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

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Disclosure: Ángel Aledo-Serrano is a Study Investigator

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Innovative Epilepsy Treatments Needed Faster and More Than Ever



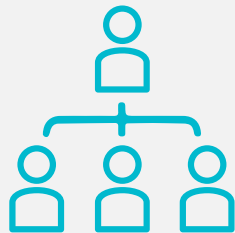
~50 MILLION PEOPLE
worldwide are affected by epilepsy



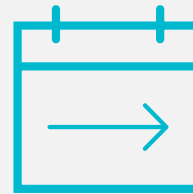
FOS and generalized epilepsy
account for >90% of epilepsy
cases in adults and children



Seizures and their frequency
are directly related to QoL and
outcomes in epilepsy patients



A significant number of patients remain
refractory, rapidly cycling through
treatment lines; 48% reach 3rd-line and
25% reach 5th-line ASM therapy



~35% of patients change
medications annually



63% require two or more
medications

Vormatrigine: Functionally Selective Sodium Channel Modulator in Development for Focal Onset Seizures (FOS) and Generalized Epilepsy

Vormatrigine

Focal and generalized epilepsies

No titration

Small molecule

Functional state modulator

Significantly more potent than competitive molecules in highly translatable pre-clinical models

Rapidly achieves therapeutic concentrations after once-daily dose with no food effect – **see also Poster P0022**

Ability to significantly exceed therapeutic concentrations while well tolerated – **see also Poster P0022**

Favorable tolerability profile and minimal drug-drug interaction risk with common ASMs – **see also Poster P0023**

ASM=antiseizure medication. Vormatrigine is an investigational drug and has not been approved by any regulatory body for use.

Kahlig et al. AAN 2023; Patel et al. AAN 2024; Hansen et al. IEC 2025; Hansen et al. AES 2025; Bialer et al. *Epilepsia*. 2024;00:1-27; Bialer et al. *Epilepsia*. 2026;00:1-51

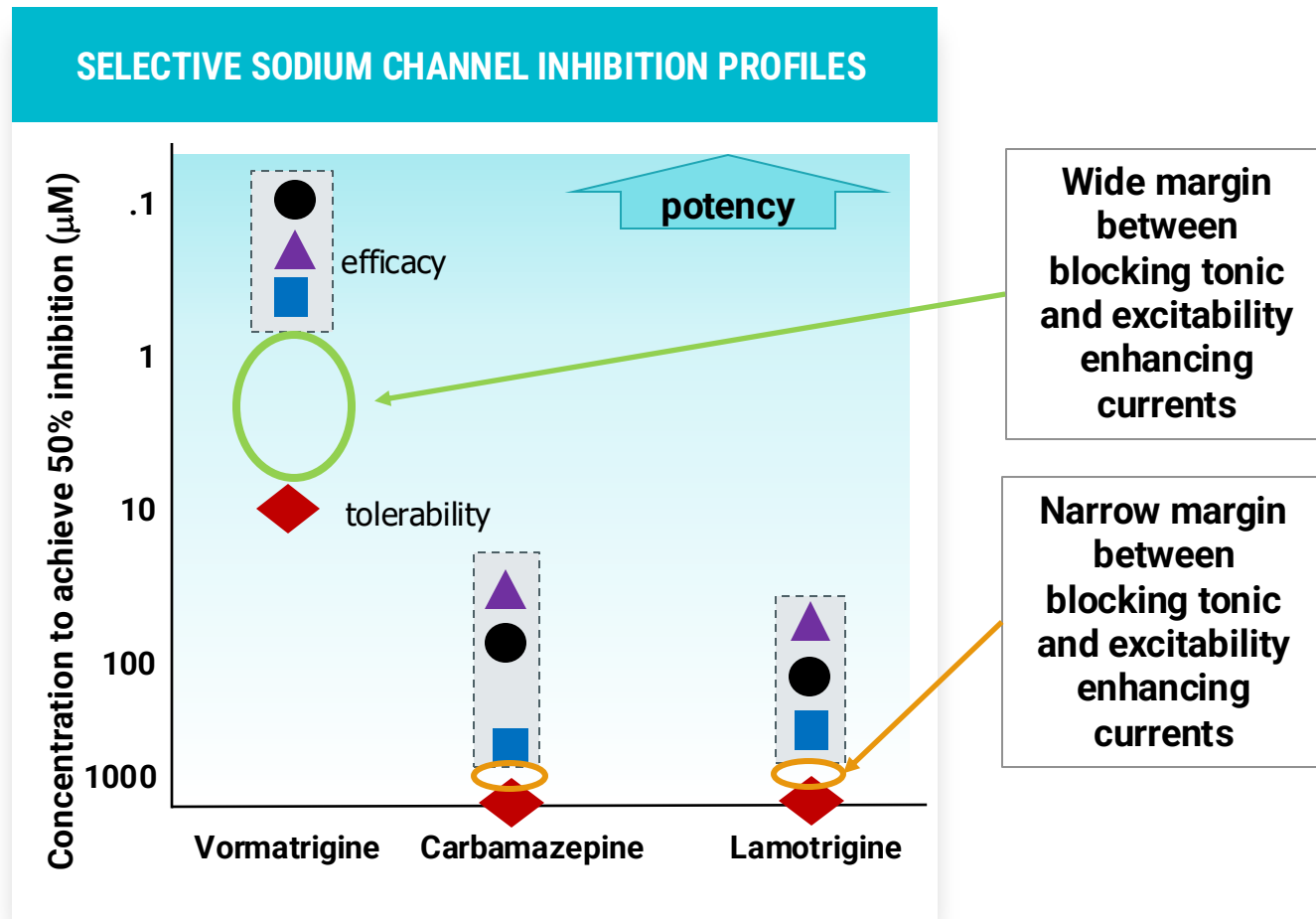
EEC 2026 Poster P0022; EEC 2026 Poster P0023

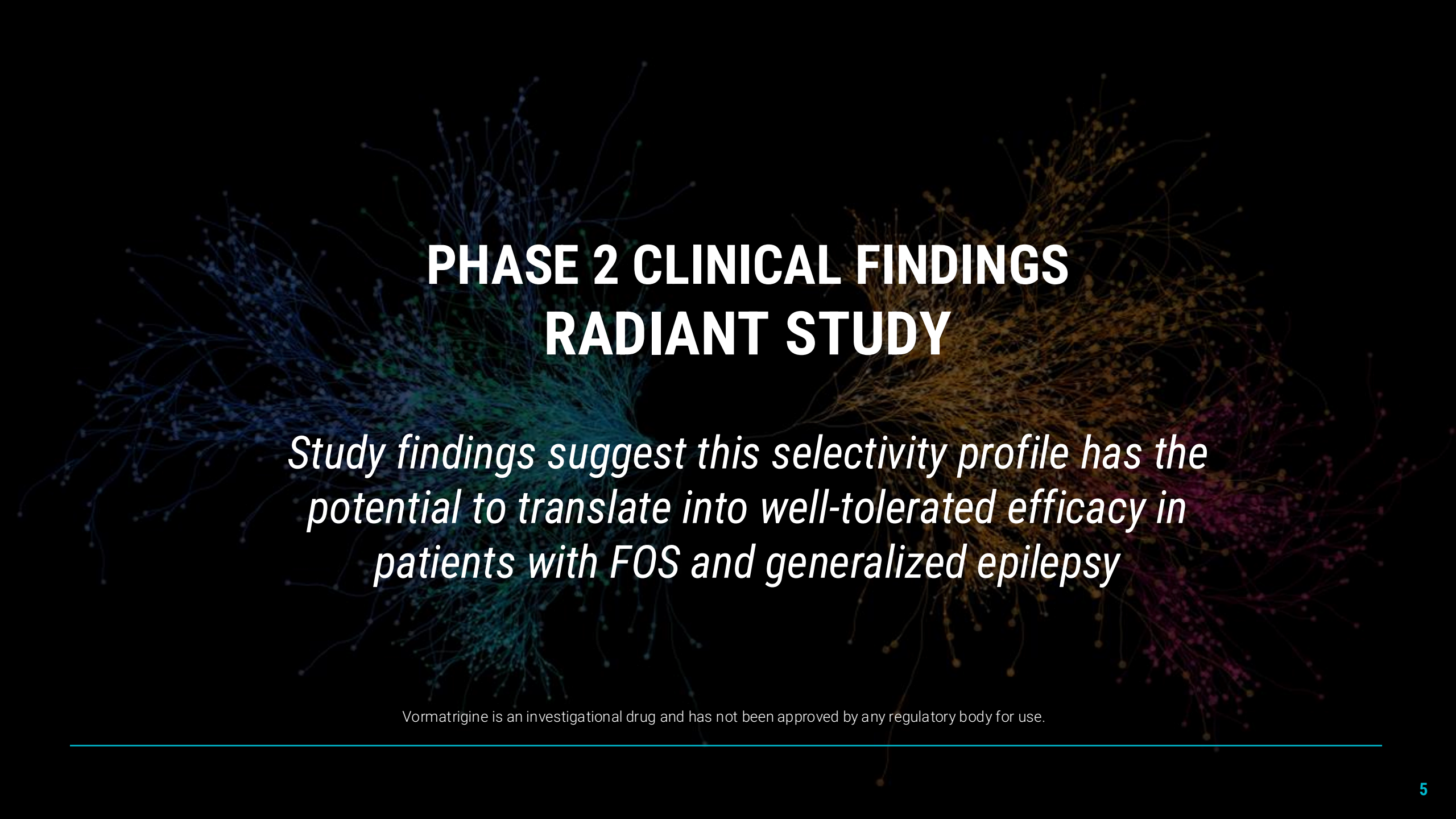
Differentiated Profile Enabling Wide Therapeutic Index

- ◆ **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





PHASE 2 CLINICAL FINDINGS RADIANT STUDY

Study findings suggest this selectivity profile has the potential to translate into well-tolerated efficacy in patients with FOS and generalized epilepsy

Vormatrigine is an investigational drug and has not been approved by any regulatory body for use.

RADIANT Study Overview



Primary Endpoint:

- Median percent change in monthly (28 days) seizure frequency from Baseline to Treatment Period

Secondary Efficacy Endpoints:

- Proportion of subjects experiencing seizure freedom, 100% reduction in monthly (28 days) seizure frequency from Baseline to Treatment Period

Key Inclusion Criteria

- A diagnosis of FOS or idiopathic PGTS according to ILAE Classification (2017), and progressive epilepsy cause ruled out on CT or MRI
- Male or female aged 18-75 years inclusive
- ≥ 2 countable seizures per month for FOS patients, or 1 countable generalized tonic-clonic seizure per month in the 3 months prior to screening for PGTS patients
- On 1–3 stable doses of ASMs for ≥ 4 weeks prior to screening

Participant Demographics and Baseline Characteristics

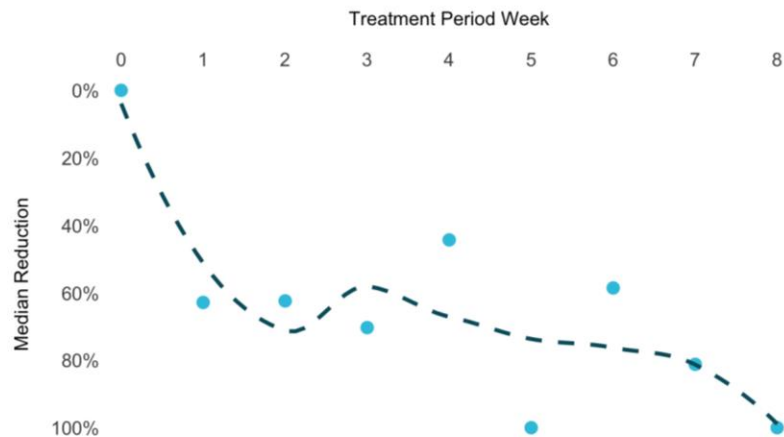
RADIANT participants represented the real-world refractory group

		VORMATRIGINE (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*	77%
	SV2A	59%
	GABA modulators	29%
	Others	12%
Baseline seizure	Median (IQR)	9 (4, 21)

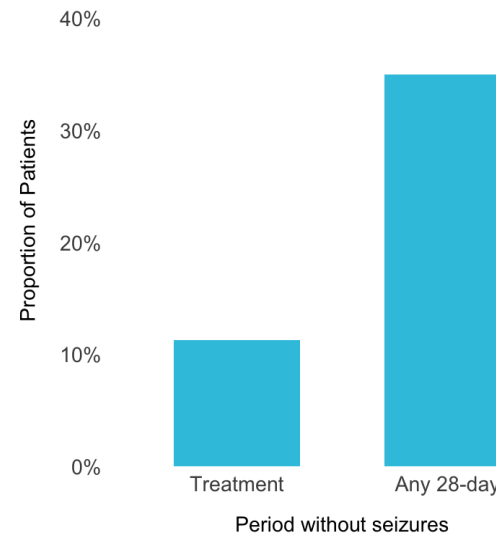
***35% of FOS patients were on cenobamate at baseline**

Rapid and Sustained Seizure Reduction and Seizure Freedom over the Initial 8-Week Treatment Period

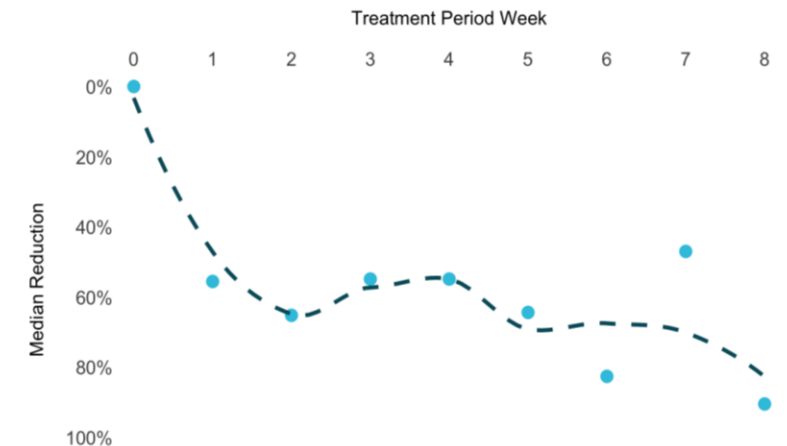
MEDIAN % FOCAL SEIZURE REDUCTION OVER THE FIRST 8 WEEKS OF TREATMENT (N=62)



PATIENTS WITH 100% FOCAL SEIZURE REDUCTION (N=62)



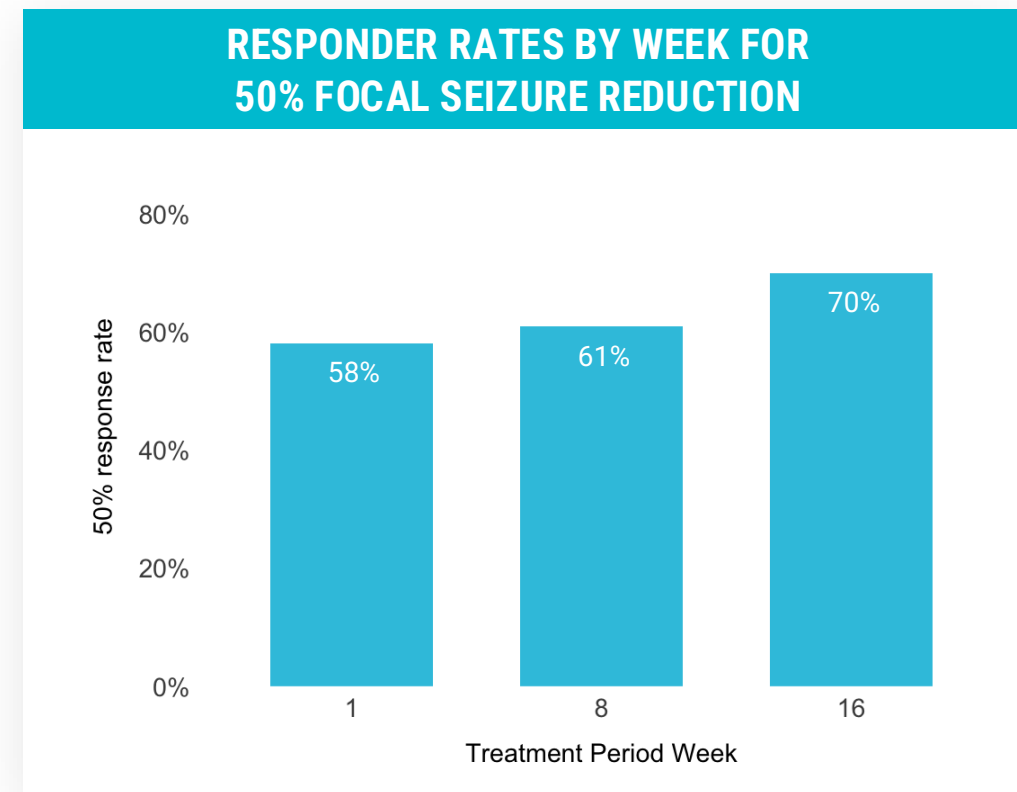
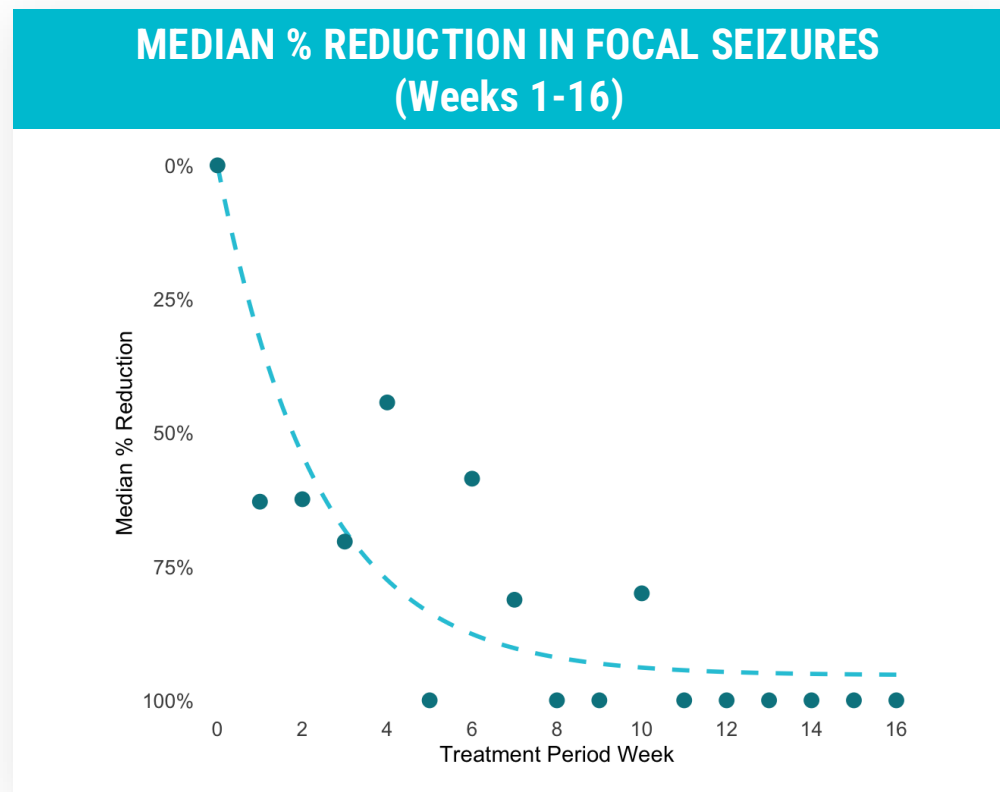
MEDIAN % GENERALIZED SEIZURE REDUCTION OVER THE FIRST 8 WEEKS OF TREATMENT (N=3)



Consistent Effect in Patients with Generalized Epilepsy

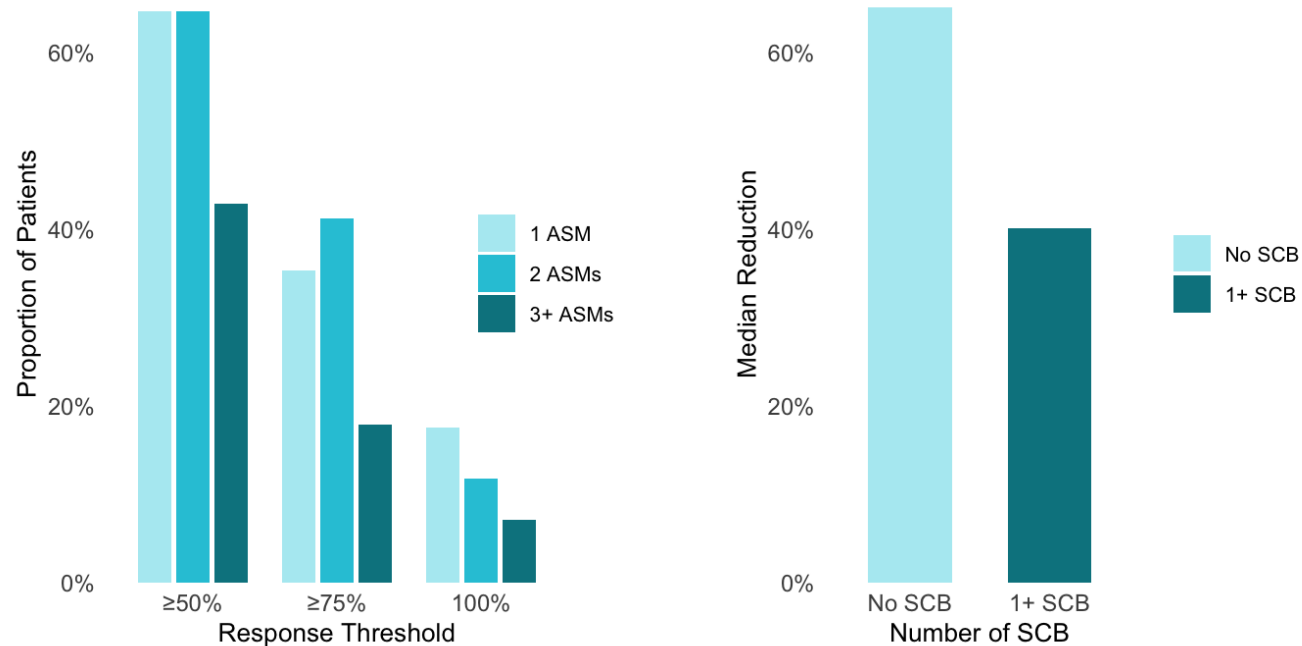
Seizure Reduction Improved Steadily & Maintained Through Week 16

Weekly Analyses Including Participants at Sites Participating in the Open-Label Extension Showed 100% Median Seizure Reduction after 10 Weeks



Efficacy Profiles on Background Therapy

RESPONDER PROPORTIONS ON BACKGROUND ASMs AND SCBs (8 WEEKS)



- Patients were on an average of 2.1 ASMs
- >30% of patients on best approved drug (cenobamate)

RADIANT Tolerability Summary

	VORMATRIGINE 30 mg (N=65)
Discontinuation	16 (25%)
Patients with ≥1 TEAE	44 (68%)
Patients with severe AEs	4 (6%)
Serious AEs (SAEs)	4 (6%)
Related SAE	1 (1.5%) ¹
CNS-Related AEs	39 (60%)
Dizziness	21 (32%)
Somnolence	8 (12%)
Headache	9 (14%)
Other Safety Signals	
Confusional state	1 (2%)
Eye disorders (all)	6 (9%)
Renal/urinary (all)	2 (3%)
Titration	None
Food Effect	None
Significant DDIs	N/A ²

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

AE=adverse event; CNS=central nervous system; DDI=drug-drug interaction; TEAE=treatment-emergent adverse event

¹Episode of diplopia, resolved after reduction of lamotrigine dose; ²Patel et al. AES 2025 and PRAX data available to-date; *Not a head-to-head comparison Hansen et al. AES 2025; Hansen et al. AAN 2026; Bialer et al. *Epilepsia*. 2026;00:1-51

RADIANT Study Summary

- **Rapid and Sustained Seizure Reduction.** Rapid response after 1 week of dosing, and median reduction maintained at 100% after 10 weeks. Participants with generalized epilepsy had similar benefit of participants with FOS, suggesting broad potential across seizure types.
- **Seizure-Freedom Potential.** Roughly one-third of patients achieved ≥ 28 consecutive seizure-free days, with $\sim 11\%$ attaining complete seizure freedom.
- **Favorable Safety and Tolerability.** Low rates of TEAEs and CNS AEs, with most AEs mild to moderate and transient.

Acknowledgements

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¹Praxis Precision Medicines, Boston, MA, USA; ²Assertive Research Center, Miami, FL, USA; ³NYU Langone Comprehensive Epilepsy Center, New York, NY, USA; ⁴Epilepsy Unit, Clinical Neuroscience Department, Blua Sanitas Valdebebas, Madrid, Spain

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Questions?



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