



Vormatrigine Rapidly Reduces Seizures in Adults with Treatment-Resistant Epilepsy: Results from the RADIANT Study

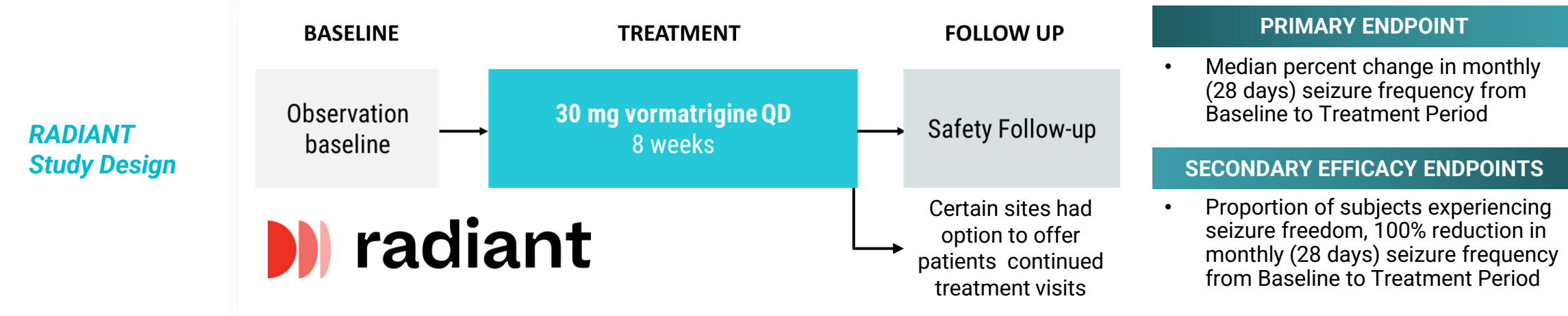
Karl Hansen¹, Bashar Mohsen², Noam Epstein¹, Maribel Hernandez¹, Megan Sniecinski¹, Kimberly Crimin¹, Minao Tang¹, Steven Petrou¹, Marcio Souza¹, Orrin Devinsky³, Ángel Aledo-Serrano⁴
¹Praxis Precision Medicines, Boston, MA, USA; ²Assertive Research Center, Miami Lakes, USA; ³NYU Langone Comprehensive Epilepsy Center, New York, NY, USA; ⁴Epilepsy Unit, Clinical Neuroscience Institute, Campus Blua Sanitas Valdebebas Hospital, Madrid, Spain

BACKGROUND

- Despite the availability of numerous antiseizure medications (ASMs), a large subset of the ~50 million people living with epilepsy worldwide still experience uncontrolled seizures.
 - Sodium channel blockers (SCBs) are central to current antiseizure treatment, yet tolerability issues and side effects restrict the extent to which patients can achieve optimal seizure control.
 - Vormatrigine selectively targets hyperexcitable sodium channels and is in development for adult FOS and generalized epilepsy with the potential to improve efficacy without compromising tolerability.
 - Recent data indicate superior preclinical and early clinical performance, favorable safety up to 45 mg, and no significant food effect.
 - Emerging data show that vormatrigine can exceed therapeutic target concentrations while remaining well tolerated without the need for titration.
 - The RADIANT study was designed to evaluate vormatrigine's efficacy, safety, and pharmacokinetics in adults with focal onset seizures (FOS) or primary generalized tonic-clonic seizures (PGTCS).
- **Here we present the latest results from all subjects dosed to date and highlight seizure-efficacy outcomes beyond the initial 56-day treatment period.**

RADIANT STUDY DESIGN

- RADIANT (NCT06908356) is a Phase 2, open-label, single-arm, multicenter clinical trial enrolling participants aged 18-75 years diagnosed with FOS or PGTCS.
- Participants received vormatrigine 30 mg daily for 8 weeks, with the study consisting of Screening/Observation (Baseline), Treatment and Follow-up periods.
- Based on local regulations and site availability, some patients were eligible to continue receiving vormatrigine beyond 8 weeks.



PARTICIPANT ELIGIBILITY AND BASELINE CHARACTERISTICS

Key Inclusion Criteria

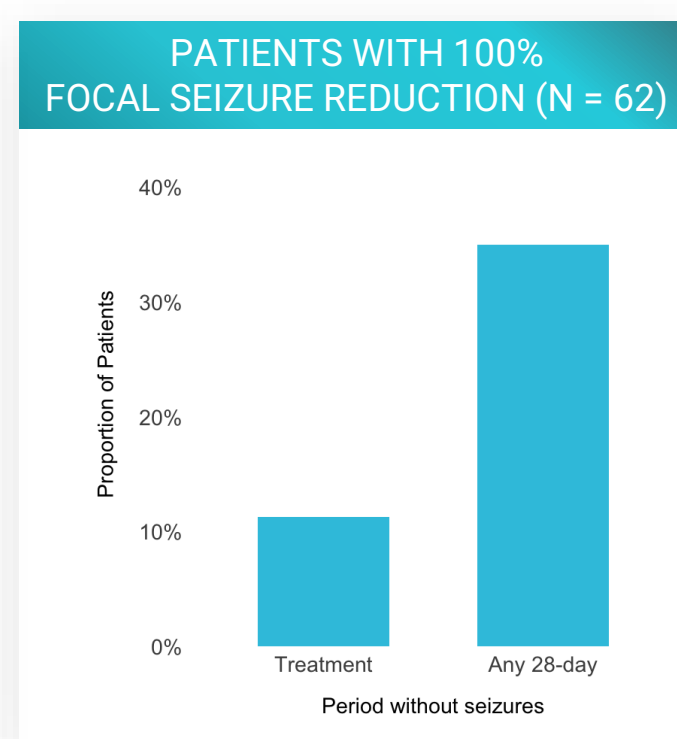
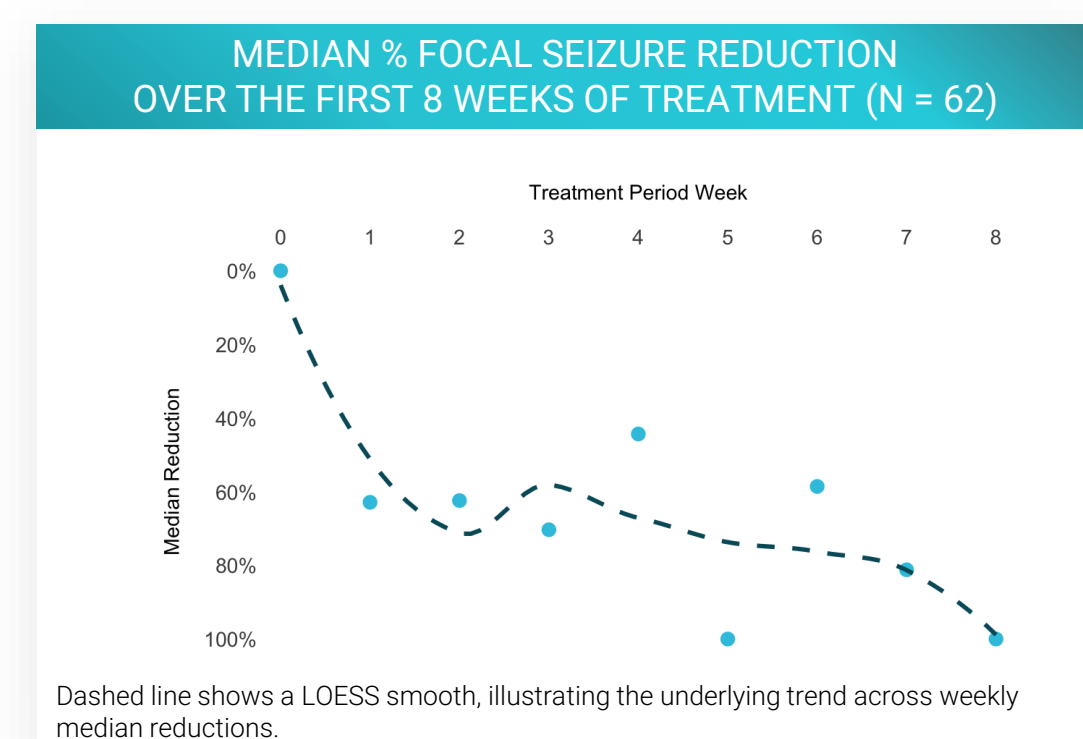
- FOS or idiopathic PGTCS, with progressive causes excluded by CT/MRI
- Aged 18-75 years
- ≥2 countable seizures in screening for FOS or ≥1 countable in screening for PGTCS patients
- On 1-3 ASMs for ≥4 weeks prior to screening

Demographics and Baseline Characteristics

	N = 65
Age (years), mean (SD)	43.0 (14.45)
Sex (Male, Female)	29, 36
# Background ASMs, mean (SD)	2.1 (0.85)
Concomitant ASM	
Sodium Channel Blocker*	77%
SV2A	59%
GABA modulators	29%
Others	12%
Baseline seizures, median (IQR)	9.0 (4, 21)

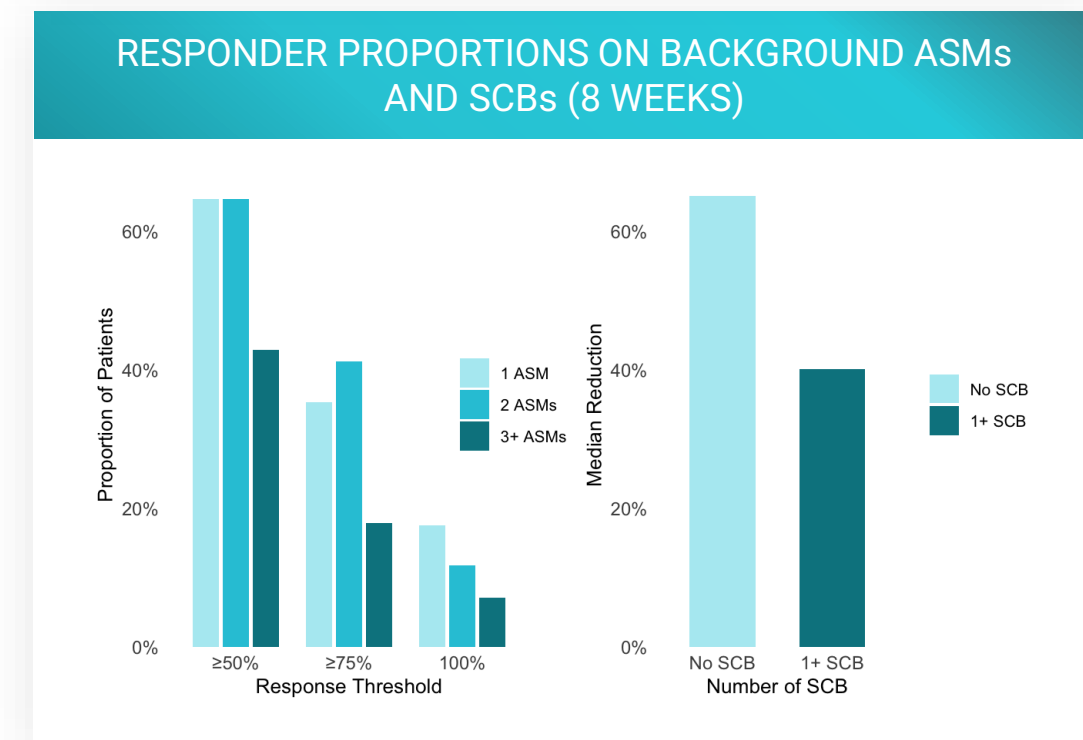
*35% of FOS patients were on cenobamate at baseline

RADIANT – VORMATRIGINE AS A POTENTIAL BEST-IN-DISEASE THERAPY



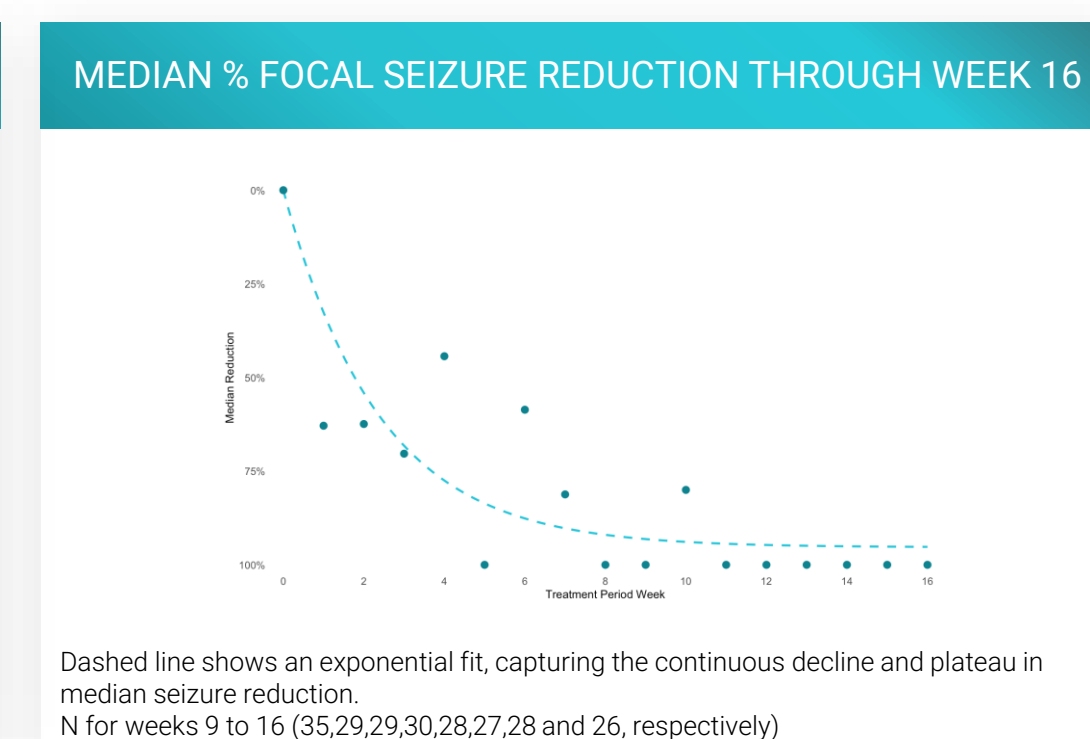
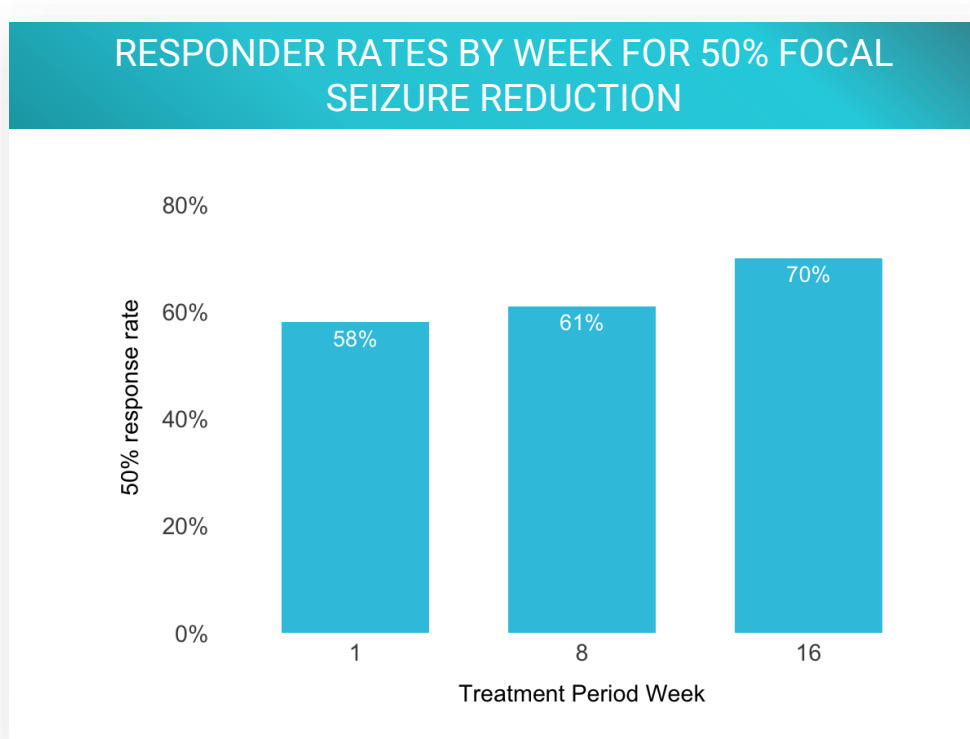
Rapid and Sustained Seizure-Reduction Profile

- Rapid response after 1 week of dosing.
- Median seizure reduction improves steadily; ~100% by Week 10 and maintained through Week 16.
- Seizure-free intervals emerge early, with over one-third of patients achieving ≥28 days without seizures.
- Seizure-freedom in over 11% of patients within the treatment period.

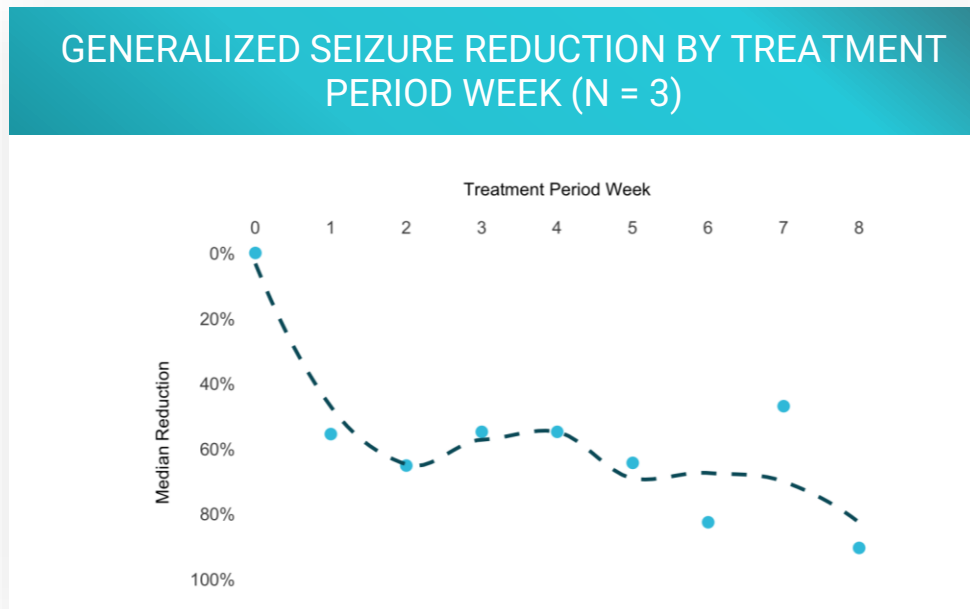


Efficacy Profiles on Background Therapy Support Vormatrigine's Intrinsic Activity and Monotherapy Potential

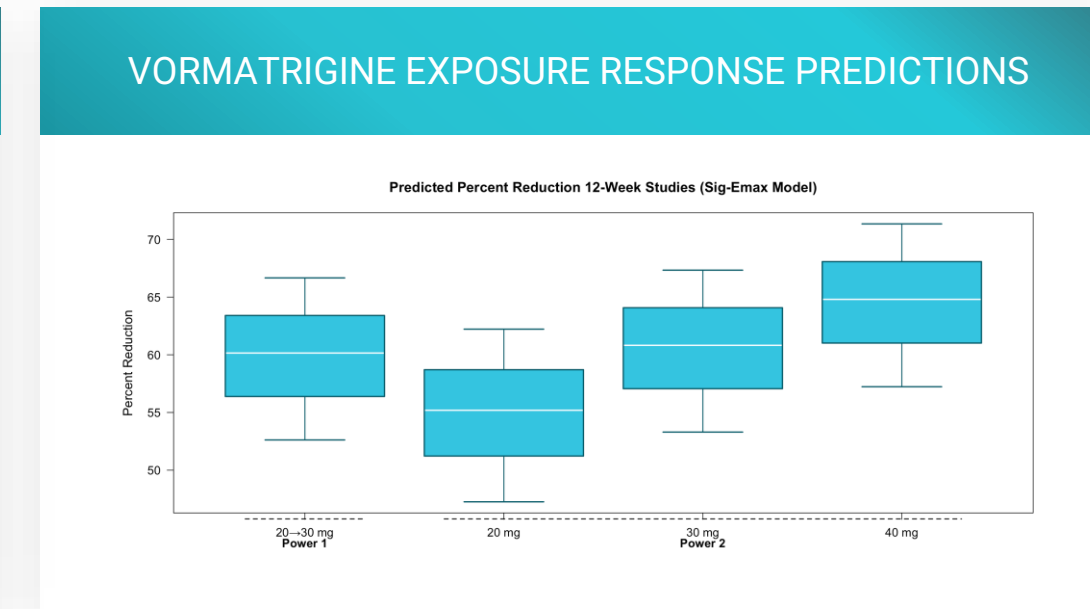
- Participants were on an average of 2.1 ASMs with >30% on cenobamate.
- Highest responder rates were observed with fewer background ASMs, indicating clearer expression of the drug's intrinsic effect.
- Greater median reductions with no SCB compared to 1+ SCB, revealing the drug's full pharmacologic impact.
- Strong response in combination with 1+ SCB supports both flexibility in combination use and independence from polytherapy.
- Maintained efficacy under heavier ASM or SCB loads reflects a robust stand-alone effect, consistent with monotherapy potential.



Rapid, Sustained Seizure Reduction in PGTCS Patients



Model-based Simulation Supports POWER1 and 2 Designs



VORMATRIGINE SAFETY PROFILE

RADIANT Tolerability Summary – Topline Results (With Comparator Reference Data)*

	VORMATRIGINE 30 mg (N = 65)	CENOBAMATE 400 mg (N = 111)	XEN1101 25 mg (N = 124)
Study	RADIANT	Study C017 ¹	X-TOLE2 ²
Discontinuation	16 (25%)	30 (27%)	18 (14.5%)
Patients with ≥1 TEAE	44 (68%)	100 (90%)	102 (82.3%)
Serious AEs (SAEs)	4 (6%)	8 (7%)	7 (5.6%)
CNS-Related AEs			
Dizziness	21 (32%)	37 (33%)	39 (31.5%)
Somnolence	8 (12%)	41 (37%)	12 (9.7%)
Headache	9 (14%)	12 (11%)	14 (11.3%)
Tremor	0	Not reported	15 (12.1%)
Aphasia	0	Not reported	12 (9.7%)
Dysarthria	0	Not reported	8 (6.5%)
New Safety Signals (X-TOLE2)			
Confusional state	1 (2%)	Not reported	13 (10.5%)
Eye disorders (all)	6 (9%)	Not reported	24 (19.4%)
Renal/Urinary (all)	2 (3%)	Not reported	18 (14.5%)
Titration	None	12-weeks	None
Food Effect	None	None	Yes; Evening w/ food
Significant DDIs	N/A ³	Multiple	CYP3A

- Lowest rate of TEAEs and CNS AEs with modern ASMs.*
- Most AEs were mild to moderate and transient.
- All severe and serious AEs recovered and resolved.

¹Cenobamate: Krauss et al. *Lancet Neurol.* 2020;19(1):38–48; https://www.ema.europa.eu/en/documents/assessment-report/ontozry-epar-public-assessment-report_en.pdf
²XEN1101 X-TOLE2: Phase 3 topline (2026 8-K Disclosure). N from 1:1:1 randomization of 374 safety population
³Patel et al AES 2025 and PRAX data available to-date
 *Not a head-to-head comparison
 AE=adverse event; DDI=drug-drug interaction; TEAE=treatment emergent adverse event

CONCLUSIONS

- RADIANT results position vormatrigine as a best-in-disease therapy demonstrating fast-acting efficacy without titration, sustained seizure reduction over longer treatment duration, seizure-freedom potential, alongside favorable DDI, tolerability and safety profiles with once-daily dosing.
- Increasing and sustained effect observed in FOS patients, reaching 100% median weekly seizure reduction by Week 8, and maintained from Week 10 through Week 16.
- Seizure-freedom emerged early, with roughly one-third of patients achieving ≥28 consecutive seizure-free days during the treatment-period assessments, and ~11% attaining complete seizure freedom.
- Greater response rates and efficacy under minimal background therapy demonstrate vormatrigine's intrinsic activity and monotherapy potential, to be studied in the POWER3 study expected to initiate in 1H 2026.
- Patients with generalized epilepsy also demonstrated rapid and sustained seizure reduction, reinforcing the broad potential of vormatrigine across seizure types.
- Exposure response modeling predicts significant seizure reduction across a range of doses, validating the POWER1 and POWER2 study designs.

REFERENCES

- GBD 2021 Global Prevalence Data *Lancet Public Health*
- WHO 2023 Epilepsy Fact Sheet
- Seiden & Connor 2022 *Epilepsy & Behavior*
- Kahlig et al AAN 2023
- Hansen et al IEC 2023
- Bialer et al 2024 *Epilepsia*
- Anderson et al AES 2023
- Hansen et al EEC 2024
- Anderson et al AES 2024
- Hansen et al AAN 2025
- EU CTR 2024. EudraCT 2021-001433-39. Neurocrine Biosciences
- Krauss et al 2020 *Lancet Neurol*
- XEN1101 X-TOLE2: Phase 3 topline (2026 8-K Disclosure)
- Patel et al AES 2025

Acknowledgments We thank the participants and their families and the RADIANT Study Team for their contributions to this work.

Funding All studies were funded by Praxis Precision Medicines. Medical writing and editorial assistance were provided by Lillian G. Matthews and Jamie Church in accordance with Good Publication Practice (GPP).

Disclosures OD, BM and AA have served as Praxis consultants or are Study Investigators. All other authors are current employees of Praxis Precision Medicines and may be Praxis stockholders.

- @PraxisMedicines
- Praxis Precision Medicines
- Praxismedicines.com
- clinicaltrials@praxismedicines.com



Presented at:
American Academy of Neurology Meeting
18-22 April 2026
Chicago, Illinois

