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Presented at the:
BIOMARIN SCIENTIFIC EXHIBIT
"Genetic Epilepsies – Updates in Science and Diagnosis"

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

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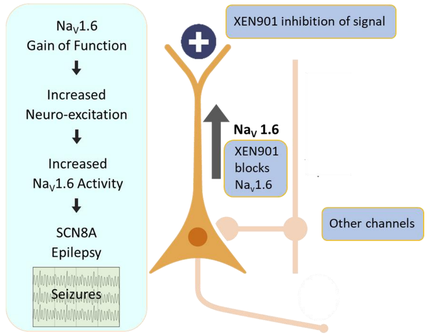
Informational Poster Prepared by Xenon Pharmaceuticals Inc.

BACKGROUND

XEN901: A novel selective sodium channel inhibitor

- XEN901 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
- FDA feedback supports near-term pediatric program
- On Dec. 2, 2019, Neurocrine Biosciences obtained an exclusive license to XEN901.

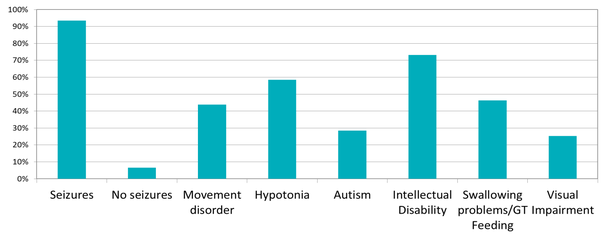


SURVEY OBJECTIVES AND METHODS

- 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

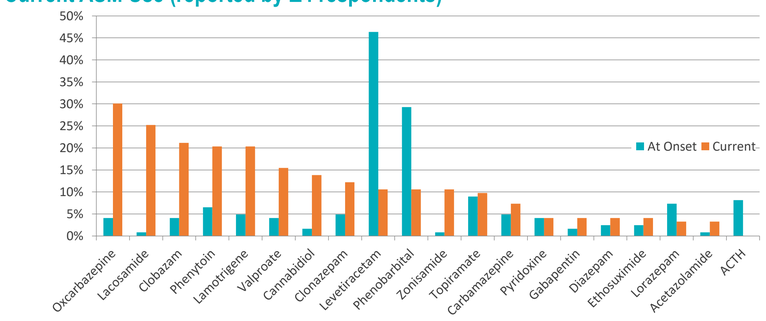
Spectrum of Clinical Presentation



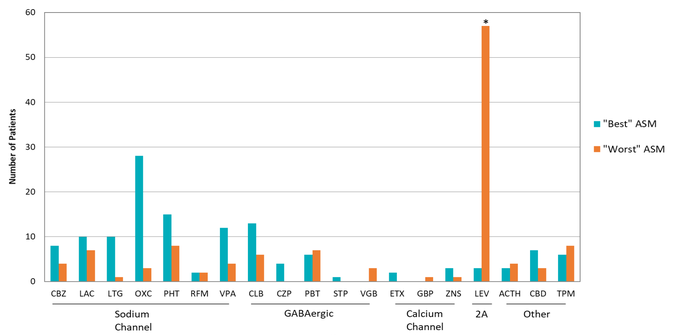
Preliminary Demographics and Seizure Burden of Survey Patients

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 of these, generalized tonic-clonic seizures were most common initial seizure type (53%), followed by partial seizures (20%)
Spectrum of Seizure Onset (for those with onset in 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

Current ASM Use (reported by ≥4 respondents)

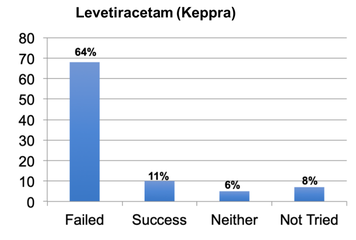


"Best" and "Worst" Medications for Seizure Control*

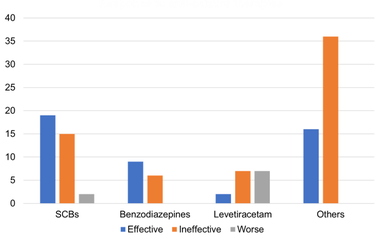


* Reported as "worst" due to undesirable side effects or lack of efficacy

Response to Anti-Seizure Medications (Data From Other Studies)

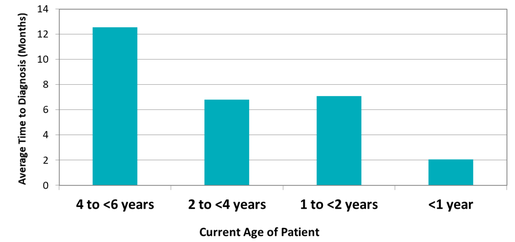


SCN8A Registry



SCN8A Multidisciplinary Clinic

Genetic Diagnosis



Approximate time to diagnosis after first seizure is decreasing

Behind the Seizure™ Program

- Behind the Seizure™ program is a collaboration with Invitae, Xenon, BioMarin and Stoke that offers no-cost testing to all children with seizures up to 60 months of age
- 180+ gene panel launched in February 2019
- Access to genetic testing allows identifying cause of seizures and implementation of specific treatments in many cases
- Supports patient ID for clinical studies
- Builds physician data base

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
- 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 the middle of 2020 in order to start a proposed clinical trial for XEN901 in SCN8A-DEE patients.

XENON