Relutrigine Demonstrates Robust Seizure Reduction and Seizure Freedom in DEEs: Results from the EMBOLD Study

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Background

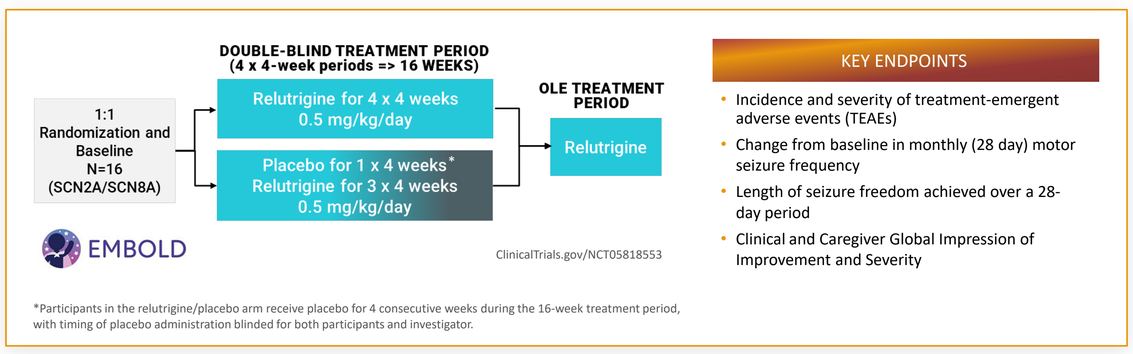
- Developmental and epileptic encephalopathies (DEEs) are devastating neurological disorders presenting in infancy and early childhood characterized by severe, frequent seizures and increased early mortality.
- Relutrigine is a differentiated sodium channel modulator with demonstrated superior selectivity for disease-state sodium channel hyperexcitability, ,a known cause of seizure manifestation in all DEEs.
- Preclinical and emerging clinical data suggest a wide therapeutic window and potential for superior safety and efficacy over current standard-of-care for DEEs.
- The EMBOLD study is a Phase 2 randomized clinical trial designed to explore the safety, tolerability, efficacy, and pharmacokinetics of relutrigine in pediatric participants with seizures associated with early onset *SCN2A*-DEE and *SCN8A*-DEE.

➢ ***Findings demonstrate relutrigine is poised to be a first-line, best-in-class treatment for DEEs, with topline data in SCN2A-DEE and SCN8A-DEE showing well-tolerated, robust, short- and long-term improvement in motor seizures alongside marked seizure freedom.***

Methods

EMBOLD Study Design

- EMBOLD (NCT05818553) is a multicenter, double-blind, placebo-controlled, randomized study, followed by open-label extension (OLE), in pediatric participants with a diagnosis of early onset *SCN2A*-DEE or *SCN8A*-DEE.
- Cohort 1 participants were randomized (1:1) to receive relutrigine QD for 16 weeks, or relutrigine QD for 12 weeks and matching placebo QD for 4 weeks, with timing of placebo administration blinded for both participants and investigator.
- Dose was administered orally or via gastrostomy/jejunostomy tube (G/J-tube), with dose adjustment permitted from initial dose of 0.5mg/kg/day to a maximum of 1.0 mg/kg/day for patients enrolled in Cohort 1.
- EMBOLD study participants had the option to be enrolled to undergo the study assessments in a hybrid fashion (with in-clinic and at-home visits) or with at-home visits only (fully decentralized trial, DCT).
- Cohort 1 topline findings and results from the ongoing OLE period are presented.



*Participants in the relutrigine/placebo arm receive placebo for 4 consecutive weeks during the 16-week treatment period, with timing of placebo administration blinded for both participants and investigator.

First and Only DEE Trial to Offer DCT Option To Meet Patients Where They Are

Figure 1. EMBOLD Cohort 1 Study Design – DCT At Home. 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.

Participant Eligibility and Baseline Characteristics

Key Inclusion Criteria

- Documented severe DEE with mutations in *SCN2A* or *SCN8A* genes
- Age 2-18 years inclusive; weight ≥10 kg
- ≥8 countable motor seizures in 4 weeks preceding screening AND during 28-day baseline observation period
- On stable ASM doses for ≥1 month prior to screening

Table 1. Demographics and Baseline Characteristics

	Placebo (n = 8)	Total (n = 16)
Age, mean (min, max)	6.1 (3, 12)	5.9 (2, 14)
DEE		
SCN2A, n (%)	4 (50)	7 (44)
SCN8A, n (%)	4 (50)	9 (56)
Gender (Male / Female, %)	5/3 (63/37)	9/7 (56/44)
Age at seizure onset (n)		
0 – 3 months	7	13
4 – 12 months	1	2
>12 months	0	1
Patients with ASM use at baseline		
1 or 2 ASM	2	4
3 or 4 ASM	5	11
Baseline motor seizures per 28-day, median (min, max)	58.7 (15, 844)	53.5 (13, 844)
Baseline log-transformed motor seizures per 28-day, mean (SE)	4 (0.4)	3.3 (0.3)
Baseline CGI-S, mean (min, max)	5.5 (4, 6)	5.6 (4, 6)

CGI-S, Clinical Global Impression of Severity

Relutrigine Continues to be Well Tolerated

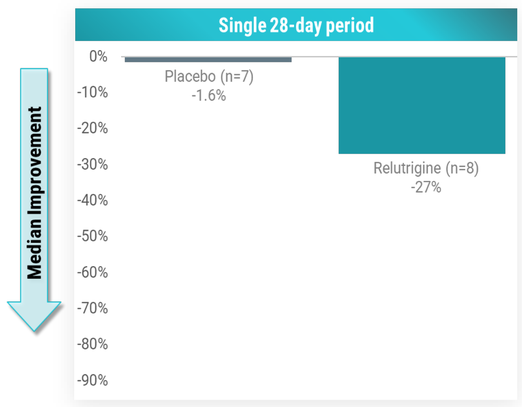
- AEs mostly mild to moderate.
- No dose reduction of relutrigine required, and >50% of participants increased dosing to 1 mg/kg/day.
- All SAEs determined to be not drug-related and were consistent with disease background.
- No clinically significant safety findings in vital signs, clinical laboratory results, physical exams, ECGs.

Table 2. EMBOLD Tolerability Summary – Topline Results

	PLACEBO (n = 8)	RELUTRIGINE (n = 16)
ANY TEAE	*4 (50%)*	*14 (88%)*
TEAEs > 2 Patients		
Infections*	3 (38%)	8 (50%)
Vomiting	1 (13%)	5 (31%)
Pyrexia	0	5 (31%)
Somnolence	0	4 (25%)
Constipation	0	3 (19%)
Nasopharyngitis	2 (25%)	1 (6%)

One severe TEAE of status epilepticus related to an infection
*Infections include bronchiolitis, conjunctivitis, gastroenteritis, influenza, metapneumovirus infection, nasopharyngitis, otitis media, pneumonia, respiratory tract infection, rhinovirus infection scarlet fever, tonsillitis, upper respiratory tract infection. Active treatment duration was at least 7 times longer than placebo duration with respect to total period of observation.

Robust Motor Seizure Reduction and Seizure Freedom



Significant reductions in motor seizures

46%

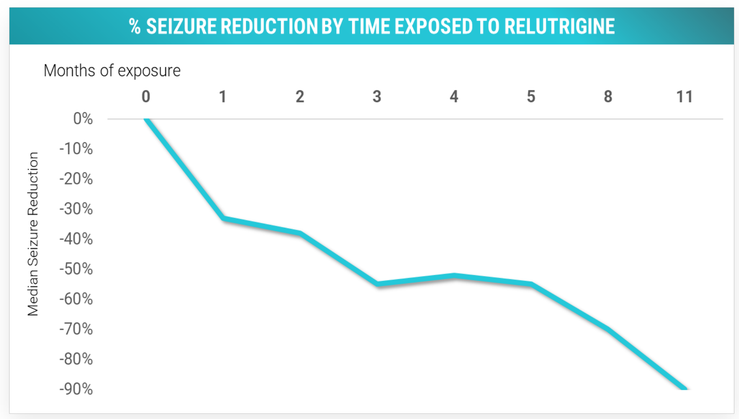
placebo-adjusted reduction in motor seizures over double-blind period*

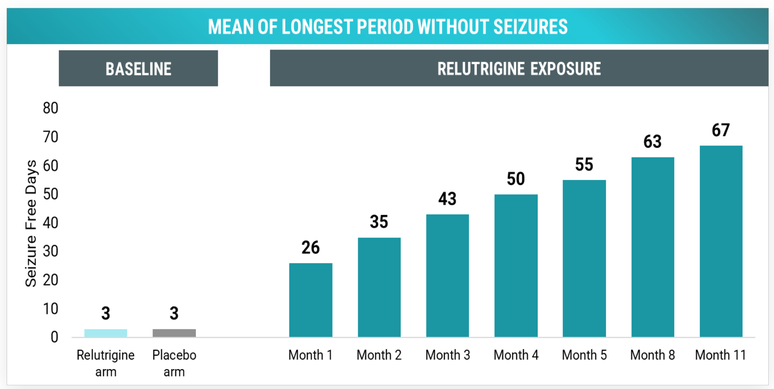
- 1,778 motor seizures at baseline (n=15)
- 7 patients increased the dose of relutrigine to 1 mg/kg during the double-blind period

*Percent reduction derived from log-transformed placebo-adjusted relutrigine effect

Sustained seizure reduction with continued exposure on top of standard of care*

*Assessment of motor seizures over the controlled plus OLE period as of April 24, 2025





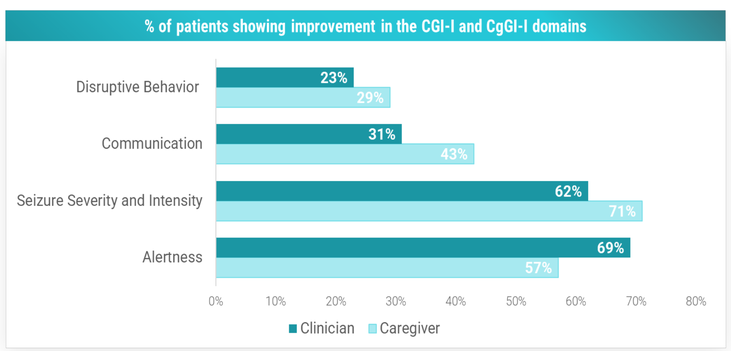
Sustained seizure-free periods reflecting clinical and daily life improvements*

- Topline data at 16 weeks showed 33% of patients were seizure-free after initiating relutrigine
- Seizure freedom sustained with continued relutrigine exposure

*Assessment of motor seizures over the controlled plus open-label OLE period as of April 24, 2025

Meaningful gains in overall well-being of patients, despite severity and historical lack of improvement with available treatments

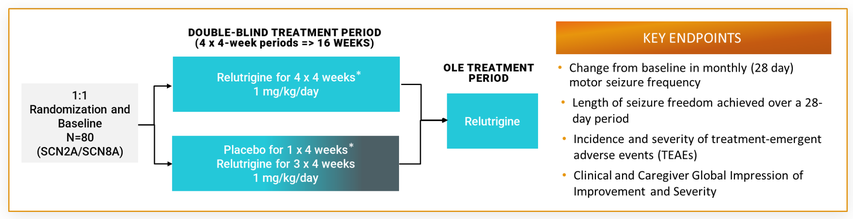
- ~30-70% improvements reported by clinicians and caregivers across multiple domains on CGI-I and CgGI-I, respectively



Clinical Global Impression of Improvement (CGI-I) and Caregiver Global Impression of Improvement (CgGI-I) assessed at Week-16 visit

Conclusions

- **Relutrigine poised to be a first-line, best-in-class treatment for broad DEEs.**
- **EMBOLD Cohort 1 trial results demonstrate relutrigine is well tolerated across *SCN2A*-DEE and *SCN8A*-DEE groups, with robust, short- and long-term improvements observed in motor seizures alongside marked seizure freedom.**
- **EMBOLD Cohort 2 registrational study designed to confirm relutrigine's efficacy continues to enroll; topline results expected no later than the first half of 2026.**
- **EMERALD registrational study in broad DEEs has been initiated and is set to complete enrollment in 2026 (see poster P505).**



https://www.resiliencestudies.com/embold

Figure 2. EMBOLD Cohort 2 Study Design. *Participants randomized (1:1) to receive relutrigine QD for 16 weeks, or relutrigine QD for 12 weeks and matching placebo QD for 4 weeks, with timing of placebo administration blinded for both participants and investigator.

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Acknowledgments We thank the participants and their families, the EMBOLD 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 and George Fahmy in accordance with Good Publication Practice (GPP3).

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

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