
- **Formulated for pediatric use**
- **Small molecule**
- **Functional state modulator**

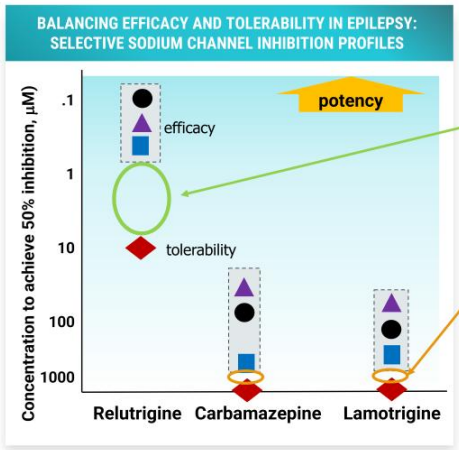
- Superior selectivity for hyperactive Na_V channels, a known cause of seizure manifestation in all DEEs regardless of etiology
- Demonstrated robust seizure reduction and unprecedented seizure-freedom per 28-day period
- Generally well-tolerated with mostly mild to moderate AEs, no drug-related SAEs 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, NaV=voltage-gated sodium channel, SAE=serious adverse event

Differentiated profile enabling wide therapeutic index

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

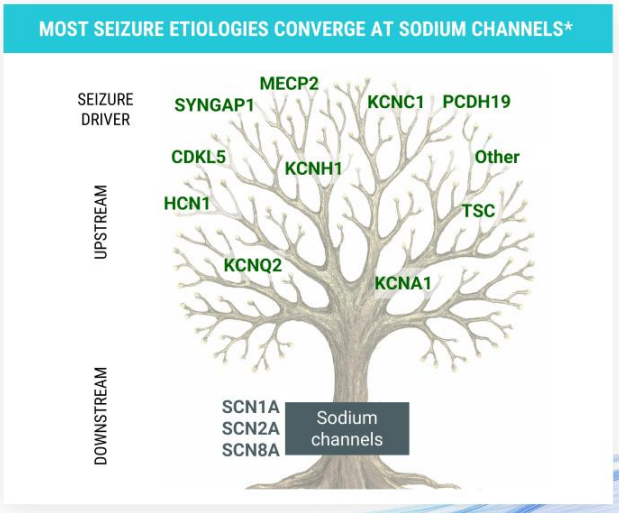
Pathological Excitability Currents
- Currents:
  - Persistent
  - Voltage
  - Use-dependent
- Promote hyperexcitability
- Inhibition drives anti-seizure efficacy



Praxis data on file
hNav=human voltage-gated sodium channel, µM = micromolar, TI=therapeutic index

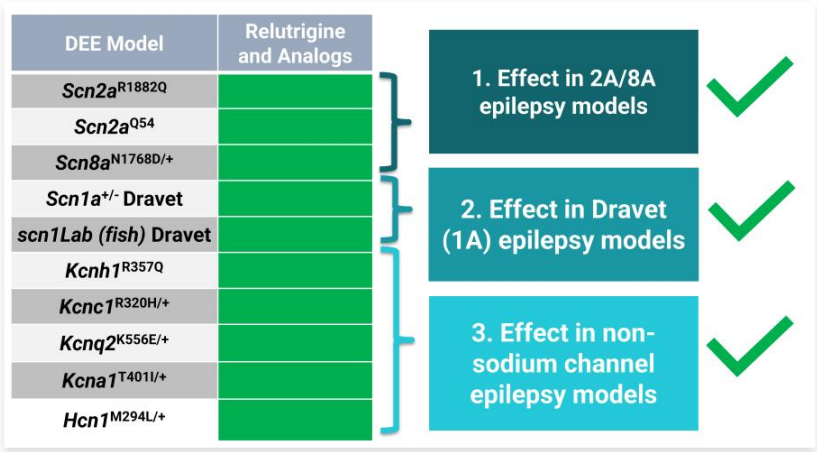
Relutrigine's potential for broad applicability across multiple etiologies

- 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
- 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, NaV=voltage-gated sodium channel

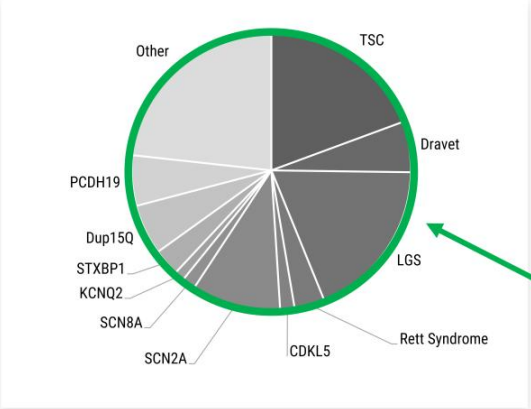
Consistent efficacy in diverse number of DEE models



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.

Current US DEE market is over 200,000 patients

Expected to increase in coming years as care and diagnosis improve



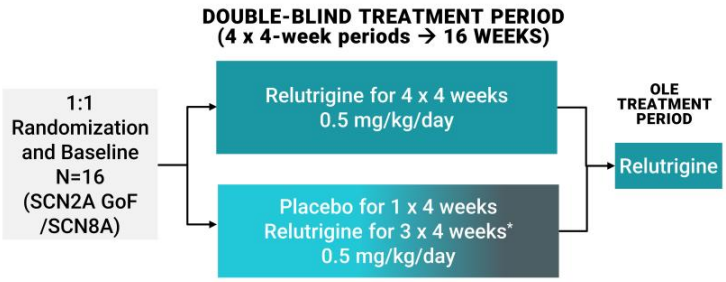
- Different levels of severity along the disease spectrum
- Opportunity for multiple approaches to address unmet need

EMERALD study expected to provide evidence to support a broad label

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

EMBOLD Cohort1 study design: controlled trial targeting DEE seizure burden in patients receiving standard of care ASMs

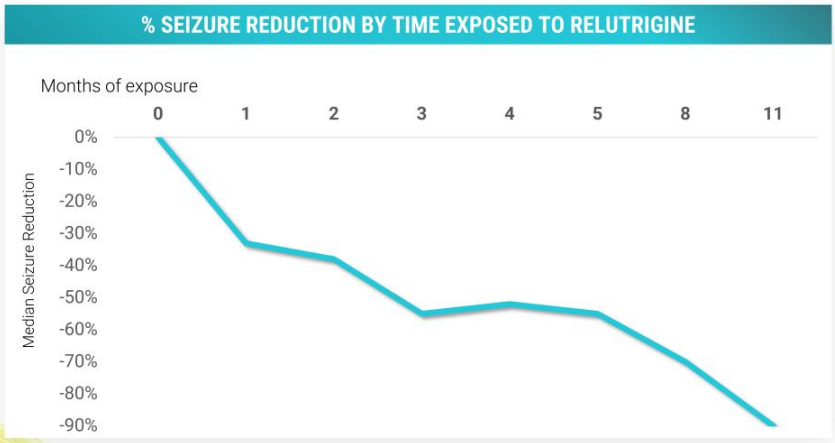


KEY ENDPOINTS:

- Incidence and severity of treatment-emergent adverse events (TEAEs)
- 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

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

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

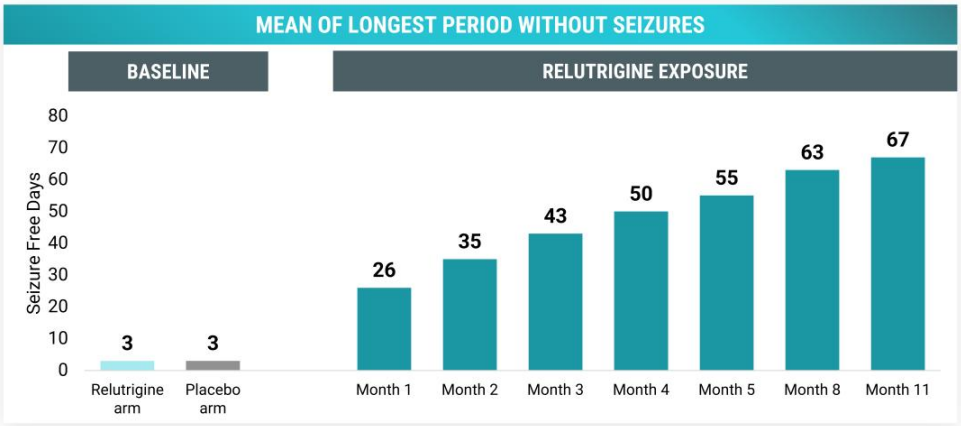
No dose reduction of relutrigine required

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

EMBOLD

PRAXIS 44

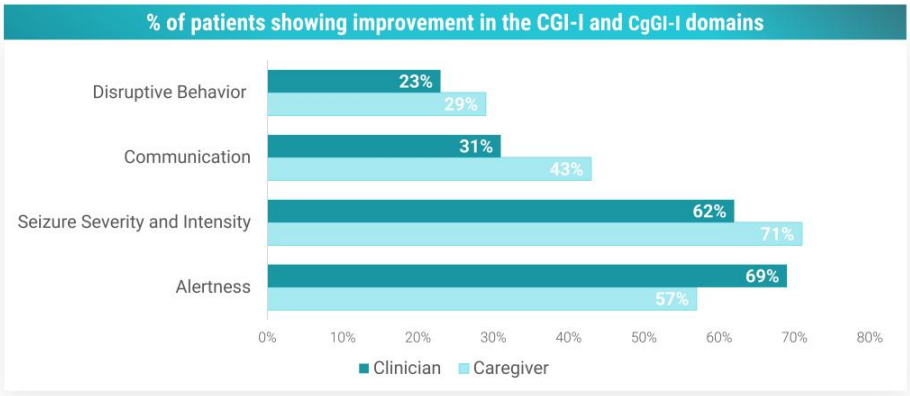
EMBOLD Cohort 1 results: sustained seizure-free periods reflect both clinical and daily life improvements



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

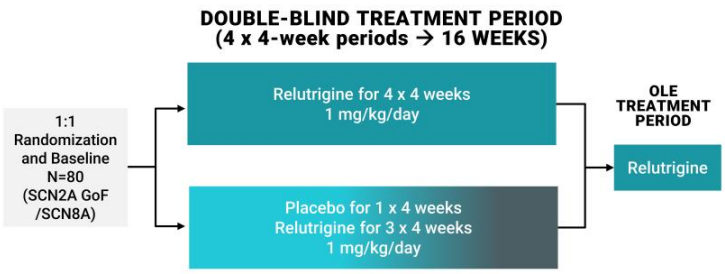
Relutrigine treatment led to disease modifying impact

Meaningful gains in overall well-being of patients, despite severity and historical lack of improvement with available treatments



Clinical Global Impression of Improvement and Caregiver Global Impression of Improvement assessed at Week-16 visit

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

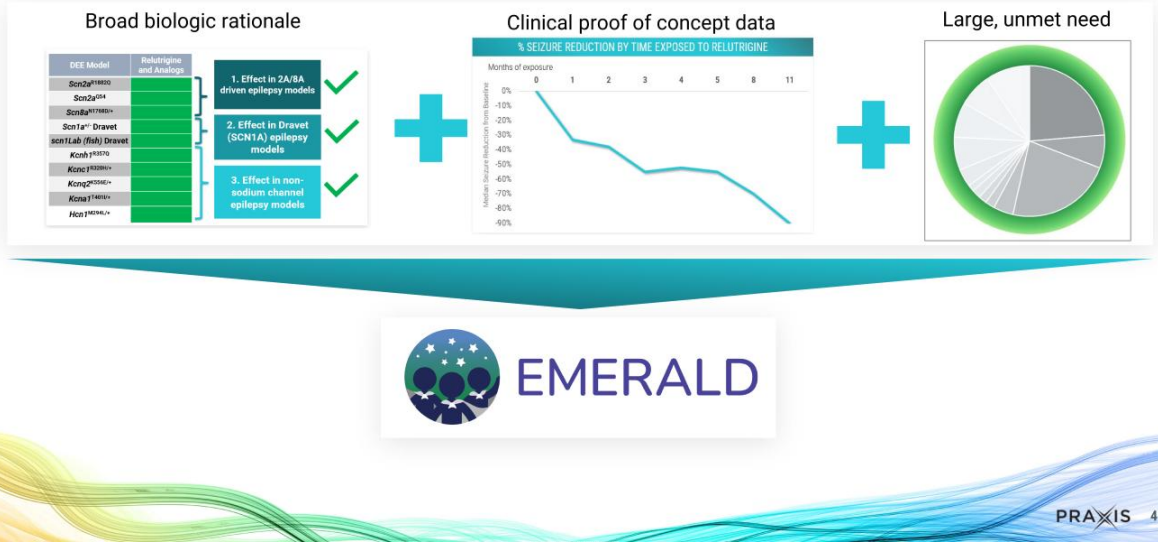


KEY ENDPOINTS:

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

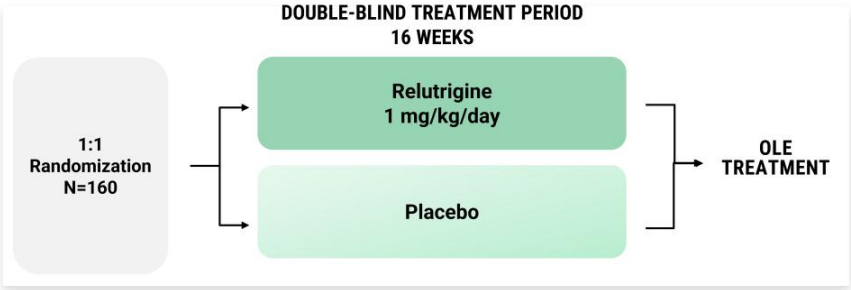
ClinicalTrials.gov Identifier: NCT05818553. https://clinicaltrials.gov/ct2/show/NCT05818553
ASM=anti-seizure medication, QD=daily

Relutrigine's clinical profile expanding with EMERALD study



EMERALD

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

Elsunersen is the first drug designed for SCN2A GoF DEE

ELSUNERSEN

SCN2A GoF

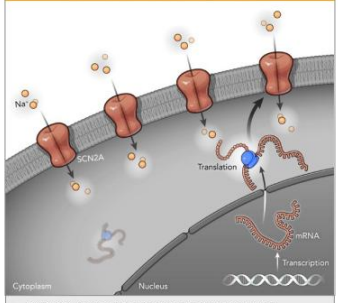
INTRATHECAL

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

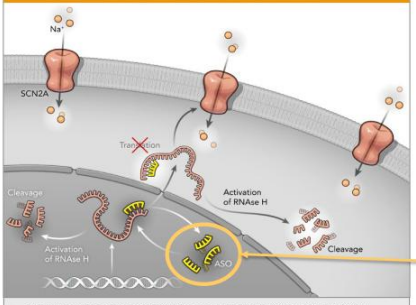
Precision targeting of SCN2A GoF patients positions elsunersen as a potential disease-modifying therapy

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

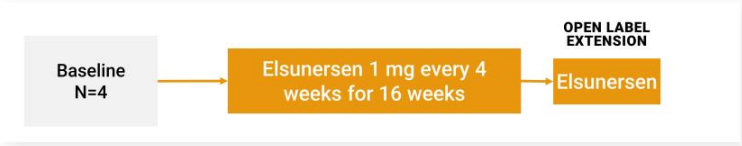
ASO TREATED: NORMALIZED SCN2A ACTIVITY

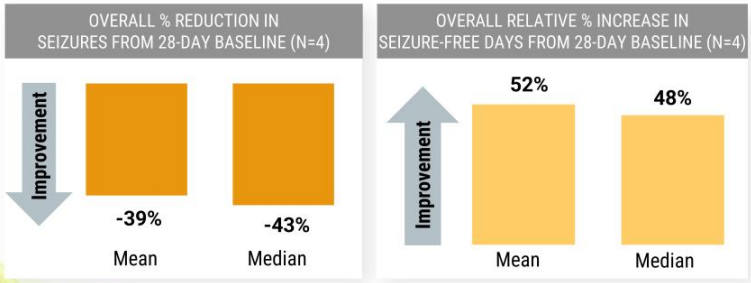


- Elsunersen selectively interacts with SCN2A mRNA causing RNase H1 mediated degradation
- The number of SCN2A sodium channels is reduced, which normalizes ion flow and reduces seizure activity

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

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**

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**
- **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

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


PRAXIS
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