Emergency Use Case of Relutrigine, a Functional State Sodium Channel Modulator, in an Infant with *SCN2A*-DEE and Refractory Seizures and Recurrent Status Epilepticus

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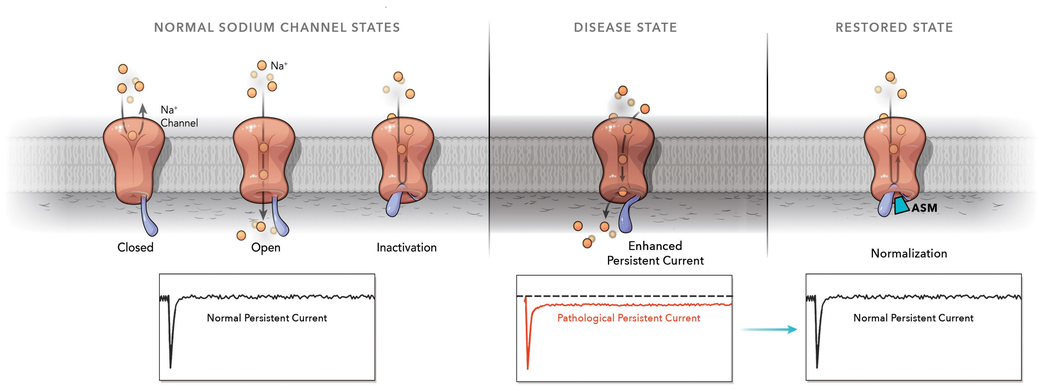
Background

- Developmental and epileptic encephalopathies (DEEs) are devastating neurological disorders presenting in infancy and early childhood, characterized by severe, frequent seizures and increased mortality, as well as developmental delay, intellectual disability, and other comorbidities.
- Certain pathogenic variants in voltage-gated sodium channel (Na_V) genes can increase Na_V activity leading to the neuronal hyperexcitability observed in severe DEEs.
- Relutrigine is a functionally selective, precision Na_V modulator, in development for the treatment of DEEs, with demonstrated superior selectivity for disease-state Na_V hyperexcitability.
- Preclinical and clinical data have demonstrated potential for relutrigine to be a first- and best-in-class treatment for DEEs (**P157**).
- Here we describe the first emergency use case of relutrigine in an infant with *SCN2A*-DEE and refractory seizures and recurrent *status epilepticus* (SE).

RELUTRIGINE MECHANISM OF ACTION



Persistent sodium current (I_{Na}) is a critical driver of pathological hyperexcitability in CNS disorders

Relutrigine First Emergency Use Case: New Zealand

Case presentation: SCN2A-DEE and refractory seizures and recurrent status epilepticus

- An infant with SCN2A-DEE began receiving relutrigine in February 2024 at age 4 months, on a named patient, emergency-use basis following a medical history of refractory seizures with multiple episodes of SE requiring ICU hospital admissions and IV medications to resolve the clinical status.
- In the 7 days preceding relutrigine treatment initiation, the patient had been in SE on three separate occasions and was receiving clobazam (2 mg/kg/day), lacosamide (12.4 mg/kg/day) and phenytoin (3.7 mg/kg/day) without any impact on seizure frequency and severity.
- Other ASMs tried in the first months of life without response included: levetiracetam 80 mg/kg/day, carbamazepine 25 mg/kg/day, vigabatrin up to 100 mg/kg/day, topiramate 10 mg/kg/day, and sodium valproate 40 mg/kg/day.

Pharmacokinetic Summary

- Blood samples were collected for sparse measurement of relutrigine plasma concentrations.
- PK data demonstrated generally dose-dependent exposure.
- Plasma concentrations were quantifiable following multiple doses of 0.5 to 3 mg/kg/day relutrigine.
- Concentrations exceeding therapeutic levels were achieved and well tolerated.

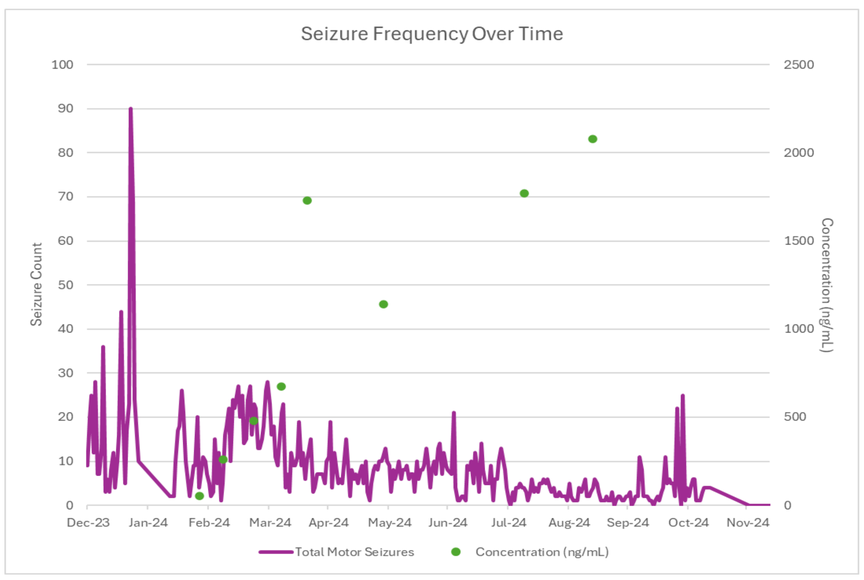


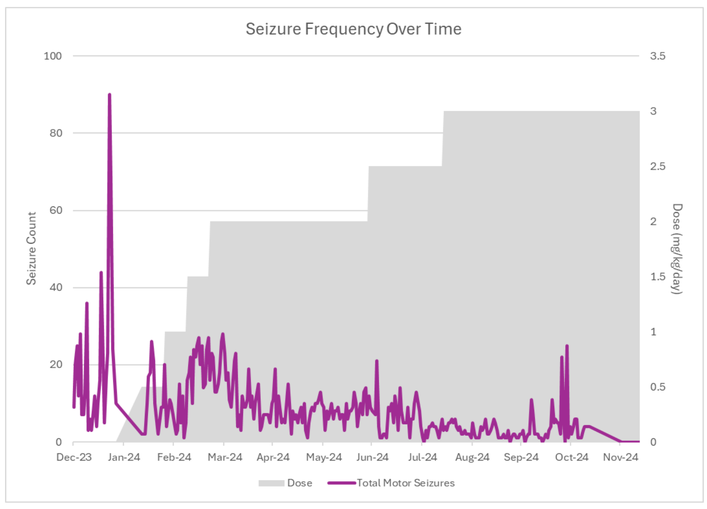
Figure 2. Patient clinical course in relation to relutrigine plasma concentration over the first year. Change in total motor seizure frequency following relutrigine dosing regimen over time, with PK timepoints overlaid.

Demonstrated Tolerability and Seizure Reduction

Marked reduction in seizures alongside a well-tolerated profile

- Following weaning off phenytoin, treatment with relutrigine commenced at a starting dose of 0.5 mg/kg/day, with increasing increments of 0.5 mg/kg every two to four weeks, up to a dose of 3 mg/kg/day as of August 2025.
- Thus far, the patient has been receiving relutrigine once a day over a period of 19 months.
- Following relutrigine treatment initiation and over the course of the first year, there was a marked reduction in episodes of SE and hospital admissions, with demonstrated durable reduction in seizure frequency (***Fig. 1***), as well as a decrease in emergency medications administered.
- Over this period, 24-hour EEG showed an interval reduction in seizure frequency, with an overall >50% reduction in seizures at 3mg/kg/day.
- In addition, the patient has been more alert and awake, responding to, and looking towards, familiar voices.
- To date, overall seizure burden remains stable with relutrigine continuing to be well-tolerated with no clinically significant findings on blood draws, urine or ECG analysis, and no drug-related or severe adverse events.

A



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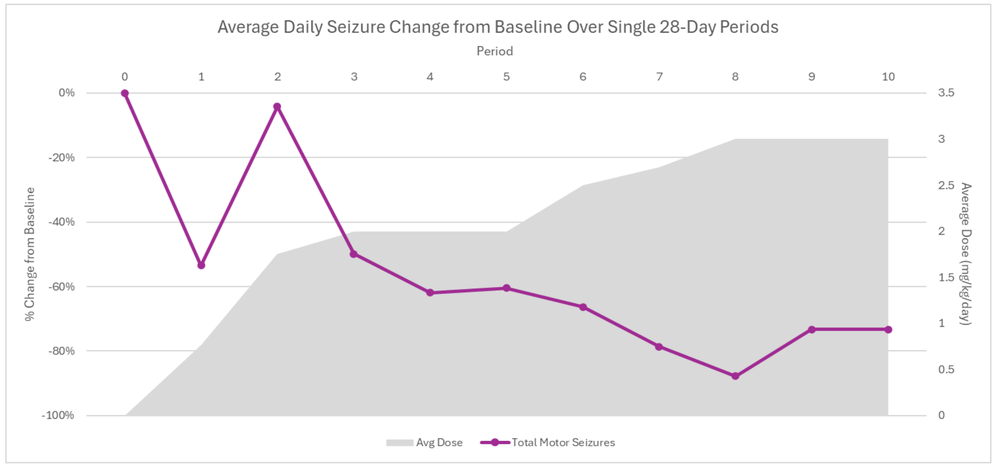

Figure 1. Patient clinical course following introduction of relutrigine dosing regimen and effects on motor seizures over the first year. **(A)** Change in total motor seizure frequency over time following relutrigine dosing regimen. **(B)** Percentage change in average daily seizures over single 28-day periods following relutrigine dosing regimen demonstrating durable seizure reduction. Period 2 included hospitalization and seizures following immunization. Period 9 included hospitalization for elective gastronomy insertion, with prolonged seizures in the context of aspiration pneumonia as a procedural complication.

Conclusions

- **Relutrigine is poised to be a first- and best-in-class treatment for DEEs, with early clinical experience in the first emergency use case indicating a well-tolerated profile and marked seizure reduction, including cessation of previous SE.**
- **Ongoing follow up will determine long-term effects on seizure frequency and intensity, and associated comorbidities.**

RELUTRIGINE	Demonstrated robust seizure reduction and unprecedented seizure-free status per 28-day period (see also **P157**)
ORAL SOLUTION, NO TITRATION, ONCE DAILY	Superior selectivity for hyperactive Na_V channels, a known cause of seizure manifestation in all DEEs regardless of etiology
ADMINISTRATION FORMULATED FOR PEDIATRIC USE	Generally well-tolerated with mostly mild to moderate AEs, no drug-related SAEs and no relutrigine dose reduction required (see also **P157**)
SMALL MOLECULE FUNCTIONAL STATE MODULATOR	Three Rare Pediatric Drug designations for SCN1A (Dravet Syndrome), SCN2A DEE and SCN8A DEE

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Funding Relutrigine was made available under emergency use provisions from Praxis Precision Medicines. Medical writing and editorial assistance were provided by Lillian G. Matthews in accordance with Good Publication Practice (GPP3).

Disclosures SF, BS, DP, HJ, RH, 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