

## SCN2A Related Disorders – FDA Patient-Led Listening Session

04/28/2021

### Objective of session:

The objective of the session was to provide FDA staff with the opportunity to peer into the lives of patients and families living with SCN2A related disorders in order to understand the impact of the disease, as well as the dire need for treatment. As members of the SCN2A community, it's imperative that we develop an understanding of meaningful treatment outcomes and how they can vary vastly across the spectrum of SCN2A disorders.

### Summary of topics discussed:

#### 1. Seizures

- The age of onset is critical for determining the functional consequence of the genetic variant. This can help to inform the selection of the optimal antiepileptic drug (AED), though many clinicians outside of larger children's hospitals may be uninformed and unfamiliar with this distinction.
- Many drugs don't work, or patients cycle through several before ever being diagnosed, and then they only work for a short period of time before seizure control is lost.
- Some AEDs actually aggravate seizure activity dramatically in some patients, and even in rare cases cause status epilepticus.
- Families report caregiver fatigue as they struggle to gain seizure control and face the reality that the AEDs do nothing to improve global developmental outcomes that matter the most to caregivers.

#### 2. Communication

- Based on an informal survey of SCN2A caregivers, the inability to communicate was the most devastating to caregivers.
- The frustration associated with being unable to communicate can often make behaviors and seizures worse.

#### 3. Cognition

- Most patients with SCN2A related disorders have an intellectual disability characterized by significant cognitive impairment.
- Lack of safety awareness and disregard for danger creates the frequent opportunity for serious injurious and life-threatening accidents.
- Many patients never surpass the functioning of a six-month-old.

#### 4. Behavior/Autism

- Behavior problems are frequently reported including self-injurious behaviors and aggression toward others.

- Given the inability for many patients to adequately communicate, caregivers may never know the root cause of the frustration and therefore must continually handle behavioral outbursts without any relief for the patient.

## 5. Sleep

- Sleep disturbance is commonly reported across the entire spectrum of SCN2A related disorders. Lack of sleep is often associated with worsening behaviors and seizures, as referenced above.
- Poor sleep has a detrimental impact on the entire family and for some has led to the departure from the workforce.

## 6. Gastrointestinal

- Between autonomic dysfunction or AED side effects, most patients suffer from either slow or fast gut motility which translates into constipation or diarrhea.
- Gastrointestinal reflux disease (GERD) is also reported to cause extreme distress and discomfort, further worsening behaviors, and triggering seizures.

## 7. Caregiver Stress

- Many parents spent their children's first months residing in the NICU when their babies were born having seizures.
- Some families had typically developing children who suddenly became very ill and were thrust into the world of serial hospital admissions.
- Many parents have their own medical and mental health diagnoses as a result of the stress created by trying to keep their children alive.

## 8. Risk/Benefit with Treatment Options

- Given the devastating impact of SCN2A related disorders, caregivers of children with SCN2A have a high tolerance for drug-related risk. Many families have already been forced to make difficult decisions regarding treatments in order to control seizures.
- Caregivers emphasize that while total seizure control is ideal, reduction of seizures would still be valuable.
- The majority of parents, when given the choice between stopping all seizures or improving quality of life by targeting symptoms or reducing side effects, choose quality of life.
- While more effective and less toxic epilepsy drugs are needed, there is an unmet need to treat the other aspects of SCN2A related disorders. This will require looking at other treatment outcomes beyond the control of epilepsy, such as improvement in cognition, sleep and motor function, GI, and other SCN2A related outcomes.

### **Partner organization:**

*FamilieSCN2A Foundation*

## **FDA divisions represented:**

### **1. Office of the Commissioner (OC) – 6 offices**

- Office of Patient Affairs (*organizer*)
- Office of Chief Scientist/Office of Regulatory Science and Innovation
- Office of Clinical Policy & Programs
- Office of Combination Products
- Office of Orphan Products Development
- Office of Pediatric Therapeutics

### **2. Center for Biologics Evaluation & Research (CBER) – 4 offices/divisions**

- CBER/OCD - Office of the Center Director (OCD)
- CBER/OCBQ/DIS/PSB – Office of Compliance and Biologics Quality/Division of Inspections and Surveillance/Program Surveillance Branch
- CBER/OTAT/DCEPT/CHB – Office of Tissues and Advanced Therapies/Division of Clinical Evaluation And Pharm Toxicology/Clinical Hematology Branch (CHB)
- CBER/OTAT/DCEPT/GMBII – Office of Tissues and Advanced Therapies/Division of Clinical Evaluation And Pharm Toxicology/General Medicine Branch II (II (GMBII))

### **3. Center for Devices and Radiological Health (CDRH) – 2 offices/divisions**

- CDRH/OC/OSPTI/DAHRSSP - Office of Strategic Partnerships and Technology Innovation/ Division of All Hazards Response, Science and Strategic Partnerships (DAHRSSP)
- CDRH/OSPTI/DAHRSSP/PSE - Office of Strategic Partnerships and Technology Innovation/ Division of All Hazards Response, Science and Strategic Partnerships/Patient Science and Engagement (PSE)

### **4. Center for Drug Evaluation and Research (CDER) – 11 offices/divisions**

- CDER/OMP/OPDP/DAPRII – Office of Medical Policy/Office of Prescription Drug Promotion/Division of Advertising & Promotion Review II (DAPRII)
- CDER/OND/ODES/DCOA – Office of New Drugs/Office of Drug Evaluation Science/Division of Clinical Outcome Assessment Staff (DCOA)
- CDER/OND/ON/DNI - Office of New Drugs/Office of Neuroscience/Division of Neurology I (DNI)
- CDER/OND/ON/DNII - Office of New Drugs/Office of Neuroscience/Division of Neurology II (DNII)
- CDER/OND/ON/DP - Office of New Drugs/Office of Neuroscience/Division of Psychiatry (DP)
- CDER/OND/ORDPURM/DPTRDPURM - Office of New Drugs/Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine/ Division of Pharm Toxicology for Rare Diseases, Pediatrics, Urology, and Reproductive Medicine (DPTRDPURM)
- CDER/OND/ORPURM/DRDMG – Office of New Drugs/Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine/ Division of Rare Diseases and Medical Genetics (DRDMG)
- CDER/OND/ORO/DRORDPURM - Office of New Drugs/Office of Regulatory Operations/Division of Regulatory Operations For Rare Diseases Peds, Urology, Reproductive Medicine (DRORDPURM)
- CDER/OTS/OB/DBI - Office of Translational Sciences/Office of Biostatistics/Division of Biometrics I (DBI)
- CDER/OTS/OB/DBIV - Office of Translational Sciences/Office of Biostatistics/Division of Biometrics IV (DBIV)
- CDER/OTS/OCP/DTPM - Office of Translational Sciences/Office of Clinical Pharmacology/Division of Translational and Precision Medicine (DTPM)

## **Patients and community members represented:**

- Leah Schust Myers - Executive Director of the FamilieSCN2A Foundation, parent of a child with SCN2A
- Stephan Sanders, MD - Associate Professor, Psychiatry, University of California, San Francisco Weill Institute for Neurosciences
- Jenny Burke - Parent of an adult with SCN2A
- Angie Auldridge - Parent of a child with SCN2A
- Kris Ray - Parent of a child with SCN2A
- Shawn Egan - Parent of a child with SCN2A
- Katie Helbig - Senior Genetic Counselor, Children's Hospital of Philadelphia and Co-Director of the Epilepsy Neurogenetics Initiative (ENGIN)
- Angie Weaver - Parent of a child deceased as a result of SCN2A
- Anne Berg, PhD - Research Professor at Northwestern University

## **Disclaimer**

*Discussions in FDA Rare Disease Listening Sessions are informal. All opinions, recommendations, and proposals are unofficial and nonbinding on FDA and all other participants. This report reflects the [organization]'s account of the perspectives of patients and caregivers who participated in the Rare Disease Listening Session with the FDA. To the extent possible, the terms used in this summary to describe specific manifestations of [disease or condition], health effects and impacts, and treatment experiences, reflect those of the participants. This report is not meant to be representative of the views and experiences of the entire [disease or condition] patient population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.*