Abstract No. #4940; Program #P16.010

An Online Survey of Caregivers of Patients with SCN8A-Related Epilepsy

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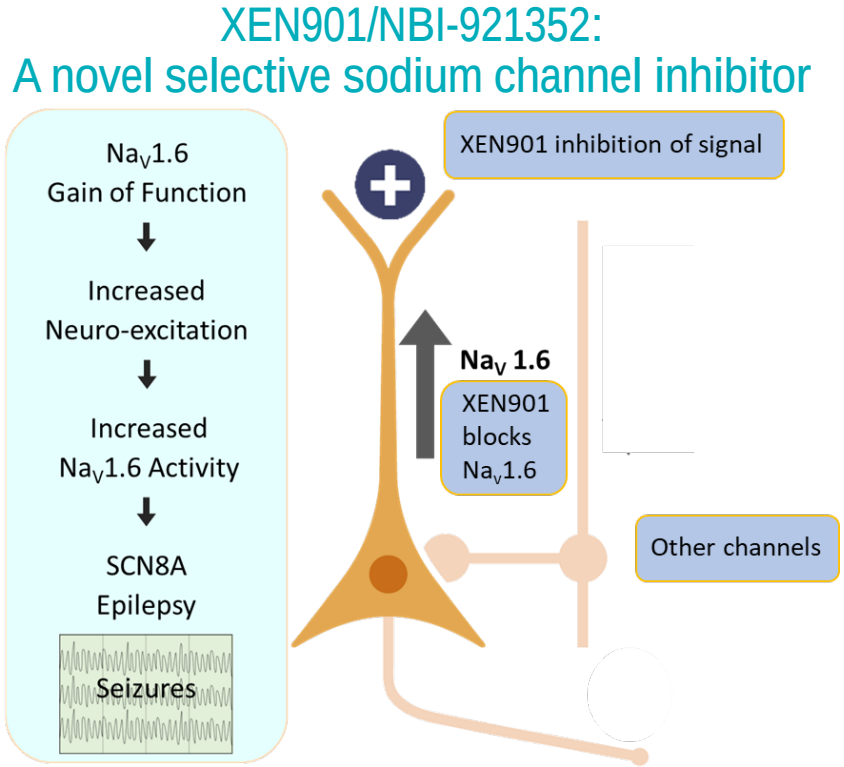
Disclosures

- Drs. Harden, Cutts, Grayson, Luzon, Butterfield, Pimstone and Aycardi are employed by Xenon Pharmaceuticals Inc. ("Xenon"). They receive salaries and may hold stock or stock options in Xenon.
- The Cute Syndrome Foundation received funds from Xenon for this patient survey and other projects/events. In addition, Dr. Savoie is a consultant for Xenon as an employee of Cute Syndrome Consultants, LLC. Cute Syndrome Consultants, LLC receives financial compensation from Xenon in exchange for Dr. Savoie's services.
- The Shay Emma Hammer Foundation and the University of Arizona received funds from Xenon for an SCN8A patient registry but not directly for this patient survey. In addition, Dr. Hammer is, in a personal capacity, a consultant for Xenon and receives financial compensation from Xenon in exchange for his services.
- Dr. Schreiber, in a personal capacity, is a consultant for Xenon and receives financial compensation from Xenon in exchange for his services.
- Dr. Hammer and Dr. Schreiber, in their personal capacities, are consultants for Neurocrine Biosciences, Inc. and receive financial compensation from Neurocrine Biosciences in exchange for their services.
- Dr. Haubenberger is employed by Neurocrine Biosciences, Inc. He receives a salary and may hold stock or stock options in Neurocrine Biosciences.
- Neurocrine Biosciences, Inc. has an exclusive license to XEN901 and other pre-clinical selective $Na_V1.6$ inhibitors and dual $Na_V1.2/1.6$ inhibitors.
- All trademarks are the property of their respective owners.

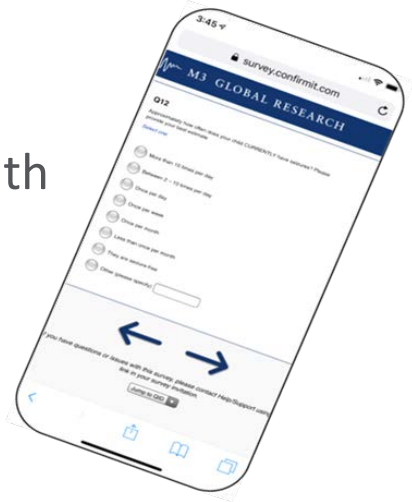
Background

- XEN901 was developed as a precision medicine to selectively address the etiology of SCN8A-DEE
- Selective inhibition of $Na_V1.6$ channel
- Does not inhibit other sodium channels
- On Dec. 2, 2019, Neurocrine Biosciences obtained an exclusive license to XEN901 (now known as NBI-921352)



Survey Objectives and Methods

- A caregiver survey was performed to obtain additional phenotypic information regarding the history of SCN8A-related epilepsy as well as Anti-Seizure Medication (ASM)
- Demographics, comorbidities, seizure onset and frequency, ASM use
- 36 question survey, conducted by Xenon in collaboration with The Cute Syndrome Foundation
- Implemented by M3 Global research and reviewed and approved by Veritas Independent Review Board
- Families recruited by targeted email outreach, social media campaign and an educational webinar
- Survey responses collected over a three-week period in late 2019



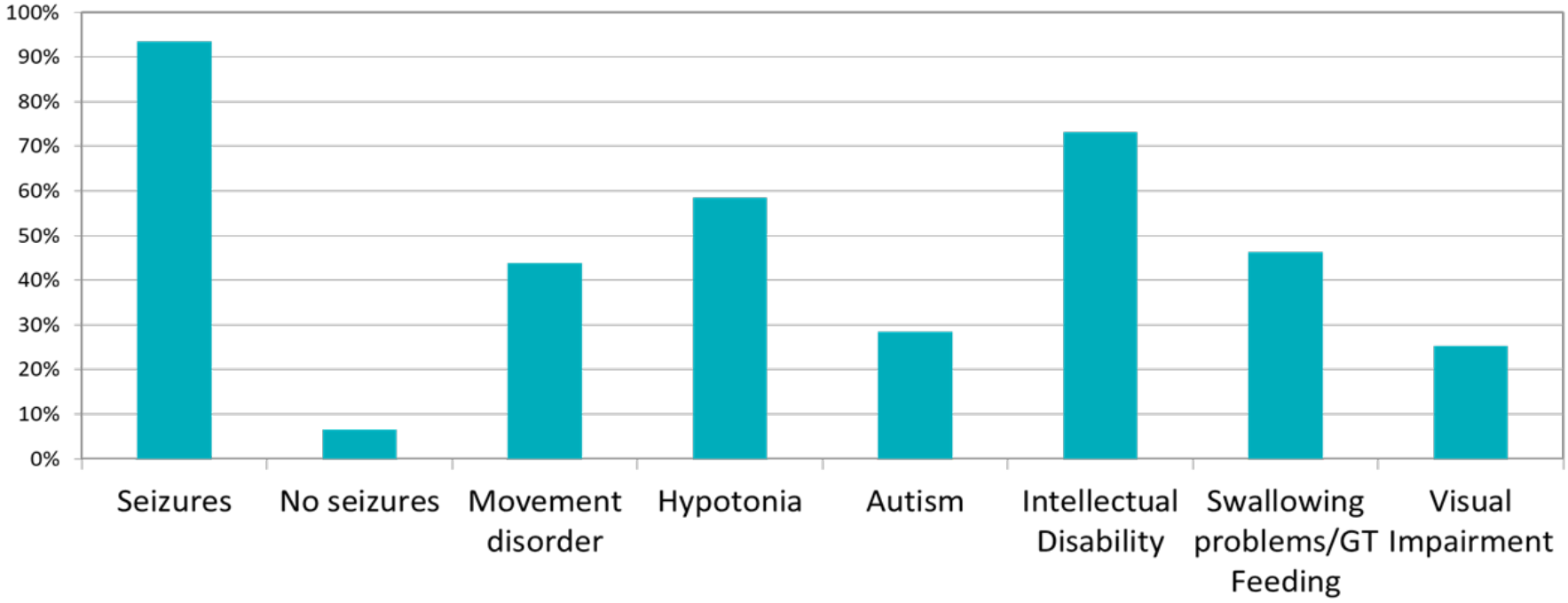
Results

Preliminary Demographics and Seizure Burden of Survey Patients

Demographics	
Data available	125 complete responses for analysis; exclusions as follows: 2 non-English speaking origin
Locations (n=123)	USA (93); Canada (12); UK (12) Australia (6)
Patient Age, n (%)	30 (24%) younger than 4 years 93 (76%) older than 4 years
Seizure history, n (%)	8 (7%) report no seizure history 115 (93%) report seizure history
Spectrum of Seizure Onset (for those with onset in the first 2 years; n=107)	Average age of seizure onset was ~4 months Range was 1 day to 24 months
Initial seizure frequency (n=115)	15% had more than 10 seizures per day 30% had between 2-10 seizures per day 12% had 1 seizure per day
Current seizure frequency (n=109)	63% had seizures over past 30 days 71% had seizures over past 90 days 79% had seizures over past 180 days

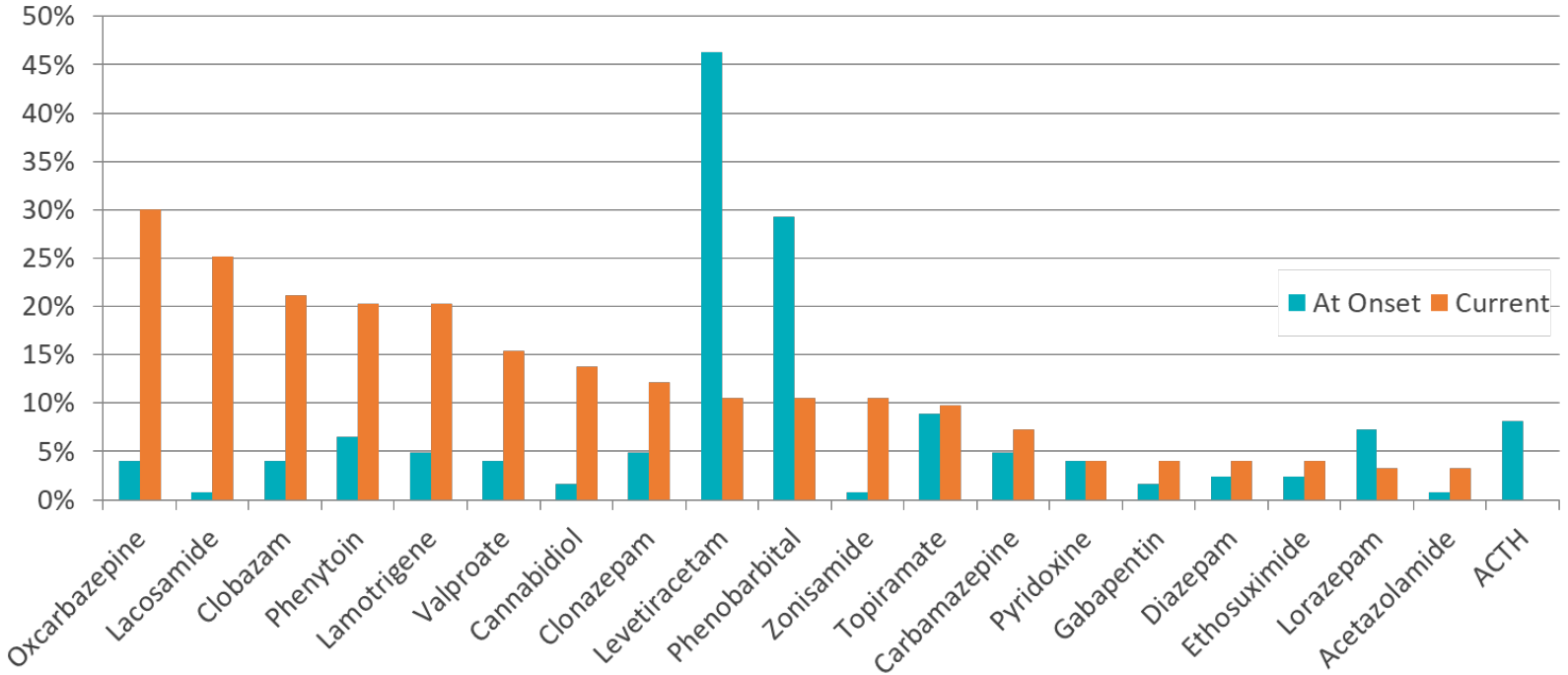
Results

Spectrum of Clinical Presentation



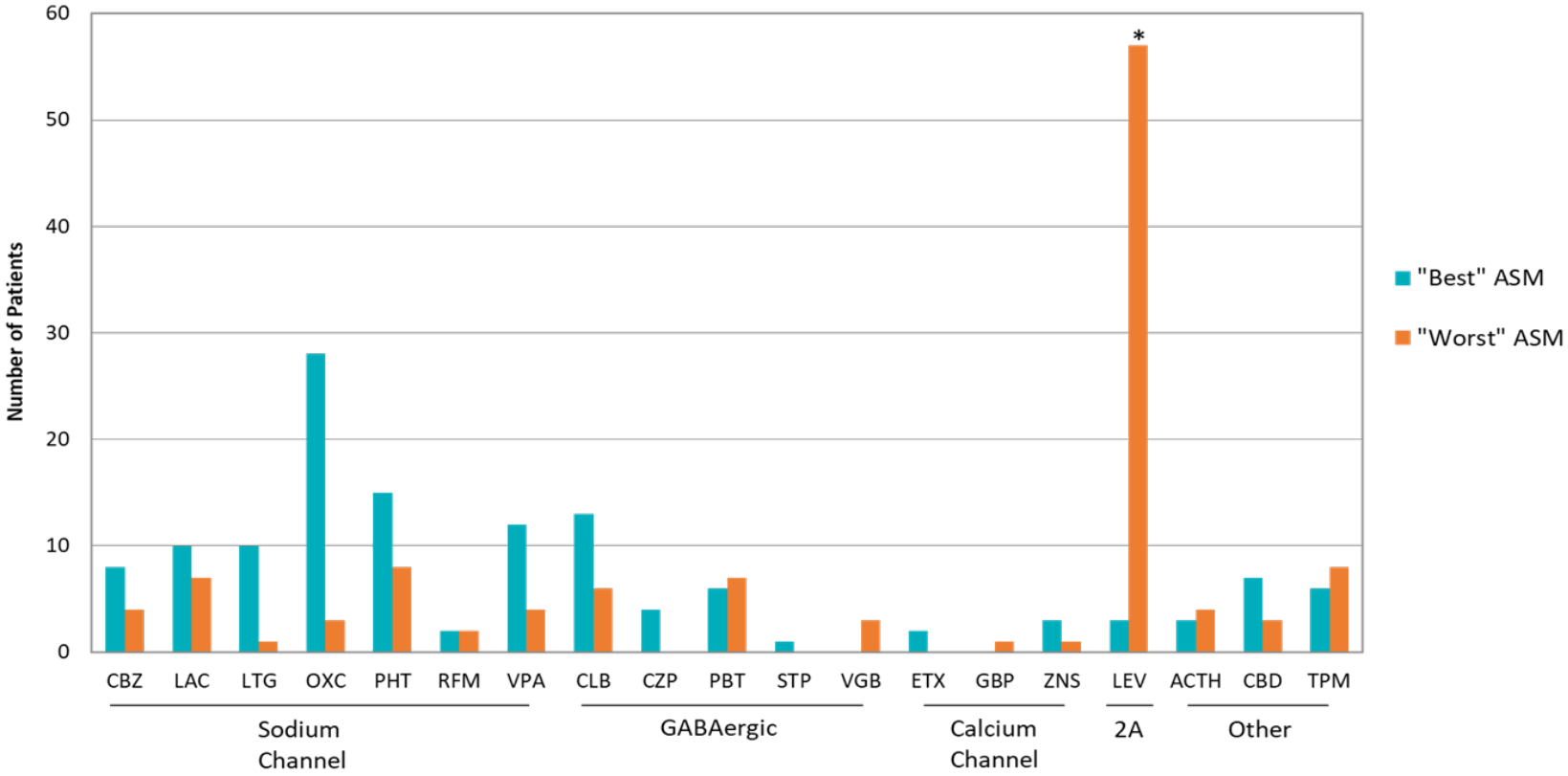
Results

Current ASM Use (reported by ≥4 respondents)



Results

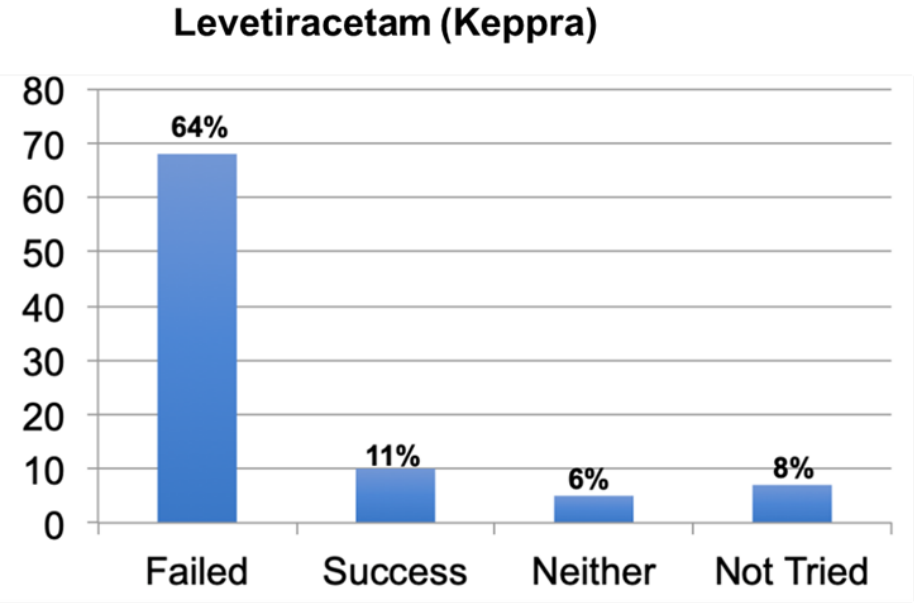
“Best” and “Worst” Medications for Seizure Control*

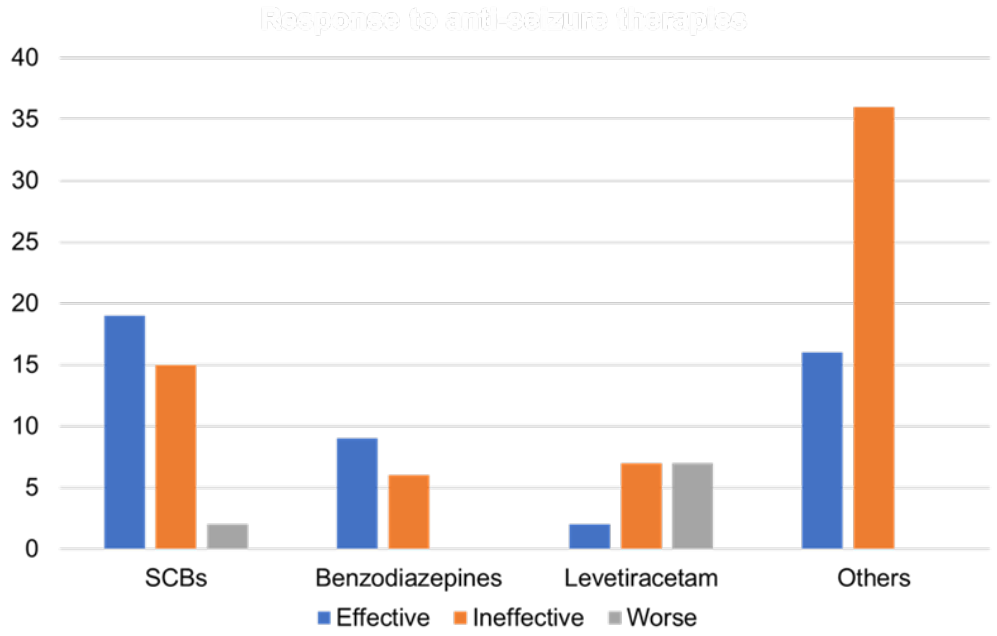


* Reported as “worst” due to undesirable side effects or lack of efficacy

Response to Anti-Seizure Medications

(Data From Other Studies)



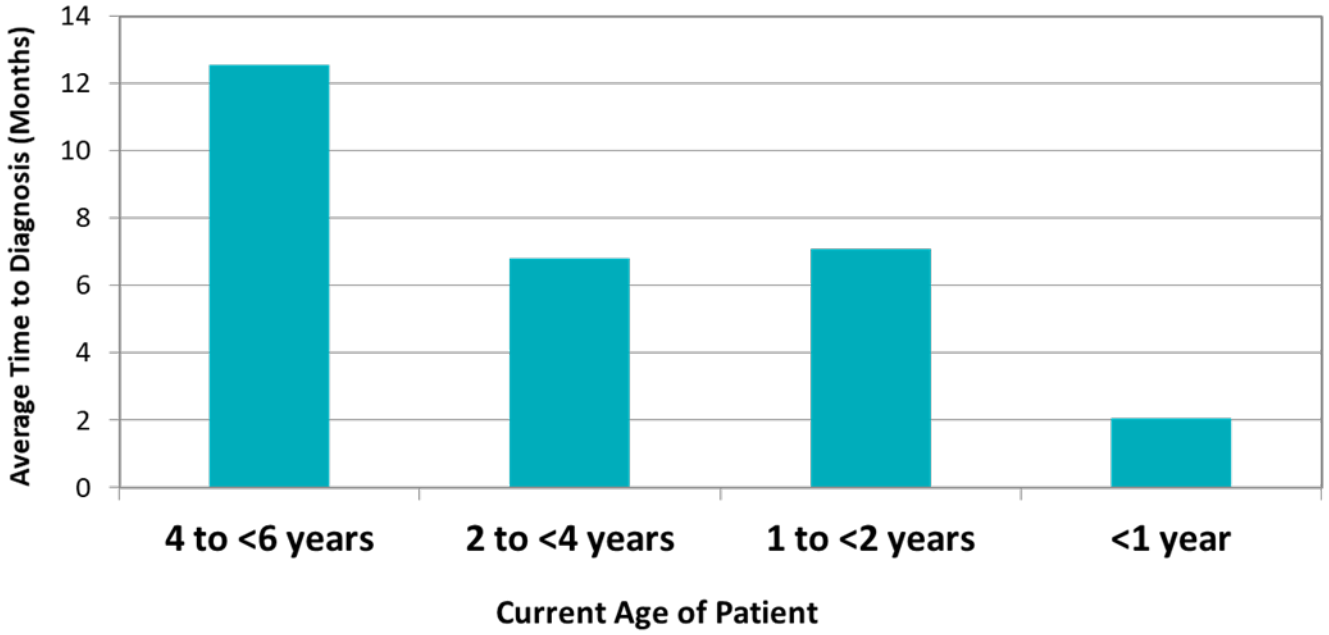


SCN8A Registry

SCN8A Multidisciplinary Clinic

Genetic Diagnosis

Approximate time to diagnosis after first seizure is decreasing



Conclusions

- Survey helps to improve the knowledge of disease course and phenotypic heterogeneity
- Time to genetic diagnosis from first seizure is decreasing over time
- Broad use of ASMs is apparent in this population and survey confirmed observations from previous studies that Levetiracetam (Keppra), although commonly used as a first line treatment, may not be recommended for use in SCN8A-related epilepsy
- Study limitations include retrospective report with possible memory bias

Phase 2 Clinical Planning:

- Survey was informative regarding clinical trial design
- Completed development of a pediatric-specific granule formulation of XEN901/NBI-921352
- Completed juvenile toxicology studies to support pediatric development activities
- PK study in healthy adult volunteers with the new pediatric formulation ongoing
- Neurocrine Biosciences anticipates filing an IND application with the FDA in mid-2020 in order to start a Phase 2 clinical trial in SCN8A-DEE patients in the second half of 2020