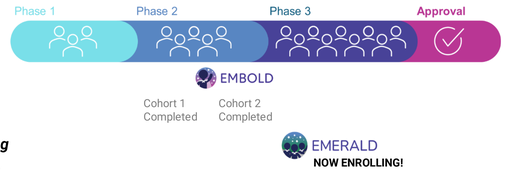
# EMERALD: A Phase 3, Randomized, Multi-Center, Double-Blind, Placebo-Controlled Clinical Trial to Evaluate the Efficacy, Safety, Tolerability, and Pharmacokinetics of Relutrigine in Participants with Developmental and Epileptic Encephalopathies

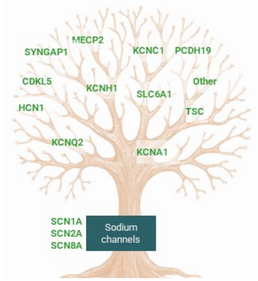
**Samata Kamireddy, Brian Spar, Kelley Del Real, Steven Petrou, Marcio Souza**
**Praxis Precision Medicines, Boston, MA, USA**

## BACKGROUND

- Developmental and epileptic encephalopathies (DEEs) are a group of chronic, devastating conditions presenting during childhood 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 2/3 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 (Poster 10-010).

➢ ***Expanding on these findings, EMERALD is a currently enrolling Phase 3 trial evaluating relutrigine for seizure control, safety, tolerability, and pharmacokinetics in DEE participants.***

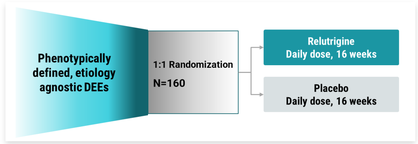



## METHODS

*EMERALD 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.

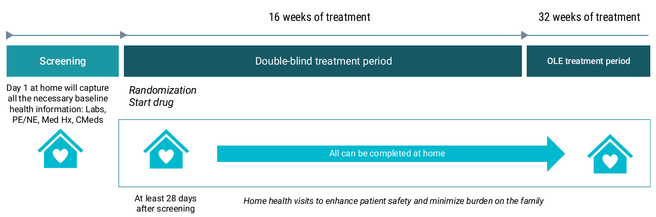



**PRIMARY ENDPOINT**

- Change from baseline in monthly motor seizure frequency

**KEY SECONDARY ENDPOINTS**

- Change in seizure-free days from baseline
- Incidence and severity of treatment-emergent adverse events

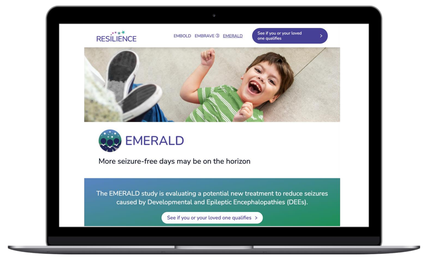



CMeds=concomitant medications; Med Hx=medication history; NE=neurological exam; PE=physical exam

***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.

## 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***




***Currently Enrolling Patients in the United States, Brazil and Australia***

### 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

## CONCLUSIONS

- **Relutrigine is poised to be a first-line, best-in-class treatment for broad DEEs.**
- **The EMERALD registrational study in broad DEEs is expected to be completed by the end of 2026.**
- **Positive EMBOLD results triggered early stop for efficacy, and the FDA has accepted the NDA and granted priority review for relutrigine, for the treatment of SCN2A- and SCN8A-DEEs.**

**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 in SCN2A- and SCN8A-DEE (*see also* ***Poster 10-010***)
- 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* ***Poster 10-010***)
- FDA Orphan Drug and Rare Pediatric Disease Designations for SCN2A-DEE, SCN8A-DEE, and Dravet syndrome, plus FDA Breakthrough Therapy and EMA Orphan Drug Designations for SCN2A-DEE and SCN8A-DEE

## REFERENCES

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

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