



Efficacy and Safety of Relutrigine in Pediatric Participants with SCN2A- and SCN8A-Related Developmental and Epileptic Encephalopathies: Pivotal EMBOLD Cohort 2 Study

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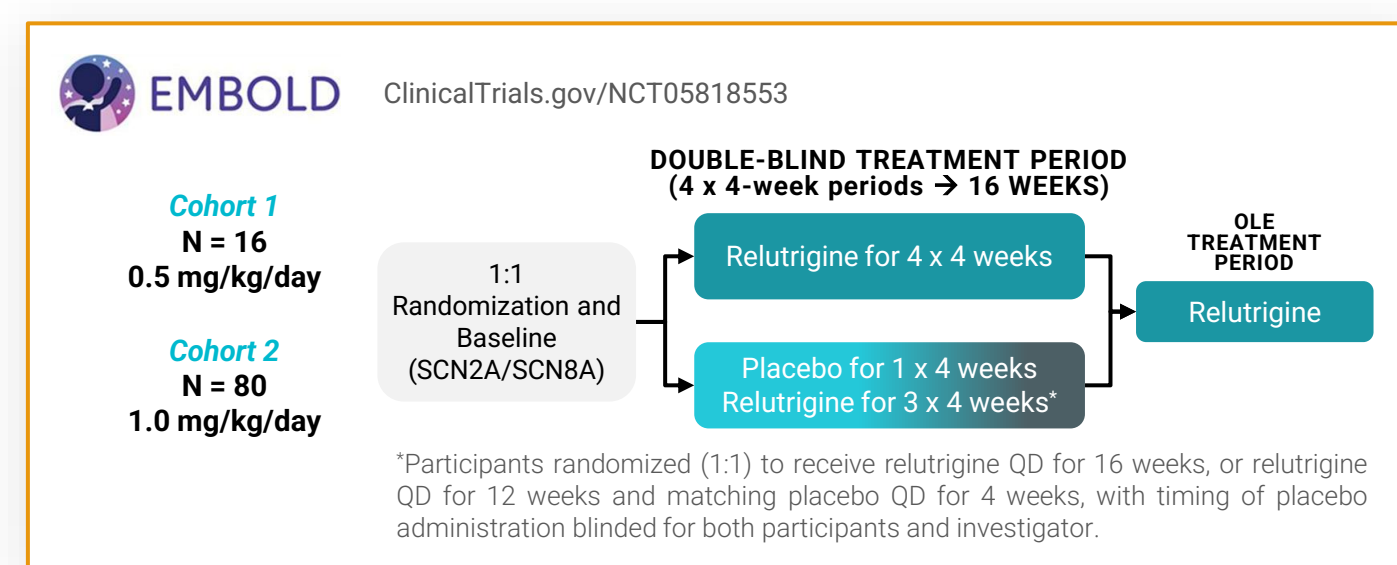
BACKGROUND

- Developmental and epileptic encephalopathies (DEEs) are severe childhood epilepsies marked by frequent, refractory seizures and high early mortality.
- Relutrigine is a next-generation sodium channel modulator designed to selectively target the disease-driven hyperexcitability that causes seizures in DEEs.
- Emerging clinical data demonstrate a wide therapeutic window and the potential for superior safety and efficacy over current treatments.
- EMBOLD is a Phase 2/3 randomized clinical trial evaluating relutrigine's safety, tolerability, efficacy, and pharmacokinetics in children with SCN2A-DEE and SCN8A-DEE.
- Findings show relutrigine is well-tolerated and delivers strong, rapid, and sustained seizure reduction, supporting its potential as a first-line, best-in-class therapy for DEEs.**

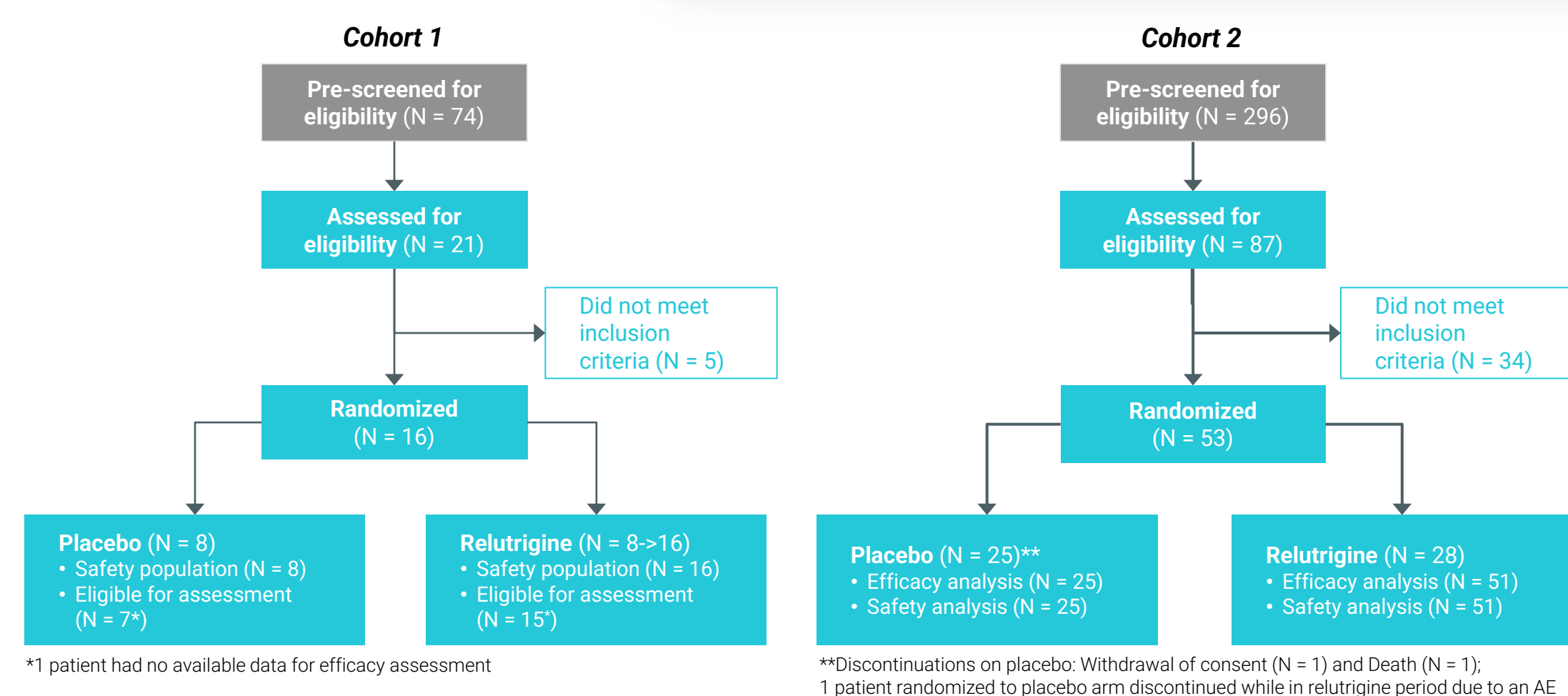
METHODS

EMBOLD Study Design

- EMBOLD (NCT05818553) is a multicenter, randomized, double-blind, placebo-controlled study with an open-label extension, in children with SCN2A-DEE or SCN8A-DEE.
- Cohorts 1 and 2 were randomized (1:1) to relutrigine QD for 16 weeks, or relutrigine QD for 12 weeks + matching placebo QD for 4 weeks (placebo period timing blinded to families and investigators).
- Dosing:
 - Cohort 1:** Starting dose of 0.5 mg/kg/day with optional increase to 1.0 mg/kg/day; administered orally or via G/J tube.
 - Cohort 2:** Starting dose of 1.0 mg/kg/day and maintained through the double-blind period; administered orally or via G/J tube.



Disposition Per Cohort



BASELINE CHARACTERISTICS

Demographics and Baseline Characteristics

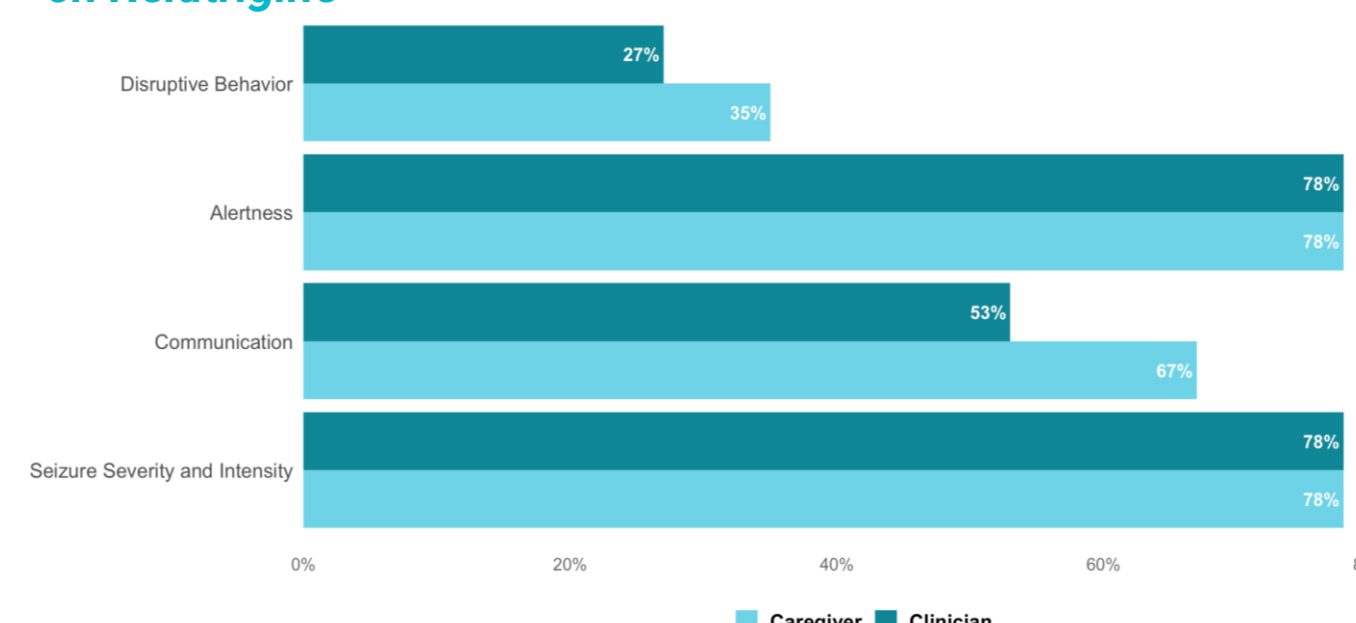
	Cohort 1		Cohort 2	
	PLACEBO (N = 8)	RELUTRIGINE (N = 16)	PLACEBO (N = 25)	RELUTRIGINE (N = 51)
Age, mean (min, max)	6.1 (3, 12)	5.9 (2, 14)	6.6 (1.7, 18)	6.0 (1, 18)
DEE				
SCN2A, n (%)	4 (50%)	7 (44%)	7 (28%)	13 (25%)
SCN8A, n (%)	4 (50%)	9 (56%)	18 (72%)	38 (75%)
Gender (Male / Female, %)	5/3 (63%/37%)	9/7 (56%/44%)	16/9 (64%/36%)	24/27 (47%/53%)
Age at seizure onset (n)				
0 - 3 months	7	13	14	30
4 - 12 months	1	2	11	20
>12 months	0	1	0	1
Patients with ASM use at baseline				
1 - 2 ASM	2	4	9	17 (33%)
3 - 6 ASM	5	11	16	34 (67%)
Baseline log-transformed motor seizures per 28-day, mean (SE)	4.0 (0.4)	3.3 (0.3)	5.04 (0.3)	4.72 (0.19)

MARKED IMPROVEMENT IN DISEASE MODIFYING DOMAINS

Broad, Clinically Meaningful Improvements Across Behavior, Function and Overall Status

- Global status improved substantially, with both clinician and caregiver scales showing large placebo-adjusted gains in a single 28-day period by >25% in favor of relutrigine
- Marked behavioral benefit
- Strong enhancement in alertness
- Meaningful advances in communication
- Consistent reduction in seizure severity and intensity

Proportion of Participants Improving by Domain - Last Visit on Relutrigine



RELUTRIGINE CONTINUES TO BE WELL TOLERATED

Cohort 2 Demonstrates a Consistent Safety and Tolerability Profile

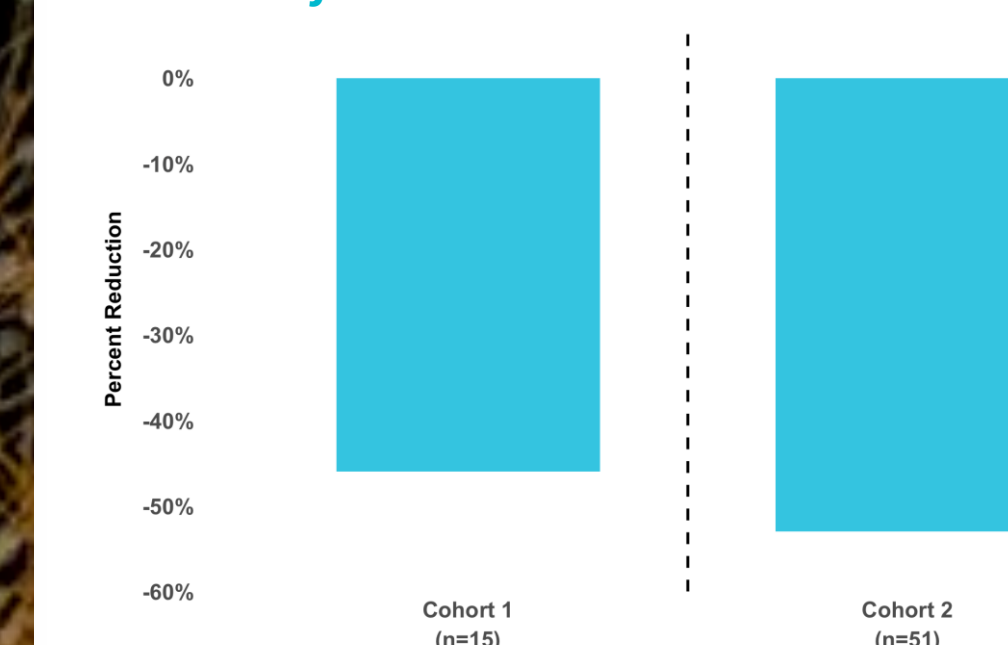
- TEAEs were mostly mild to moderate.
- All SAEs determined to be not drug-related and were consistent with disease background.
- No clinically significant safety findings in vital signs, clinical laboratory results, physical exams and ECGs.

EMBOLD Tolerability Summary - Rate of Observed Occurrence (Normalized to a Per 100-Patient-Months of Exposure)

	PLACEBO (N = 25)	RELUTRIGINE (N = 51)
TEAEs >10% of Patients		
Pyrexia	13.35	11.74
Upper Respiratory Infection	4.45	9.79
Somnolence	13.35	9.13
Irritability	4.45	5.22
Diarrhea	8.90	4.57
Constipation	8.90	3.92
Cough	None	3.92
Vomiting	8.90	3.92

CONSISTENT AND CLINICALLY MEANINGFUL EFFECT

Placebo-Adjusted Seizure Reduction - Cohort 1 and Cohort 2



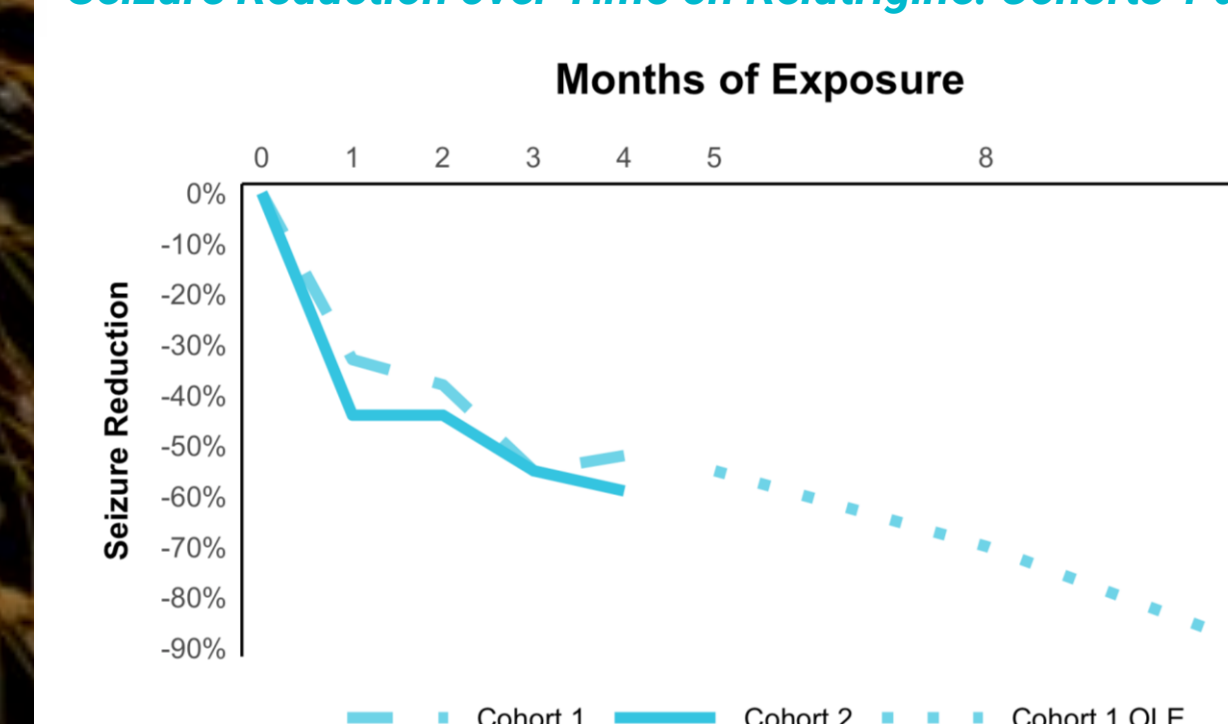
Large, Consistent and Clinically Meaningful Effect in Seizure Reduction

- Relutrigine demonstrated placebo-adjusted seizure reduction in 16 weeks of 46% (p=0.0354) in the first cohort and 53% (p<0.0002) in the confirmatory, registration cohort.
- The effect was consistent in SCN2A and SCN8A patients.

Overall Effect: Rapid, Durable Seizure Reduction with Strong Functional and Global Improvement

- Rapid and substantial early seizure reduction with sustained and progressively deepening effect over time
- Consistent treatment response across cohorts
- Meaningful functional improvement, reflected by a 66% increase in motor seizure-free days
- Robust improvement in clinician and caregiver reported global scores

Seizure Reduction over Time on Relutrigine: Cohorts 1 and 2, Cohort 1 OLE



Cohort 2 Key Secondary Endpoints

Key Secondary	Estimate	p-value
Motor seizure-free days	+66.2%	0.0340
CGI-I (Clinician)	-2.62	<0.0001
CgGI-I (Caregiver)	-3.7	0.002

CONCLUSIONS

- Relutrigine was well tolerated with rapid, significant, and increasing seizure reduction over time with broad functional improvements across behavior, alertness, communication, and overall status.
- The pattern of early onset, sustained progression, and multi-domain benefit is consistent with disease modification and supports relutrigine's potential as best-in-class therapy for both SCN2A-DEE and SCN8A-DEE.
- 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.

REFERENCES

- Scheffer et al 2017 *Epilepsia*
- Wagnon & Meisler 2015 *Front Neurol*
- Ware et al 2019 *Epilepsia Open*
- Wolff et al 2017 *Brain*
- Zuberi et al 2022 *Epilepsia*
- Takai et al 2020 *Int J Mol Sci*
- Johannessen Landmark et al 2021 *Epilepsia*
- Kahlig et al 2022 *Epilepsia*
- Frizzo et al IEC 2025

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