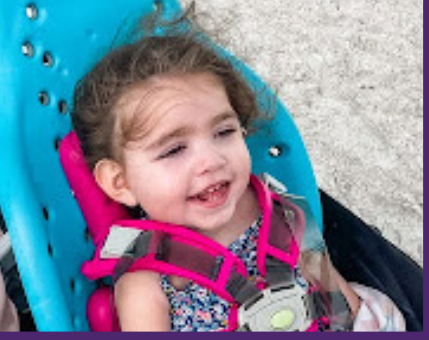
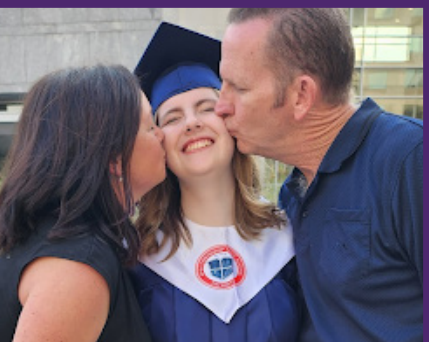












FDA Patient Listening Session Summary

SCN8A-RELATED DISORDERS

March 31, 2026

The Cute Syndrome® FOUNDATION

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Executive Summary

SCN8A-related disorders are rare neurological conditions caused by pathogenic variants in the SCN8A gene, which encodes the Nav1.6 voltage-gated sodium channel. These disorders are frequently associated with severe developmental and epileptic encephalopathies (DEE), treatment-resistant epilepsy, developmental delay, intellectual disability, autism spectrum disorder, movement disorders, respiratory complications, feeding difficulties, behavioral dysregulation, and elevated mortality risk, including sudden unexpected death in epilepsy (SUDEP).

The FDA Patient Listening Session provided an opportunity for patients, caregivers, clinicians, and advocates to communicate the real-world impact of SCN8A-related disorders directly to FDA representatives. Participants emphasized the need for flexible regulatory approaches, innovative clinical trial designs, and accelerated development pathways appropriate for ultra-rare neurological disorders with high unmet medical need.

Key Themes Identified Across Participants

- **Treatment Limitations:** Most patients require multiple anti-seizure medications yet continue to experience refractory seizures, medication toxicity, developmental disruption, and significant side effects.
- **Disease Complexity:** SCN8A affects substantially more than seizure frequency, impacting cognition, communication, behavior, feeding, respiration, mobility, sleep, and independence.
- **Caregiver Burden:** Families frequently become full-time caregivers, medical coordinators, therapists, advocates, and emergency responders while facing chronic stress and financial strain.
- **Fear of Loss:** Parents described constant anxiety surrounding SUDEP, status epilepticus, respiratory complications, and sudden decline.
- **Need for Better Endpoints:** Participants emphasized that meaningful clinical improvement may include better cognition, fewer medication side effects, improved alertness, communication, sleep, mobility, and family stability.
- **Urgency:** Families repeatedly emphasized that time matters because developmental opportunities narrow quickly and mortality risk remains high.

Introduction to SCN8A-Related Disorders

First defined in 2012, the SCN8A gene encodes a voltage-gated sodium channel (Nav1.6) and affects how neurons in the central nervous system function. SCN8A-related disorders are rare genetic neurological conditions involving pathogenic variants of the SCN8A gene.

There is still much to be discovered about SCN8A mutations and their associated effects. Clinical presentations vary significantly across individuals but commonly include epilepsy, developmental delay, intellectual disability, autism spectrum disorder, movement disorders, feeding difficulties, respiratory compromise, hypotonia, sleep disruption, and behavioral dysregulation. There are high levels of family and caregiver stress and fatigue experienced in caring for a child or family member with an SCN8A mutation. Furthermore, genetic epilepsies have a higher risk of Sudden Unexplained Death from epilepsy (SUDEP), and the rate of mortality in SCN8A patients is high relative to the size of the population.

Although fewer than 1,000 individuals have been formally identified worldwide, increasing access to genetic testing continues to expand recognition of SCN8A-related disorders, with new cases being discovered every day. It is now believed that SCN8A mutations may cause up to 1% of all epilepsies. There is currently no standard treatment for SCN8A disorders.

The Cute Syndrome Foundation

The Cute Syndrome Foundation (TCSF) is the starting point for support for new families to reach as they receive an SCN8A diagnosis. TCSF raises awareness of SCN8A mutations, funds dedicated and talented scientists researching SCN8A and supports the families around the world who are affected by this disorder.

Goals of the FDA Patient Listening Session

- Provide FDA representatives with direct insight into the lived experience of individuals and families affected by SCN8A-related disorders.
- Highlight the broad neurological, developmental, behavioral, and systemic impacts associated with the disorder.
- Identify unmet treatment needs and meaningful clinical endpoints from the patient and caregiver perspective.
- Communicate the urgency surrounding therapeutic development for this high-burden, high-mortality population.
- Encourage continued collaboration among regulators, researchers, clinicians, industry, and the patient community.

FDA Patient Listening Session Meeting Review

Summary and Key Themes

Across the session, families emphasized that SCN8A is a whole-life, whole-family disorder. Seizures are urgent and often life-threatening, but the disease burden also includes developmental delay or regression, impaired communication, movement and muscle tone differences, feeding and respiratory vulnerability, sleep disruption,

behavioral crises, caregiver vigilance, sibling impact, and grief. Participants repeatedly described a need for therapies that are more precise, less burdensome, and capable of improving daily functioning and quality of life—even when progress is incremental.

Key Regulatory-Relevant Themes

Potential areas for FDA consideration include: recognition that seizure count alone may not capture treatment benefit; inclusion of non-seizure endpoints and caregiver-observed functional changes; trial designs that reduce travel, placebo exposure, and participation burden; thoughtful risk-benefit assessment in a population already exposed to substantial medication and disease-related risk; and flexibility for very small, genetically defined subgroups.

Key Topics

- Overview of SCN8A mutation and related effects
- Experiences and needs of SCN8A patients and their caregivers from the perspective of a day-in-the-life of these individuals, and inclusive of the treatment journeys endured

SCN8A Patient Listening Session Agenda

Opening and Introductions

- **FDA Opening Remarks**
  FDA Public Engagement Staff
- **Introduction by The Cute Syndrome Foundation**
  Kacie Craig, Outgoing Executive Director

Speakers

- **SCN8A-Related Disorders Overview**
  Dr. John Schreiber, Pediatric Neurologist
- **Family and Caregiver's Journey Montage**
- **Margot's Story: Early Onset Epilepsy—Severe DEE**
  Madeleine and Chris, Margot's Parents
- **Will's Story: The Unspeakable Truth of SUDEP**
  Liz and Michael, Will's Parents
- **Megan's Story: Hope Undone by Loss of Seizure Control**
  Trisha, Megan's Mom and Megan, SCN8A Warrior
- **Beyond Seizures: Behavioral Impacts**
  Shelley Frappier and Katie, Wyatt's Mom
- **Lucy's Story: The Reality of Loss—Severe DEE**
  Danielle and Phil, Lucy's Parents
- **Max's Story: Why Time Matters**
  Dianely, Max's Mom

Closing and Q&A

- **Wrap-Up Remarks**
  Hillary Savoie, TCSF Founder and Board Chair
- **FDA Q&A Session**
  Opportunity for FDA to ask follow-up questions
- **FDA Closing Remarks**
  FDA Public Engagement Staff

Introduction

Kacie Craig, Outgoing Executive Director of the Cute Syndrome Foundation and Mom to Stella, SCN8A Warrior

Kacie introduced the goals of the session and summarized the perspectives of patients, families, and caregivers of patients living with SCN8A. She asked the FDA to consider three key takeaways from the Patient Listening Session (PLS):

FIRST: EXISTING TREATMENTS ARE FAILING THE SCN8A COMMUNITY

Many currently available treatments not only provide incomplete seizure control, but also introduce significant side effects or fail to impact the broader challenges that define daily life. Seizure reduction matters deeply, but success cannot be measured exclusively through seizure metrics if the overall burden remains overwhelming.

SECOND: WHAT PROGRESS LOOKS LIKE MATTERS

For this community, progress does not have to mean a cure, though the community continues to hope and advocate for one. Progress can be incremental. It means expanding the toolbox available to clinicians and families. Even modest gains can translate into meaningful improvements for a child and family. No meaningful change is too small.

THIRD: THE RISK OF INACTION IS REAL AND URGENT

The consequences are immediate. Lives are lost, opportunities for development are narrowed, and families are forced to navigate irreversible decline without better options. ***In the time spent planning and coordinating this meeting, the TCSF community lost 13 children—including 2 who were profiled during this session.*** The urgency is real, and time is not theoretical for the families living this experience.

Kacie noted that the patient stories shared in the PLS were selected intentionally to represent a spectrum of experiences. Families participated out of their desire to make things better for the community, even if it is too late for their own children.

Clinical Perspective

Dr. John Schreiber, Associate Chief for Neurophysiology, Children's National Hospital in Washington, D.C.

Dr. Schreiber has treated patients with SCN8A-related disorders for several years and shared his clinical experience with the FDA.

There are multiple types of SCN8A-related disorders. The phenotype most associated with epilepsy is developmental and epileptic encephalopathy (DEE), which is the also the most severe. Patients have very severe seizures starting early on in life; the average age of seizure onset is less than four months of age. These patients can have infantile spasms and multiple seizure types that are very difficult to treat, along with other associated comorbidities such as cortical vision impairment. Many are fed by G-tube. They have movement disorders and severe hypotonia. Many are non-ambulatory, and nonverbal, and have significant respiratory issues.

There are also less severe types of DEE that are considered mild to moderate. Many of those patients are able to ambulate, but still have lots of developmental challenges, including oral motor and feeding problems. They can have behavioral problems, sleep problems, and autism spectrum disorder as well.

The least severe phenotype is the self-limited focal epilepsy, which also tends to present early on in infancy.

These children have seizures that are fairly well controlled and are not often the patients who are going to be included in clinical trials. But despite the moniker of self-limited epilepsy, many do have lifelong seizures and may need medications long term.

Most of the phenotypes mentioned are gain of function and therefore respond to medications like sodium channel blockers that can help to reduce the excessive gain of function. Though for most, sodium channel blockers alone are not enough to control seizures. Many of these patients are on several medications at once, and their epilepsy may remain refractory.

There are other phenotypes that are considered to be loss of function, and those are neurodevelopmental disability without epilepsy and neurodevelopmental disability with generalized epilepsy. Those with epilepsy tend to have later-onset seizures that are generalized in onset, most commonly absence seizures. They can respond to typical medications that we would use for absence seizures but also may not be entirely controlled.

Of the genetically-mediated epilepsies, SCN8A-related epilepsies are on the more severe end of the spectrum. It is one of the few that can present in the first month of life. There is an overall increased risk of mortality in SCN8A-related disorders, particularly in the DEE. Some of those cases are due to SUDEP (sudden unexpected death in epilepsy). Other cases are progression of disease or mortality related to pneumonia and respiratory complications. Patients can be prone to bouts of status epilepticus, where seizures do not stop, leading to hospitalization, intubation, and related morbidity and mortality.

Recent research looking at quality of life in children with SCN8A-related epilepsy found a correlation between quality of life and phenotype, with the more severe phenotype causing the most severe impact on quality of life and developmental outcomes. One important study finding was that the number of anti-seizure medications negatively impacted more domains of quality of life than the actual seizure frequency itself. Understandably, a lot of the medications have potential adverse effects such as somnolence, fatigue, and many others. Anytime a patient is on more than just a couple of different medications, the potential for interactions and more adverse reactions continues to compound.

Clearly, for all those children who are not responding adequately to medications, which is a significant number, the SCN8A community needs better options, not only in terms of efficacy, but also in terms of side effects. Although there are several different sodium channel blockers available, they lack specificity, not only for the type of voltage-gated sodium channel but also for the channel properties. The hope is that better selectivity can help to minimize adverse effects and target the specific sodium channel that is dysfunctional. That could also potentially allow patients to taper off other medications that may cause more challenges for these children.

Parent and Patient Testimonials

Families' and Caregiver's Journey Montage

This summary is from a collection of interviews with multiple families. Five families are represented, sharing experiences that reflect the daily realities of many more families living with SCN8A.

FIRST SEIZURES AND DELAYED DIAGNOSES:

Parents shared stories of when their child first experienced a seizure, ranging from weeks to about seven months of life. Many had not seen or experienced seizures before, so there was some initial uncertainty as to what they were seeing. It took many families many months to get definitive diagnoses and more clarity about their child's condition.

CONTROLLING SEIZURES IS FIRST AND FOREMOST; DIFFICULT DECISIONS WEIGH HEAVY ON PARENTS:

There are so many difficult decisions caregivers of patients living with SCN8A have to make every day. One of the most difficult is medication decisions that may benefit their child or could alternatively negatively affect them. Even incremental improvements to seizures or the medications available would be welcome. The trade-offs are difficult to face, and medication is only one example of the types of decisions that impact the quality and duration of these children's lives.

SCN8A IS SO MUCH MORE THAN SEIZURES; IT AFFECTS EVERYTHING:

SCN8A impacts the entire family dynamic. Caregiver relationships are strained. Siblings are impacted in ways that cannot be known because their life with a chronically ill sibling is all they've experienced. Finances are impacted because some parents need to stop working to care for their child full-time, and the costs of caregiving can be great.

WHAT CAREGIVERS WISH PEOPLE UNDERSTOOD:

Most caregivers feel that others cannot possibly understand the life they are living because others are not experiencing it themselves, and because SCN8A caregivers buffer and shield others from the reality and extent of their challenges. They become people that they never knew they could be, simply because they have to be. SCN8A parents share feelings of isolation.

ALTHOUGH IT'S A HARD JOURNEY, CAREGIVERS FEEL HONORED TO PARENT THESE AMAZING CHILDREN:

Parents communicate that it is not a burden to care for their children living with SCN8A, that they love them deeply, but that the situation is nonetheless heavy all the time. Parents remind themselves to celebrate their children for who they are. Parents and caregivers feel that raising children with SCN8A is an honor, and the experience makes them better people, for which they are grateful.

SCAN OR CLICK TO VIEW THE FULL CAREGIVER REPORT



SCAN OR CLICK TO WATCH MARGOT'S STORY

PARENTS HAVE CONSTANT ANXIETY OF LOSING THEIR CHILD:

Many parents and caregivers of children with SCN8A carry a constant fear that either they will lose their child prematurely to SCN8A or that they themselves will die before their children, and there will be no one to care for them. There is a fear that their child won't be there the next day, whether due to SUDEP or the unpredictability of seizures or illness. Many parents do not feel anyone could possibly understand this anxiety. Parents who have lost their children miss not only their child but the day-to-day experience of caring for their child, despite the challenges.

Madeleine and Chris, Margot's Parents

Margot's Story: Early Onset Epilepsy–Severe DEE

Margot was born in March 2021 following a healthy pregnancy and an easy delivery. The first three months of her life were smooth. One morning, Margot started to make some odd facial twitches, which Madeleine recorded and showed to Margot's pediatrician, who suspected seizures. Margot's parents took her to Boston Children's Emergency Room, where she continued having facial movements every few hours. Margot had an EEG and was admitted for monitoring and additional testing. While hospitalized, she also had a full-body tonic-clonic seizure and was diagnosed with epilepsy of unknown origin. Margot responded well to the first medication she was given, so the family was hopeful. Her DNA was sent for genetic testing.

When Madeleine and Chris received the results of the genetic testing at 5 months, Margot actually had two mutations in the SCN8A gene. They immediately began researching the condition and learned how the mutation caused epilepsy and that there was extreme variability in terms of the health of SCN8A patients.

After her diagnosis, Margot's condition continued to worsen. Throughout her lifetime, she was on 11 anti-seizure medications and the ketogenic diet. She developed infantile spasms, a catastrophic form of epilepsy with almost continuous seizures. Margot had upwards of 150 seizures per day, as well as a background of noise called hypsarrhythmia that gets in the way of brain development. Margot was treated with high-dose steroids for infantile spasms, which caused tremendous rage and crying, as well as another drug that has a risk of blindness. Rescue medications and frequent trips to the ER and ICU stays were common.

Margot had extreme respiratory vulnerability due to uneven muscle tone, limited movement, and frequent pneumonia, requiring BiPAP and oxygen. She had GI issues, including daily vomiting, feeding intolerance, and eventual continuous J-tube feeds. Margot also had cortical visual impairment and limited communication. Her parents were always on

edge and turned their home into a makeshift ICU, so they could reduce hospital visits. Madeleine stated,

"I think that's the hardest, you know—not knowing how much time we have left with her and just trying to make the most of every day."

Margot's parents are interested in treatments that can fundamentally address the disease at the cause and potentially reverse the side effects, despite it being too late for Margot. They are hopeful for precision therapies, such as genetic therapies, and understand that these therapies may carry more risk. In this community, there is an urgency to this development because the risk of doing nothing is equally significant.

Despite exhaustive treatments and supportive care, Margot's disease remained refractory, and she passed away during the planning of this PLS after 4 years of living with SCN8A.



Liz and Michael, Will's Parents

Will's Story: The Unspeakable Truth of SUDEP

Initially, Will's development seemed fairly typical compared with his older brother, but at a few months of age, differences began to show. Liz mentioned this to Will's pediatrician, who said Will had mild hypotonia and recommended occupational therapy. He was not significantly far behind but was on the slower end of meeting developmental milestones.

Will's first seizure occured when he was 10 months old. He was rushed to the ER and started having status epilepticus, where he was put on paralytics to stop the seizures and intubated. Will was admitted for several days of testing with inconclusive results, and that began many years of trying to figure out what was going on for Will.

One of the first medications given to Will was a common medication for patients with seizures that ended up making his seizures worse. Over the course of Will's life, he tried seven or eight medications. His second medication gave him seizure freedom for roughly nine months. During this time, Will made some significant developmental gains. By the age of three, he had learned all of his letters. In the second stint of seizure freedom at age five, Will learned how to walk.

At the time that Will received his diagnosis at five years old, the medical literature documented only 14 children with the SCN8A diagnosis, and of those 14, a handful had died from SUDEP.

At the time that Will died, he was having about one seizure a week, which was a vast improvement because he would have maybe one bad day a week. But the rest of the time, he was able to live life, and the

SCAN OR CLICK TO WATCH WILL'S STORY

family was able to live life with him. Will loved school and had his own friends. Liz was able to go back to work when Will was in kindergarten. But then Will and his family had to start over after a breakthrough seizure ended that seizure freedom period. Will never regained seizure control after that point. He lost the ability to walk. He went back to crawling. He forgot a lot of his letters. "The seizures took such a toll on his body and his mind."

When Will was alive, Liz and Michael had the same baby monitor from Will's first seizure until the day he died. The monitor was always with them, no matter what they were doing, including next to their bed at night and in the bathroom when showering. Will died of SUDEP one night, and there was nothing that alerted them to his death. "SUDEP is a quiet thing, so in spite of us having a monitor on him, that didn't help."

"We often say that Will's absence is just as real as his presence. And we miss him every day. His room is untouched from the day he died eight years ago."

Even though it is too late for Will, Liz and Michael hope for other patients living with SCN8A that clinical trials will lead to precision medications and treatments that will help target seizures effectively without so many side effects, so they can have a better future than Will did. These kids and their families are suffering. Being able to decrease the number of seizures that these children are having would be a gift.



Megan, SCN8A Warrior and Trisha, Megan's Mom

Megan's Story: Hope Undone by the Loss of Seizure Control

Megan is 21 years old. "She was a cheerful, joyful little girl," remembered Trisha. She was nonverbal until she was about four and a half years old. But otherwise, aside from seizures and some developmental delays, Megan tried to do what all the other kids in the neighborhood were doing.

Megan began having seizures at about six months of age but was not diagnosed with SCN8A until she was 12, despite having been seen by multiple doctors. At the time of her diagnosis, there were about 45 known cases, and Megan did not resemble the other kids with the condition since most were more severely affected than Megan, both in terms of seizures and comorbidities. There were also only a few other children who had Megan's specific variant, giving them little opportunity for comparison.

Megan, like most children living with an SCN8A mutation, went through a journey of multiple medications with mixed efficacy and multiple side effects, particularly in terms of cognition and speech. Finally, with a move to another state and yet another physician, Megan was put back on a

SCAN OR CLICK TO WATCH MEGAN'S STORY

much higher dose of a drug that she had previously tried, which gave her a period of nine years of seizure freedom, and continual development that enabled her to enter college.

That instantly ended two years ago when Megan had a seizure at college and had to return home. Megan's roommates said they were not able to support her and planned to move out. Megan's family worried that she would be alone when having a seizure, and no one would be there to call 911, and she could die.

Megan and her parents are proud of her accomplishments thus far, and they know she will have more accomplishments ahead. They collectively wish for her eventual independence or partial independence. Megan is asking herself what is next for her. She has looked for a job since she was sixteen, but because Megan's speech falters and she has challenges with her vocabulary, she does not get hired despite her capabilities. She expressed feeling like she is taking the same step over and over again.

Megan's parents hope that future developments from the FDA will help with cognition as well as seizures. Megan does not mind taking medication if it prevents her from having another seizure. She would also be open to being part of a clinical trial if it helps her.

In the final planning for this event, we learned that Megan now has the job she has been working toward, giving hope to the community.



Shelley, Nico's Mom and Katie, Wyatt's Mom

Beyond Seizures: Behavioral Impacts

TCSF Director of Patient Engagement and Data Management, Shelley Frappier, interviewed 13 caregivers of children and young adults living with SCN8A. The common thread is that for many families, seizures are only part of the story. The daily burden, the exhaustion, the near-miss safety scares, the behavior challenges, and the long-term physical and emotional strain on caregivers is difficult to fully capture in words. A summary report of these findings was shared with the FDA in preparation for the PLS, and one specific example was shared during the meeting by Katie about her 14-year-old son, Wyatt. She defines what daily vigilance looks like, how safety shapes every decision, and how SCN8A impacts not just the child, but an entire family.

Wyatt has had six seizure types in his lifetime and has never experienced seizure freedom. In the beginning, managing up to 100 seizures per day was the family's greatest struggle. However, after a few years, that drastically changed as behavior problems started to take center stage. Wyatt was diagnosed with level 3 autism just after his second birthday and has since been diagnosed with pathological demand avoidance.

SCAN OR CLICK TO LEARN MORE ABOUT BEHAVIORAL CHALLENGES

He struggles with severe ADHD and impulse control. He suffers from debilitating anxiety. He has an intellectual disability that results in cognitive functioning closer to that of a six-year-old, despite being nearly 14.

An example of how his conditions manifest is if he wants something and you try to keep it from him or tell him no, he'll lash out in any way possible to protect himself—hitting, kicking, biting, hair pulling. He's not able to self-regulate, especially when he's escalated, so his family has to help him de-escalate while trying to keep everyone safe.

"The heartbreaking part is that once he's calm and sees what he's done, he always looks so sad, and it just serves as a reminder that he has no control in these situations."

Wyatt has obsessive-compulsive disorder, which often means that when he starts something, he has to finish it, but it can lead to self-harm if something doesn't feel right. For example, ripping fingernails and toenails completely off because of a snag or a hangnail. Once he starts, he can't stop until the whole nail is gone. Wyatt breaks everything, even things that he loves. He rips his clothing, breaks his toys, and has broken his safety bed, causing his mom to have to sleep with him to keep him safe. He has broken countless cabinets and pieces of furniture, and has an obsession with breaking glass, causing the family to have to eliminate glass from the house.

Wyatt is not toilet-trained and has major temper tantrums, often in public, which at 14 is not understood by most observers. On Wyatt's first day of middle school, he was pinned down by a teacher due to behavior. The school was unprepared to support Wyatt, despite their assurances that they were.

Katie shared that Wyatt is also loving, snuggly, funny, brave, smart, silly, and imaginative. She also shared the challenges so that others facing similar issues—such as not being able to take their eyes off their kids because if they do, they'll run, hurt themselves, or hurt someone else—can feel seen.



Danielle and Phil, Lucy's Parents

Lucy's Story: The Reality of Loss–Severe DEE

Lucy passed away when she was three years old due to SCN8A. She was full of joy, and her parents miss her every day. She had so many challenges in her short life, but was always smiling. Lucy arrived after a healthy pregnancy, but right after she was born, the doctors noticed irregular breathing, significant muscle tightness, and shakiness. She was taken to the NICU for multiple tests, but they did not find anything conclusive. Lucy's first obvious seizure occurred at about two weeks old when Danielle was feeding her, still in the NICU at that point. She stiffened and turned blue.

SCAN OR CLICK TO WATCH LUCY'S STORY

Every day with Lucy was all about her schedule and needs. She did not sleep much, which was very hard on both her and her parents; she slept with oxygen and a pulse oximeter. She had to take her seizure medications three times a day because she metabolized her medications so quickly, and she did six scheduled feeds throughout the day for about an hour. Danielle and Phil tried to just be parents to Lucy, but with her complex medical needs, they were also her therapists and nurses. Play often looked like doing stretches and using different equipment, or working with her communication device, even when outside therapists were not with Lucy.

Almost every week to every month, Lucy had to have labs to monitor medication levels to check for issues they might be causing. She had 13 specialists, so essentially a specialist for every system of the body. The family lived an hour and a half from the children's hospital, so they would try to coordinate appointments, but when that did not work, they found themselves driving to the hospital two or three times a week. That meant loading all of Lucy's equipment in the car, all of her medications, her G-tube, her specialty formula, and an emergency oxygen tank.

When Lucy was four or five months she started having generalized tonic-clonic seizures that would all result in status epilepticus. She would have reduced breathing during the seizures, so every seizure from that time through about nine months, the family had to call 9-1-1. There was no opportunity for Lucy to develop during this time, so she didn't hit any typical milestones. Lucy lived the first couple of months of her life in the hospital. Unfortunately, so much damage was done during that time to her brain that it seemed she was never going to catch up. Lucy was hospitalized 36 times for seizures, respiratory issues, and medication side effects during her lifetime; she was only alive for 40 months.

During one hospital visit, Danielle lost count at 100 seizures in a 24-hour period. Her doctor hit the code button and called for an emergency meeting for the team to help find a solution for Lucy. She was immediately put on the ketogenic diet, along with all of her anti-epileptic drugs, and soon her seizures went from 10 to 100 per day to three to five a week, which was a significant improvement.

Lucy got pneumonia for a third time in July of 2023 and was taken to the hospital. Her parents were not prepared for what would come next; they thought they would be taking Lucy home after a short stay. A few days in, the team met with Lucy's parents to prepare them for the worst-case scenarios. The next day, Lucy perked up, but two days later, she was experiencing heart failure, and Danielle and Phil had to say goodbye to Lucy. This will "forever be the worst memory of our lives."

The fact that there is no specific treatment for SCN8A is one of the hardest things about the condition. Treatment is based on reading

literature and knowing other patients. But at the end of the day, doctors and families are just trying things to see what might work, while not making things worse. With most patients being on multiple medications, it makes it really hard to know what to do next.

"We were extremely open to a clinical trial to the point where we actually had the initial screener appointment for one of the trials scheduled the day that I was driving Lucy to the emergency room for that last hospital stay."

Lucy's parents were interested in the trial both for the community and because perhaps it would have given Lucy a better chance to explore life. Incremental progress would still have been progress.



SCAN OR CLICK TO WATCH MAX'S STORY

Dianely, Max's Mom

Max's Story: Why Time Matters

When Max was born, his parents thought everything was normal, despite Max not sleeping. After a month, Max's pediatrician said he looked fine, but he was not showing a Moro reflex, so he referred Max to a neurologist. During the visit, Max made a movement that concerned the doctor so he ordered an EEG. The EEG showed infantile spasms. Max was rushed to be admitted the same night for multiple other tests, including genetic testing. It took several months to receive the genetic results. At the time, there were about 90 documented cases of SCN8A mutations and only one with Max's variant. Max's healthcare team didn't know anything about SCN8A; even a subsequent team with slightly more knowledge seemed to be "shooting from the hip" to help Max.

When the doctor said, "Max's chance of living doesn't look promising," Dianely began researching the condition to be the advocate Max deserved. She found her way to the Cute Syndrome Foundation on Facebook, where she found the "most amazing tribe of people there who understood exactly what we were going through and were able to guide us in ways that the professionals we were seeing at the time couldn't." Dianely felt that without this support and knowledge she gained, they may have lost Max sooner than they did.

"All of a sudden, my husband and I were forced to become nurses, doctors, therapists when we got home."

Dianely eventually quit her job so that she could provide full-time care to Max. His parents were constantly having to make difficult decisions regarding Max's care, weighing the quality of his life with the quantity. Max's mom believes that his condition turned his little brother Zach into "the most amazing human being I know. He would always come into the room wanting to make Max laugh. His goal in life was getting Max to smile or have fun." On the day that Max's heart stopped, Zach laid down

next to his brother and gave him a kiss before saying goodbye. "The pure innocence that he had was broken a little."

When Dianely was asked to participate in this PLS, Max was alive, and she was considering how to include Max in the interview. Max had been doing so well at the time. Within a matter of months, however, Max was gone. "One minute to the next, I went from Max smiling and laughing, watching his latest favorite movie…to me, kissing him goodbye."

Dianely wants others to realize that there is no manual for managing kids with SCN8A. Therefore, there has to be room for flexibility, understanding, collaboration, and teamwork. Because if it weren't for parents or caregivers who fight and advocate as hard as they do, a lot of what's been learned wouldn't exist. One of the main concerns is that kids with SCN8A are often grouped into a "bubble" with others who don't necessarily fit the same profile. Max didn't fit in that "bubble." "He was just so drugged up on a lot of these seizure medications...that were meant for adults."

She wants the FDA to see the SCN8A community as a separate entity in need of guidelines or indications to fit our needs. She believes the community understands that there are studies that take time, and that the research we support may not save our own kids, but that it could save someone else's child in the future. That is why she continues to fight, despite having lost Max.

Hillary Savoie, Founder and Board Chair

Wrap-Up Remarks by The Cute Syndrome Foundation

Hillary began by expressing emotion regarding recent losses in the SCN8A community, including those children who have passed since the planning of the PLS began. She communicated the real and personal connection that she and others have with the children suffering with this disorder and reiterated the impact SCN8A has not only on the patients, but also their parents, their siblings, and their communities. There is urgency to the need for developments in SCN8A, and she shared the need for all those present to feel that urgency along with the community.

Despite the losses the SCN8A community continues to face, there remains hope for many reasons, including the families who continue advocating for SCN8A even after the loss of their children. One such advocate is Danielle, Lucy's mother and the Incoming Executive Director of the Cute Syndrome Foundation (TCSF).

The FDA is integral to that hope. The SCN8A community believes that better, more precise treatments are possible—from therapies that may improve daily life with SCN8A through fewer seizures and reduced side effects, to innovations that can fundamentally change what is possible for

children living with the disorder. The community seeks the FDA's partnership in turning that hope into meaningful progress across every stage of the process—from bench research and clinical care to drug development and regulatory action—so that these systems work more effectively for children with SCN8A, because they cannot wait.

Hillary closed by thanking the families who agreed to share their stories and their willingness to make themselves vulnerable in hopes of moving the needle for our community, as well as a thank you to the FDA and others in attendance for taking the time to show up and learn about our community from the people who actually live it.

Q&A and Comments from FDA

Question / Comment #1:

Comment: The individual was very moved by the intense day-to-day impact of SCN8A and inspired to look beyond the mountains of data to the patients.

Q: How could FDA reduce obstacles to families participating in clinical trials?

A: Allow for decentralized, in-home, or local testing and reporting.

A: Reduce placebo exposure and instead utilize other representative data such as the available natural history study or other available data such as ongoing registries.

A: Allow for n-of-1 or n-of-fewer trials, such as those used with different genetic approaches.

A: Accelerate the review process through various means, including close collaboration with sponsors.

Question / Comment #2:

Q: How do families weigh the risks and benefits of participating in clinical trials for SCN8A?

A: Families are interested in possible therapies that reduce seizures but are also interested in other effects that have not been well characterized. For families, the safety bar is somewhat lower because they are already making risk/benefit trade-offs every day with the therapies from which they currently have to choose.

A: This sentiment was repeated by two additional family speakers. Families described already navigating medications not originally developed for the SCN8A community, including treatments requiring extended monitoring for serious side effects such as cardiac complications,underscoring that the risk calculus for investigational therapies is viewed through a very different lens than for the general population.

A: Geographic access was also raised as a significant barrier to clinical trial participation. Some children are too medically fragile to travel to distant trial sites, and the absence of local or regional trial infrastructure has prevented families from enrolling even when they were willing and motivated to do so. This reinforces the importance of decentralized trial models for this population.

A: It was also noted that the community maintains caregiver-based outcome measures and a patient registry that could support non-seizure endpoints in trial design, offering data resources beyond seizure frequency alone.

Question / Comment #3:

FDA Public Engagement Staff thanked everyone for attending and encouraged all parties to keep the conversation going. The meeting was adjourned.

Comment #4—In the chat:

An FDA member thanked TCSF and noted that they would share the learnings with their department colleagues.

Comment #5—In the chat:

It was noted that the condition, although referred to by FDA members as The Cute Syndrome, is actually known as SCN8A. The Cute Syndrome is the name of the Foundation.

Closing Perspectives

Throughout the Patient Listening Session, families consistently emphasized that SCN8A-related disorders affect every aspect of life — medically, emotionally, socially, financially, and developmentally. Participants described the SCN8A community as living with extraordinary uncertainty, constant vigilance, and repeated loss.

At the same time, families conveyed extraordinary resilience, advocacy, and hope. Even families who had lost children continued participating in the session to improve outcomes for future patients.

Participants expressed hope that continued collaboration among FDA, researchers, clinicians, industry partners, and the patient community may accelerate the development of safer, more effective, and more precise therapies capable of meaningfully changing the trajectory of SCN8A-related disorders.

Meaningful Treatment Outcomes Identified by Participants

- Reduction in seizure frequency and severity
- Reduction in status epilepticus episodes
- Fewer medication side effects and reduced polypharmacy
- Preservation or improvement of cognition and communication
- Improved sleep and alertness
- Behavioral stabilization and emotional regulation
- Improved feeding and respiratory stability
- Preservation of mobility and developmental progress
- Reduced caregiver burden and emergency interventions
- Reduced mortality risk, including SUDEP

Considerations for Clinical Trials and Regulatory Flexibility

Participants discussed numerous barriers associated with traditional clinical trial structures in ultra-rare neurological diseases. Families emphasized that extensive travel, repeated hospital visits, placebo exposure, and rigid eligibility criteria may unintentionally exclude severely affected patients.

Participants encouraged consideration of decentralized trial models, remote monitoring, home-based assessments, use of natural history data, adaptive trial designs, and alternative statistical approaches appropriate for small populations.

Families also expressed willingness to accept meaningful therapeutic risk given the severity, progression, and mortality associated with SCN8A-related disorders.

In Attendance

FDA Attendees

OFFICE OF THE COMMISSIONER (OC)–3 OFFICES

- OC/OEA/PES–Office of External Affairs/Public Engagement Staff (organizer)
- OC/OCMO/OOPD–Office of the Chief Medical Officer/Office of Orphan Products Development
- OC/OCMO/OPT–Office of the Chief Medical Officer/Office of Pediatric Therapeutics

CENTER FOR BIOLOGICS EVALUATION AND RESEARCH (CBER)–2 OFFICES

- CBER/OCD–Office of the Center Director
- CBER/OTP/PSPS–Office of Therapeutic Products/Policy and Special Projects Staff

CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)–6 OFFICES

- CDER/OND–Office of New Drugs
- CDER/OND/ON/DNI–Office of New Drugs/Office of Neuroscience/Division of Neuroscience I
- CDER/OND/ON/DNII–Office of New Drugs/Office of Neuroscience/Division of Neuroscience II
- CDER/OND/ORDPRUM/DRDMG–Office of New Drugs/Office of Rare Diseases, Pediatrics, Urology and Reproductive Medicine/Division of Rare Diseases and Medical Genetics
- CDER/OTS/OB/DBI–Office of Translational Science/Office of Biostatistics/Division of Biostatistics I
- CDER/OTS/OCP–Office of Translational Science/Office of Clinical Pharmacology

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH (CDRH)–2 OFFICES

- CDRH/OPEQ/OHTI/DHTIC–Office of Product Evaluation and Quality/Office of Health Technology I/Division of Health Technology IC
- CDRH/OSPTI/OEID/DPCD–Office of Strategic Partnership and Technology Innovation/Office of Equity and Innovative Development/Division of Patient Centered Development

Non-FDA Attendees

REAGAN UDALL FOUNDATION

NATIONAL INSTITUTES OF HEALTH (NIH)

- NIH/NCATS–National Center for Advancing Translational Sciences

SPEAKERS

- Kacie Craig, Outgoing Executive Director of the Cute Syndrome Foundation and Mom to Stella, SCN8A Warrior
- Dr. John Schrieber, Associate Chief for Neurophysiology from Children's National Hospital in Washington, D.C.
- Madeleine and Chris, Margot's Parents
- Liz and Michael, Will's Parents
- Megan, SCN8A Warrior and Trisha, Megan's Mom
- Shelley Frappier, Nico's Mom and Katie, Wyatt's Mom
- Danielle and Phil, Lucy's Parents
- Dianely, Max's Mom
- Hillary Savoie, TCSF Founder and Board Chair

LISTEN ONLY ATTENDEES–ORGANIZATION REPRESENTATION

- The Cute Syndrome Foundation–Note Taker and Technical Support
- SCN8A Alliance
- Rare Epilepsy Network
- Epilepsy Foundation
- University of Arizona Genetics Core

Disclaimer

Discussions during the FDA Patient Listening Session were informal and nonbinding. This summary reflects the perspectives and experiences shared by participating patients, caregivers, clinicians, and advocates. It is not intended to represent the experiences of all individuals living with SCN8A-related disorders.

To the extent possible, terminology and descriptions contained within this document reflect the language used by participants during the session.

Financial Disclosures

The Cute Syndrome Foundation (TCSF) would like to disclose that Longboard/Lundbeck, Neurocrine Biosciences, and Praxis Precision Medicines provided TCSF sponsorships to help support the planning and videography expenses of this Patient Listening Session. TCSF and multiple participants receive funding including grants, sponsorships, and consulting fees from a variety of sources, including sponsors; however, none of the participants on today's Patient Listening Session are receiving compensation for participation or attendance in this meeting.

Caregiver and Patient Recruitment Statement

Caregivers and patients were invited to participate in this Patient Listening Session to represent the broad clinical spectrum and lived experiences of SCN8A. The Cute Syndrome Foundation (TCSF), familiar with many families' journeys, invited speaking participants based on their unique experiences to illustrate the diversity and complexity of SCN8A.

Due to time constraints, only a few caregivers could share full narratives during the session. To provide broader representation, additional perspectives were included through a caregiver montage video and a caregiver report. The montage video highlights five families through recorded interviews, offering additional caregiver insights.

For the caregiver report, every family in TCSF's network (625 families) was invited to participate in a brief interview to share their experiences beyond seizures. Of these, 13 families chose to contribute approximately one hour of their time between August and December 2025. These 13 caregivers represented a broad range of experiences across the SCN8A spectrum.

Originally, two bereaved family perspectives were planned; by the time of the session, four participating family speakers had experienced the loss of their children.