POWER1 – A Double-Blind, Randomized, Multicenter Phase 2/3 Study Evaluating the Efficacy and Safety of Vormatrigine in Adults with Focal Onset Seizures

Karl Hansen, Michael Steidle, Silvana Frizzo, Henry Jacotin, Dharit Patel, Noam Epstein, Hong Sun, Steven Petrou, Marcio Souza

Praxis Precision Medicines, Boston, MA 02110 USA

Background

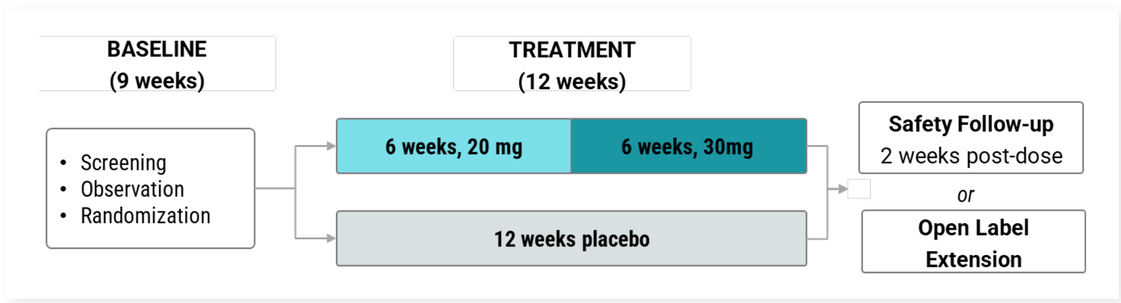
- There are ~50 million individuals worldwide living with epilepsy, the majority of whom have focal epilepsy.
- Focal onset seizures (FOS) are characterized by localized neuronal hyperexcitability, with current standard-of-care limited by tolerability issues and need for titration to avoid side effects.
- Vormatrigine, a functional state modulator that selectively targets the hyperexcitable state of CNS sodium channels, is currently in development for adult FOS and generalized epilepsy.
- Recent data highlight a superior preclinical and early clinical profile compared to currently approved antiseizure medications (ASMs), demonstrate a favorable safety and tolerability profile in doses up to 45 mg, with no clinically significant food effect.
- Notably, emerging data demonstrate vormatrigine's ability to significantly exceed therapeutic concentrations while being well tolerated, without the need for titration.

➢ ***POWER1 is an ongoing global, multicenter, double-blind, randomized, parallel design Phase 2/3 registrational study evaluating the efficacy, safety, and pharmacokinetics of vormatrigine in adults with FOS***

Methods

POWER1 Study Design

- POWER1 (NCT06999902) is a global, multicenter, double-blind, randomized, parallel design Phase 2/3 study enrolling ≈230 participants aged 18-75 years with FOS, currently taking 1-3 ASMs.
- Participants are randomized 1:1 to receive vormatrigine QD, at 20mg for the first 6 weeks and 30 mg for the second 6 weeks, or matching placebo for 12 weeks.
- The study will consist of Screening/Observation (Baseline), Treatment and Follow-up periods.
- Participants will have the option to continue study treatment in an open-label extension (OLE) study.



PRIMARY ENDPOINT

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

KEY SECONDARY ENDPOINT

- Proportion of subjects experiencing a ≥50% reduction in monthly (28 days) focal seizure frequency from Baseline Period to Treatment Period
- Percent change in monthly focal seizure frequency from Baseline Period to the Treatment Period

Figure 1. POWER1 Study Design and Endpoints. Further secondary and exploratory endpoints will examine the effect of vormatrigine on additional efficacy and safety and tolerability outcomes.

Participant Eligibility

Table 1. POWER1 Study Eligibility

KEY INCLUSION CRITERIA

- A diagnosis of focal onset epilepsy according to International League Against Epilepsy (ILAE) Classification (2017), and progressive epilepsy cause ruled out on CT or MRI
- Male or female aged 18-75 years inclusive
- On 1–3 stable doses of ASMs for at least 4 weeks prior to screening

KEY EXCLUSION CRITERIA

- Planned or recent epilepsy surgery or recent neurostimulator placement
- Pseudo- or psychogenic seizures, uncountable cluster seizures only or episode of convulsive status requiring hospitalization/intubation in the past 12 months
- History of schizophrenia, obsessive-compulsive disorder, or other serious mental health disorders
- Significant cardiac conduction abnormalities or family history of sudden death
- Use of prohibited drugs
- Pregnant or breastfeeding at the time of Screening, positive serum pregnancy test at Screening or planning to become pregnant within 14 days of the last study drug dose

POWER1 Online Pre-Screener

Healthcare providers can help their patients see if they qualify by referring them to the online pre-screener at epilepsy-research.com

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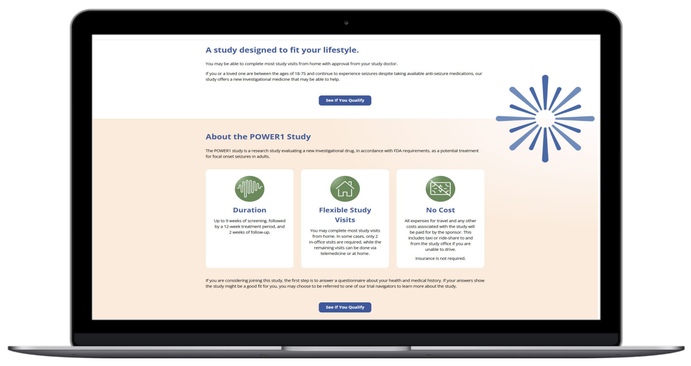

Patient-centered Study Design

Customized study design to meet patient needs

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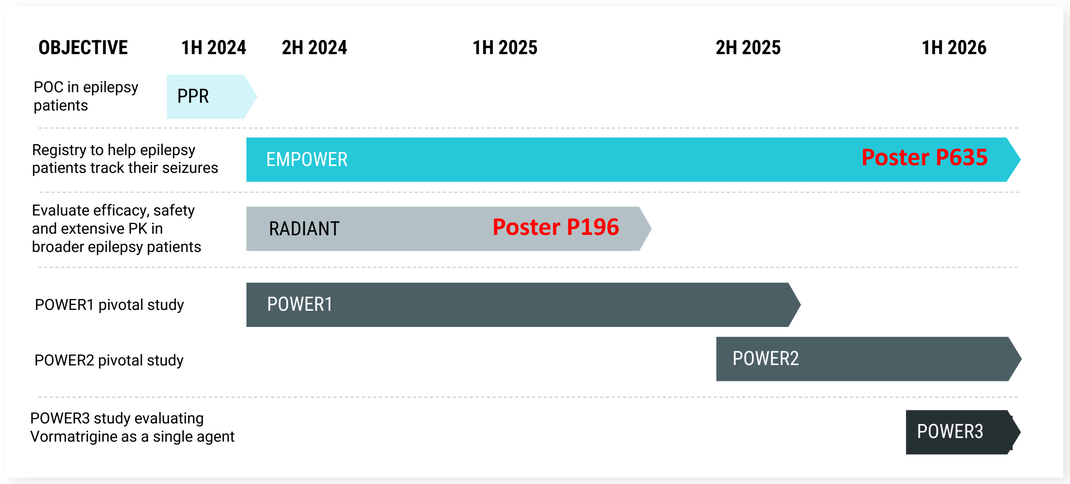
- ❖ Designed with patients' needs in mind
- ❖ Patients may complete most study visits from home
- ❖ Streamlined at-home nurse services
- ❖ Increased access for potential patients normally excluded

Conclusion

- **Expanding on preclinical and preliminary clinical data, as well as the latest positive RADIANT study results, the POWER1 study will examine the efficacy, safety and pharmacokinetics of vormatrigine as a best-in-class precision ASM for FOS.**
- **POWER1 is enrolling well and is on track to complete in 4Q2025.**

VORMATRIGINE ENERGY PROGRAM



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

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