EMERALD: A Phase 3, Randomized, Multi-Center, Double-Blind, Placebo-Controlled Clinical Trial to Evaluate the Efficacy, Safety, Tolerability, and Pharmacokinetics of Relutrigine in Participants with Developmental and Epileptic Encephalopathies

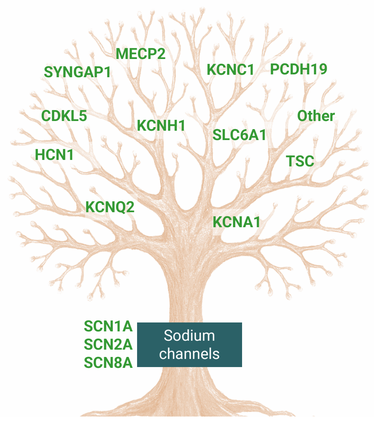
Samata Kamireddy, Brian Spar, Kelley Del Real, Steven Petrou, Marcio Souza

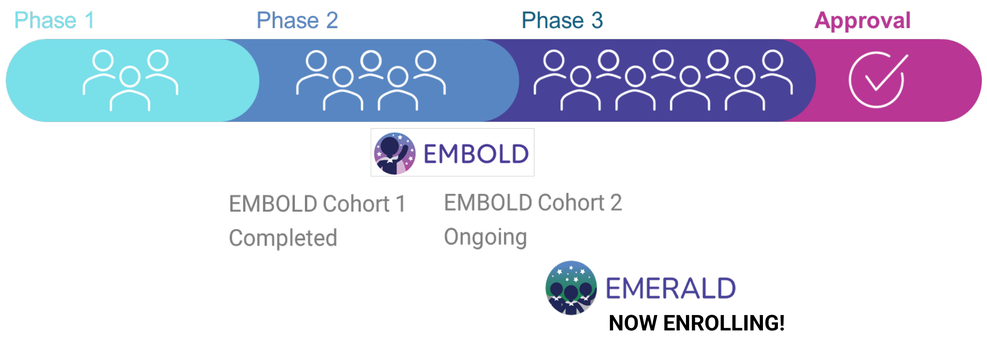
Praxis Precision Medicines, Boston, MA 02110 USA

Background

- Developmental and epileptic encephalopathies (DEEs) are a group of chronic, devastating conditions presenting during infancy and characterized by severe, frequent seizures, developmental delay or regression, and increased early mortality.
- Relutrigine is a differentiated functional state sodium channel modulator in late-stage development for DEEs, with demonstrated superior selectivity for disease-state hyperexcitability, a known cause of seizure manifestation in all DEEs.
- By targeting a common pathway implicated in DEE symptomology, relutrigine has the potential to be applicable across a broad range of DEEs.
- Topline data from the EMBOLD Phase 2 study in patients with *SCN2A*-DEE and *SCN8A*-DEE showed well-tolerated, robust, short- and long-term improvement in motor seizures alongside marked seizure freedom (**P157**).

➢ ***Expanding on these findings, EMERALD is the rapidly expanding Phase 3 registrational trial evaluating relutrigine for seizure control, safety, tolerability, and pharmacokinetics in DEE participants.***

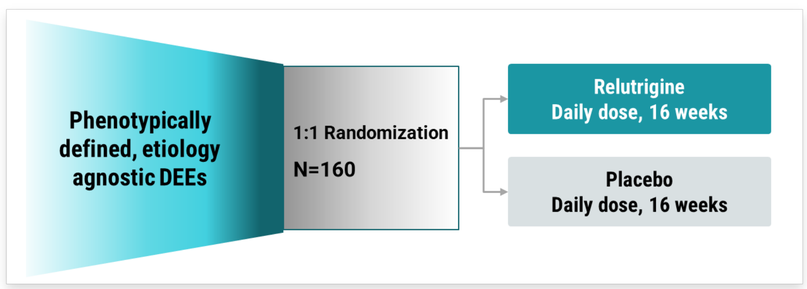




Methods

EMBOLD Study Design

- EMERALD (NCT07010471) is a Phase 3, randomized, multi-center, double-blind, placebo-controlled study enrolling ~160 eligible male and female participants aged 2-65 years with a diagnosis of DEE and onset of seizures <12 years old.
- It will include an initial Screening Period (including 28-day Baseline Observation), Part A (Double-Blind Treatment Period, 16 weeks), Part B (Open Label Extension, OLE Treatment Period, 32 weeks), and Safety Follow-up.
- Participants will be randomized (1:1) to receive either relutrigine (1 mg/kg/day starting dose; dose modification permitted up to 1.5 mg/kg/day) or placebo QD.
- Participants will have the option to undergo study assessments at home, in-clinic or as a combination of both.

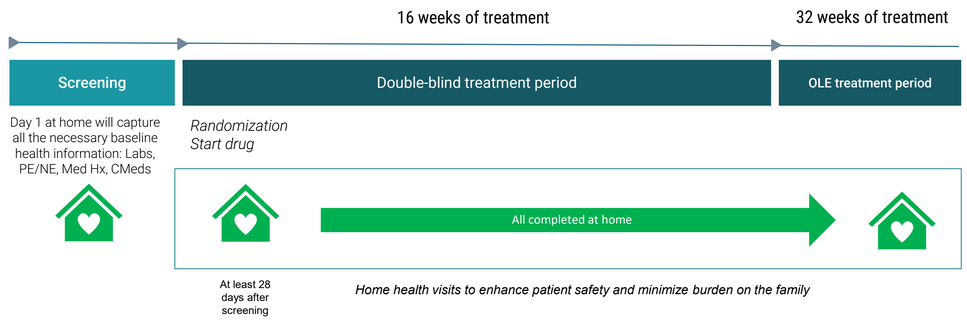


PRIMARY ENDPOINT

- Change from baseline in monthly motor seizure frequency

KEY SECONDARY ENDPOINTS

- Proportion of subjects experiencing a ≥50% reduction in monthly (28 days) seizure frequency from baseline
- Change in seizure-free days from baseline

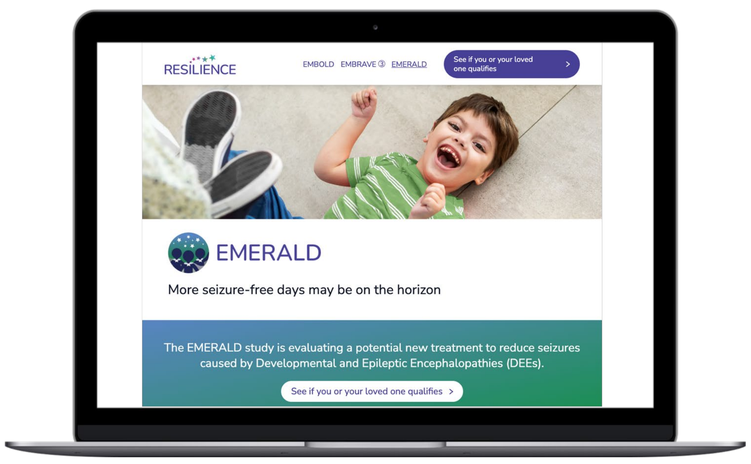


PE=physical exam; NE=neurological exam; Med Hx=medication history; CMeds=concomitant medications

Figure 1. EMERALD Study Design and Endpoints. The decentralized nature of the trial allows all study related procedures to be done at home, with doctors and nurse visits ensuring the trial is conducted in a manner more convenient for families. Further secondary and exploratory endpoints in the EMERALD trial will examine the effect of relutrigine on additional efficacy and safety and tolerability outcomes, including clinician and caregiver global impression scores, incidence and severity of TEAEs, changes in findings on physical and neurological exams, vital signs, clinical labs, ECG and incidence of suicidal ideation or behavior as measured by C-SSRS.

EMERALD Online Pre-Screener

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



Key Inclusion Criteria

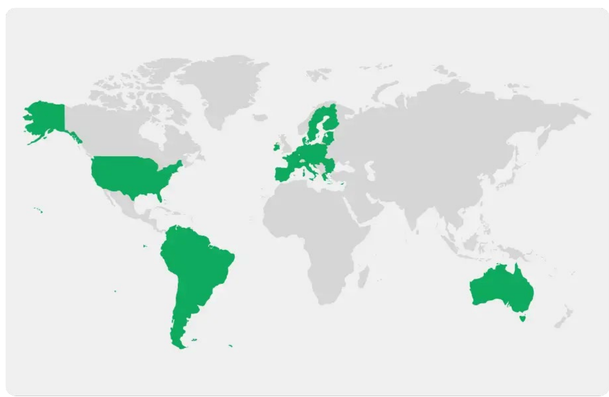
- Documented **diagnosis of a DEE**
- **2-65 years of age** at the time of screening
  Seizure onset <12 years of age
- **Has at least 4 motor seizures** in the 4-week baseline observation period
- No restriction on # of other ASMs, except taking no more than 2 sodium channel blockers

Key Exclusion Criteria

- 2 or more episodes of convulsive *status epilepticus* requiring hospitalization and intubation in the 6 months prior to Screening

EMERALD global footprint enabling efficient trial execution

Patients can choose between at-home, in-clinic, or combined participation



Conclusions

- **Relutrigine is poised to be a first-line, best-in-class treatment for broad DEEs.**
- **The EMERALD registrational study in broad DEEs has been initiated and is set to complete enrollment in 2026.**

RELUTRIGINE

- SMALL MOLECULE FUNCTIONAL STATE MODULATOR
- NO TITRATION
- ONCE DAILY
- LIQUID FORMULATION, ADMINISTERED ORALLY OR BY G/J-TUBE

- Demonstrated robust seizure reduction and unprecedented seizure-free status per 28-day period (see also **P157**)
- Superior selectivity for hyperactive Na_V channels, a known cause of seizure manifestation in all DEEs regardless of etiology
- Generally well-tolerated with mostly mild to moderate AEs, no drug-related SAEs and no relutrigine dose reduction required (see also **P157**)
- Three Rare Pediatric Drug designations for SCN1A (Dravet Syndrome), SCN2A DEE and SCN8A DEE

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Acknowledgments We thank the participants and their families, the EMERALD Study Team, as well as our collaborators 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 in accordance with Good Publication Practice (GPP3).

Disclosures SK, BS, KD, SP and MS are current or former employees/consultants of Praxis Precision Medicines and may be Praxis shareholders

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

Presented at:
International Epilepsy Congress
30 Aug - 3 Sept 2025
Lisbon, Portugal