



National Tay-Sachs &
Allied Diseases Association

JUVENILE ONSET GM1 Gangliosidosis and GM2 Gangliosidosis (Tay-Sachs and Sandhoff)

PATIENT-LED LISTENING SESSION

Thursday, August 28, 2025





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Goals and Objectives

NTSAD's intention, as a community, was to educate the FDA about the juvenile onset forms of GM1 gangliosidosis and GM2 gangliosidosis (Tay-Sachs and Sandhoff) with the following goals and objectives:

- A clinical understanding of the juvenile onsets of GM1 gangliosidosis and GM2 gangliosidosis (Tay-Sachs and Sandhoff) and the impact on children diagnosed with these ultra-rare diseases.
- Parents' lived experiences as their children progressively lose milestones once gained due to GM1 and GM2, and
- The unmet and urgent need for treatment options, and their fear of an uncertain future.



Meeting Topics

The topics covered in the Patient Listening Session painted a full picture of the disease across the five families who spoke to the FDA. They included:

- A clinical overview of the juvenile onsets of GM1 and GM2 (Tay-Sachs and Sandhoff)
- Onset of symptoms, progression of the diseases, and how quickly children lose the ability to walk, talk, safely eat orally, and use fine motor skills and cognitive ability to understand and comprehend what is happening to them
- Disease progression - from the onset of symptoms to observing children's loss of ability to participate in daily life like their peers and to watching them become completely reliant on 24/7 care by the time they reach their early teens and, for some, into adulthood
- Absence of approved therapies other than symptom management

Themes and Messages

- Clumsiness, decline in motor skills, and affected speech are common early signs
- Progression of the disease is relentless resulting in loss of autonomy for children who at those ages strive to be as independent as possible
- Fear of the future and the terrifying thought of losing their children to these diseases
- Urgency to address alternative approaches to trial design when it comes to these ultra-rare diseases
- Parents feel the idea of a placebo-controlled trial is unjust when it comes to fatal diseases with no approved therapies
- Encouraging FDA to look at what realistic and meaningful outcomes as a measure of a drug's success when it comes to ultra-rare diseases such as GM1 gangliosidosis Type II and juvenile onset Tay-Sachs and Sandhoff



It's hard to watch the children regress and lose their smiles. We just wish we could help them.





Introduction, Kathleen Flynn, CEO, NTSAD

Welcome to today's Patient-led Listening Session focused on the juvenile onsets of GM1 gangliosidosis and Tay-Sachs and Sandhoff diseases — collectively known as GM2.

I'm Kathleen Flynn, CEO of the National Tay-Sachs and Allied Diseases Association. Founded in 1957, NTSAD is one of the oldest rare disease advocacy organizations in the U.S., and our mission is to lead the fight to treat and cure GM2, GM1, and Canavan diseases by driving research, forging collaboration, and supporting families. While Externally-Led Patient-Focused Drug Development meetings for GM1 and GM2 were held in 2023 and 2024, respectively, today's session focuses specifically on the juvenile forms—marked by rapid progression, severe neurological decline, and a profound impact on quality of life. Although research is advancing, currently there are no approved treatments for these conditions.

We are grateful to the U.S. Food and Drug Administration for granting us the opportunity to host this Patient Listening Session, and we especially thank members of CBER, CDER, and other Centers for joining us. Today, you'll hear from an expert clinician, five courageous parents sharing firsthand experiences of caring for children with juvenile GM1 or GM2, and NTSAD's Annual Family Conference Camp Director.

With gratitude, we recognize Azafaros and IntraBio for their financial support, our patient advocacy partners – 11 members of the Global GM1 and GM2 Alliance who represent eight countries, as well as several families who participated in the survey provided with today's materials.

Most importantly, we thank the families who are speaking today. Their compelling statements reflect not just the urgency of the unmet need for approved therapies, but also the strength and resilience of this rare disease community. We hope this session informs future regulatory considerations — and brings us closer to meaningful treatments for these children.



Clinical Overview, Cynthia Tifft, MD, PhD, NHGRI

As you recall gangliosides are critically important structures on the plasma membranes of neurons, but they must be recycled. Inability to recycle, leads to storage in cellular lysosomes and death of neurons.



Both GM1 and GM2 gangliosidosis are rare, autosomal recessive disorders that block the first two steps in ganglioside degradation as shown in the upper left corner of this pathway slide.

Mutations in *GLB1* lead to a deficiency in b-galactosidase that removes the terminal galactose from GM1 ganglioside. Mutations in *HEXA* or *HEXB* lead to a deficiency in b-hexosaminidase A that removes the next sugar in the chain, GalNAc. The diseases are rare, neurodegeneration is relentless, and uniformly fatal. There are no approved therapies.

GLB1 encodes b-galactosidase that works in a complex with two other proteins, *PPCA* and *Neu1*, to break down GM1 ganglioside. Inability to do that leads to the features of GM1 including cerebral atrophy, neurodegeneration, a cherry red macula (in infantile disease), hepatosplenomegaly, skeletal dysplasia (particularly involving the spine and the hips), and later in the disease course, cardiomyopathy.

HEXA and *HEXB* encode the alpha and beta subunits of the heterodimeric enzyme, b-hexosaminidase A, required for the breakdown of GM2 ganglioside. GM2 ganglioside stores in neurons as multilamellar cytoplasmic bodies or MCBs. MRI imaging in these patients shows macrocephaly, global atrophy, or cerebellar atrophy depending on disease onset.

GM1, Tay-Sachs, and Sandhoff diseases are a continuum where residual enzyme activity is inversely proportional to disease severity with the least amount of residual enzyme leading to the most severe disease. For convenience, the diseases are divided into subtypes by age of onset and the rate of disease progression. Today, we will focus on the subtypes [in red]: late-infantile and juvenile type II GM1 and juvenile GM2 (Tay-Sachs and Sandhoff disease). The symptoms of all 3 diseases are similar as you can see.

The diseases are variable in progression as shown in this schematic, with infantile onset disease being relatively homogeneous, late-infantile disease in “red” being more variable, and juvenile onset disease in “green” having the most variability both in disease onset and progression.

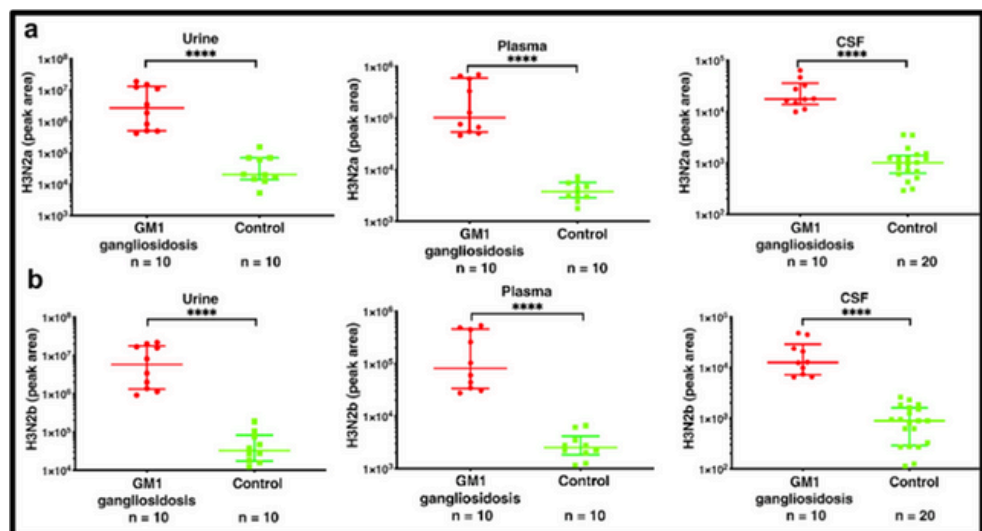


To illustrate, here I am showing you our natural history study including 44 patients with late-infantile and juvenile onset GM1 conducted at the NIH Clinical Center over 10 years¹. You can appreciate three things in this busy slide: (1) symptom onset is variable as shown by the dashed line beginning at the left, (2) reaching a diagnosis, shown by the vertical black bar, often takes years following symptom onset, and (3) many of the children have progressed to having seizures (shown by the yellow dot) before a diagnosis is even made. With newer genetic techniques such as exome and genome sequencing, we are hopeful that patients will receive earlier diagnoses before skills are lost that may not be regained even with effective therapy.

The story with juvenile onset GM2 disease is similar, with death often by the second decade.² Ambulation is impaired by age 6 with children becoming wheelchair-bound within 5 years. Dysarthria, loss of the ability to verbally communicate, that is so devastating for families, begins at age 4 and by age 9 children can no longer speak as shown in the bottom right panel. Again, the wide error bars indicate the variability in disease progression.

With broad clinical variability we can potentially turn to biomarkers as surrogate endpoints. The quantitation of GM1 and GM2 ganglioside in CSF is about as close as we can get to ganglioside storage in brain, and I was heartened by a recent publication summarizing GM1 and GM2 as biomarkers in CSF by the Office of Clinical Pharmacology at CDER in Clinical Translational Science³. GM1 ganglioside is increased in CSF in affected patients. In the right panel I am showing you data from our ongoing gene therapy trial. Note that the pre-treatment values at week 0 for juvenile onset patients are 2 to 3 times control levels, and for infants the values are even higher.

(The panel shows an oligosaccharide biomarker H3N2b, unique to GM1 disease in patients and animal models, that are much higher than control subjects in urine, plasma, and CSF.)⁴





Likewise, in GM2 gangliosidosis, the upper portion of this graph, in the solid-colored lines, are values of GM2 ganglioside in spinal fluid in a GM2 gene therapy trial published just last week. Visit A is the pre-treatment value for GM2 in CSF: between 100 and 300 ng/mL. GM2 levels in a control population are essentially “0” since it is basically a pass-through reaction between GM1 and GM3 ganglioside.

Clinical trials for GM1 and GM2 are limited, and most are no longer recruiting. GM1 and GM2 are among the many other rare diseases that have fallen victim to being dropped by industry, not because they don't work, but because they are not financially viable. Off label use of some compounds is being tried by parents, often at great expense, since there are no approved therapies. Supportive care is the mainstay of therapy for these children.

And lastly, we do not have time to waste as you will hear from our families. [The] parents [of one of my patients] went on to conceive two additional children, both affected with TSD; the recurrence risk is 1 in 4 or 25% for each pregnancy. They chose to terminate these pregnancies and donated brain tissue for research. The thin layer chromatography gel shows that even at 17 weeks' gestation GM2 ganglioside is being stored in the brain. RNA sequencing shows that gene expression is more immature than controls and that signaling pathways are disrupted. We need to find these children quickly to begin therapy and optimize outcomes.

1D'Souza P, Farmer C, Johnston JM, Han ST, Adams D, Hartman AL, Zein W, Huryn LA, Solomon B, King K, Jordan CP, Myles J, Nicoli ER, Rothermel CE, Mojica Algarin Y, Huang R, Quimby R, Zainab M, Bowden S, Crowell A, Buckley A, Brewer C, Regier DS, Brooks BP, Acosta MT, Baker EH, Vézina G, Thurm A, Tiftt CJ. GM1 gangliosidosis type II: Results of a 10-year prospective study. *Genet Med.* 2024 Jul;26(7):101144. doi: 10.1016/j.gim.2024.101144. Epub 2024 Apr 16. PMID: 38641994; PMCID: PMC11348282.

2Maegawa GH, Stockley T, Tropak M, Banwell B, Blaser S, Kok F, Giugliani R, Mahuran D, Clarke JT. The natural history of juvenile or subacute GM2 gangliosidosis: 21 new cases and literature review of 134 previously reported. *Pediatrics.* 2006 Nov;118(5):e1550-62. doi: 10.1542/peds.2006-0588. Epub 2006 Oct 2. Erratum in: *Pediatrics.* 2007 Oct;120(4):936. PMID: 17015493; PMCID: PMC2910078.

3Stern, S., Crisamore, K., Li, R.-J., Pacanowski, M. and Schuck, R. (2025), Evaluation of the Landscape of Pharmacodynamic Biomarkers in GM1 and GM2 Gangliosidosis. *Clin Transl Sci*, 18: e70176. <https://doi.org/10.1111/cts.70176>

4Kell P, Sidhu R, Qian M, Mishra S, Nicoli ER, D'Souza P, Tiftt CJ, Gross AL, Gray-Edwards HL, Martin DR, Sena-Esteves M, Dietzen DJ, Singh M, Luo J, Schaffer JE, Ory DS, Jiang X. A pentasaccharide for monitoring pharmacodynamic response to gene therapy in GM1 gangliosidosis. *EBioMedicine.* 2023 Jun;92:104627. doi: 10.1016/j.ebiom.2023.104627. Epub 2023 May 31. PMID: 37267847; PMCID: PMC10277919.

Regier DS, Proia RL, D'Azzo A, Tiftt CJ. The GM1 and GM2 Gangliosidoses: Natural History and Progress toward Therapy. *Pediatr Endocrinol Rev.* 2016 Jun;13 Suppl 1(Suppl 1):663-73. PMID: 27491214; PMCID: PMC8186028



Summary of Family Statements

Five parents shared their perspectives, experiences, and fears for their children as they navigate the world of these ultra-rare diseases. Their statements are summarized.

Kelly | Son diagnosed in the fall of 2022 at 7 years old | Juvenile Tay-Sachs

Kelly shared the first symptoms they noticed were a decline in fine motor skills and his speech and a hesitation before speaking. After nearly a year, an MRI, and genetic testing, they read the diagnosis online. Her son struggles with coordination and balance, has lost his fine motor skills, and requires attention around the clock. He suffers from severe emotional swings and is unaware of his surroundings or his safety. He has regressed and has lost any of the skills he gained prior to the diagnosis. They live every day with the fear of losing him to the disease and hope a therapy will be approved in time to help him.

Jennifer | Daughter diagnosed in 2021 at 10 years old | Juvenile Sandhoff

The first symptom Jennifer noticed in her daughter was clumsiness – occasional stumbling and losing her grip holding things like a pencil. It progressed to struggling while getting off and on the school bus, “slushy” speech, and a growing persistent tremor in her hands and throughout her whole body. Jennifer shared how the progression has happened so fast and heartbreakingly – even hugs are tough with weakened arms and grip. While her daughter is a warrior and finds ways to enjoy the things every 13-year-old enjoys, she fears for the future. Jennifer shared her frustration with the struggle to access any therapy that could be available to them – the financial costs, the fear that any drug they use may exclude them from clinical trials, and the trepidation at the thought of receiving placebo when time is not on their side.

Yasmina | Daughter diagnosed in 2020 at 6 years old | Juvenile Tay-Sachs

Leading up to 2020, Yasmina noticed that her daughter was unsteady on her feet, and her speech became slurred. She has lost the ability to speak, walk, or even enjoy her favorite arts activities. Now, Yasmina can only interpret her daughter’s needs through her eyes, and even then, it’s a guessing game. Being a single parent, the multiple hats Yasmina wears is exhausting – aside from being a mother, she is a therapist, nurse, educator, entertainer, and recently biggest advocate. Navigating the medical and Medicaid system is daunting and a full-time job. Yasmina stressed her fear and frustration thinking about her daughter being randomized into a clinical trial that may cost her time and further regression. Like the other parents, simple stabilization would be invaluable and mean more time.



Summary of Family Statements cont'd

Ryan | Daughter diagnosed in 2019 at the age of 4 years old | Juvenile GM1

Her turned in foot, walking on tiptoes, and falling more often were the first signs that something was wrong with Ryan's daughter. Her speech began to fail, and she became harder to understand. Not too long after, a simple blood test revealed the diagnosis. After wrestling with the news, Ryan and his wife searched the globe for something that could save their child. In 2021, they found a clinical trial for a small molecule drug that was being tested in adults with late onset Tay-Sachs and opened for a small number of children like his daughter. Within a month of receiving the drug, they witnessed improvements in her gait and her speech. They went from fearing losing their daughter to GM1 Type II to watching her blossom as a 10-year-old as the disease appeared to stop progressing. These results should matter, stressed Ryan, and urged regulatory arms to adapt to the "specific" realities of these diseases. They now live with the fear that they may lose access to the drug that is having a positive effect on their daughter. He closed with, "I ask you to look beyond the limitation of the data and see what is right in front of us. Because without this drug, our story would look hugely different today."

Merlie | Daughter diagnosed in 2010 at 8 years old | Juvenile GM1

The first symptoms appeared at age five with clumsiness, issues with simple motor skills, and stuttering. Balance was off. Even Merlie's daughter expressed that her feet and hands weren't listening to her. It took 13 years to finally reach a confirmation of the diagnosis. Fast-forward 15 years and Merlie's daughter is completely dependent on her parents as her caregivers. She is non-verbal, tube-fed, and not ambulatory at all. She requires 24/7 care without much respite for Merlie and her husband. However, they do not let the disease define their daughter or their lives. They power through and provide experiences to give their adult daughter an enjoyable and exciting life. Hot air balloon rides, trips to Disney, and many music events. And as Merlie shared, if her daughter could scratch that itch on her nose or regain her speech, those would be meaningful outcomes for them.

Karen Horton | Camp Director, NTSAD Annual Family Conference

We felt the perspective of Karen was important to share as she has seen children living with GM1 Type II and juvenile onset Tay-Sachs and Sandhoff attend Camp Active every year the NTSAD Annual Family Conference. She shared how she witnessed them walk independently into camp one year and then return year after year becoming increasingly more dependent on mobility assistance – walkers, wheelchairs. She sees them struggle with speaking, becoming nonverbal, and lose the fine motor skills they once had when playing or creating in Camp Active. Karen urged the FDA to allow more flexibility when it comes to clinical trials for these rare diseases, and to make the difference families need – today and in the future.



Listening Session Attendees

Speakers in Attendance (in order of speaking)

Kathleen Flynn | CEO, National Tay-Sachs & Allied Diseases Association (NTSAD)
Cynthia Tifft, MD, PhD | National Human Genome Research Institute, NIH
Kelly | mother to a child diagnosed with juvenile Tay-Sachs
Jennifer | mother to a child diagnosed with juvenile Sandhoff
Yasmina | mother to a child diagnosed with juvenile Tay-Sachs
Ryan | father to a child diagnosed with juvenile GM1 gangliosidosis
Merlie | mother to an adult child diagnosed with juvenile GM1 gangliosidosis
Karen Horton, RN | Camp Director, NTSAD Annual Family Conference
Sara Scaparotti | NTSAD Board President

NTSAD Staff in Attendance

Becky Benson | Family Support and Engagement Manager
Erin Demers | Development Manager
Valerie Greger, PhD | Research Director
Diana Jussila | Director of Family Services

FDA Attendees

Office of the Commissioner (OC) – Three Offices

- OC/OEA/PES – Office of External Affairs/Public Engagement Staff (organizer)
- OC/IO – Immediate Office
- OC/OCMO/OPT – Office of the Chief Medical Officer/Office of Pediatric Therapeutics
- Center for Biologics Evaluation and Research (CBER) – Three Offices
- CBER/OCBQ/DIS/PSB – Office of Compliance and Biologics Quality/Division of Inspections and Surveillance/Program Surveillance Branch
- CBER/OTP/OGT/DGT2/GTIB – Office of Therapeutic Products/Office of Gene Therapy/Division of Gene Therapy 2/Gene Transfer and Immunogenicity Branch
- CBER/OTP/OPT/DPT1/PTB1 – Office of Therapeutic Products/Office of Pharmacology/Toxicology/Division of Pharmacology/Toxicology 1/Pharmacology/Toxicology Branch 1
- Center for Drug Evaluation and Research (CDER) – Five Offices
- CDER/OND/ODES/DCOA – Office of New Drugs/Office of Drug Evaluation Science/Division of Clinical Outcome Assessment
- CDER/OND/ON/DNI – Office of New Drugs/Office of Neuroscience/Division of Neuroscience I
- CDER/OND/ON/DPTN – Office of New Drugs/Office of Neuroscience/Division of Pharmacology Toxicology for Neuroscience
- 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/DBIV – Office of Translational Sciences/Office of Biostatistics/Division of Biostatistics IV



Listening Session Attendees, cont'd

FDA Attendees, cont'd

Center for Devices and Radiological Health (CDRH) – 11 Offices

- CDRH/OM/DAS/CONT – Office of Management/Division of Acquisition Services/Das Contractors
- CDRH/OPEQ/OHTI/DHTIA – Office of Product Evaluation and Quality/Office of Health Technology I/Division of Health Technology IA
- CDRH/OPEQ/OHTI/DHTIB – Office of Product Evaluation and Quality/Office of Health Technology I/Division of Health Technology IB
- CDRH/OPEQ/OHTI/DHTIC – Office of Product Evaluation and Quality/Office of Health Technology I/Division of Health Technology IC
- CDRH/OPEQ/OHTIII - Office of Product Evaluation and Quality/Office of Health Technology III
- CDRH/OPEQ/OHTIII/DHTIIIA - Office of Product Evaluation and Quality/Office of Health Technology III/Division of Health Technology IIIA
- CDRH/OPEQ/OHTIII/DHTIIIB - Office of Product Evaluation and Quality/Office of Health Technology III/Division of Health Technology IIIB
- CDRH/OPEQ/OHTIV/DHTIVC - Office of Product Evaluation and Quality/Office of Health Technology IV/Division of Health Technology IVC
- CDRH/OPEQ/OHTV/DHTVA - Office of Product Evaluation and Quality/Office of Health Technology V/Division of Health Technology VA
- CDRH/OPEQ/OHTV/DHTVB - Office of Product Evaluation and Quality/Office of Health Technology V/Division of Health Technology VB
- CDRH/OSPTI/OEID/DPCD – Office of Strategic Partnership and Technology Innovation/Office of Equity and Innovative Development/Division of Patient Centered Development
- Human Foods Program (HFP) – One Office
- HFP/OPIE/OIE/PHTS – Office of Policy and International Engagement/Office of International Engagement/Public Health and Trade Staff

Non-FDA Attendees

- Reagan Udall Foundation
- National Institutes of Health (NIH)
- NIH/NCATS – National Center for Advancing
- Translational Sciences



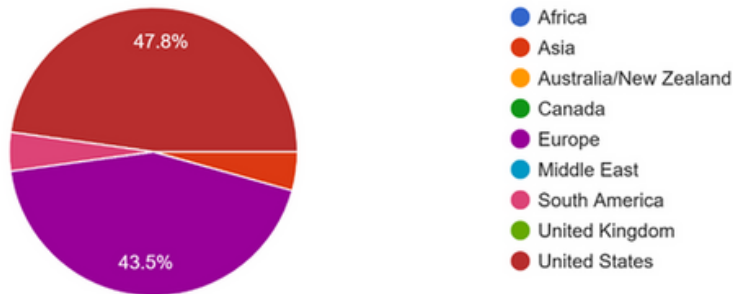


Survey: Community Voices Shared

NTSAD conducted a community survey, which was shared with the FDA as part of the supplemental materials submitted two weeks prior to the Listening Session. Parents and caregivers of children diagnosed with the juvenile form of GM1 gangliosidosis or GM2 gangliosidoses participated in the survey and granted NTSAD permission to share the results.

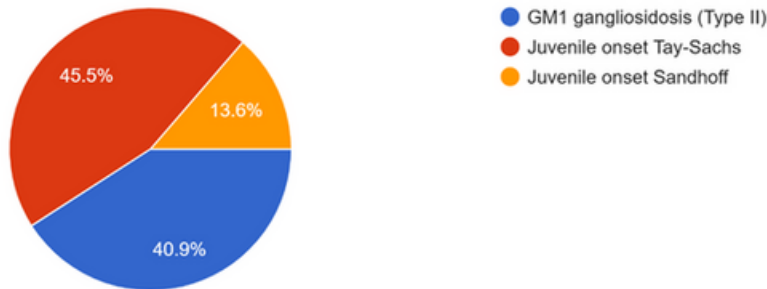
Where do you currently live?

23 responses



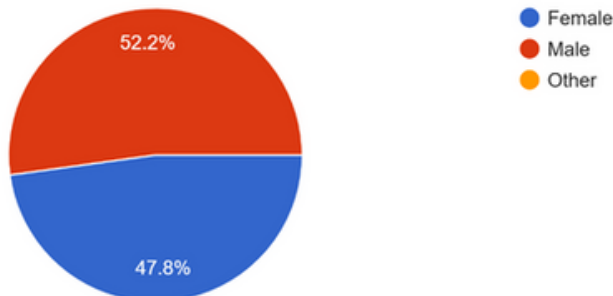
Your child was diagnosed with:

22 responses



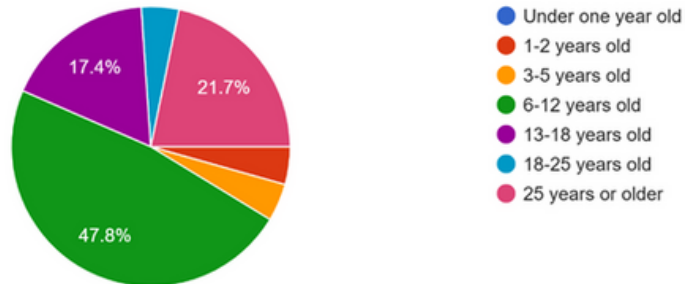
Your child is:

23 responses



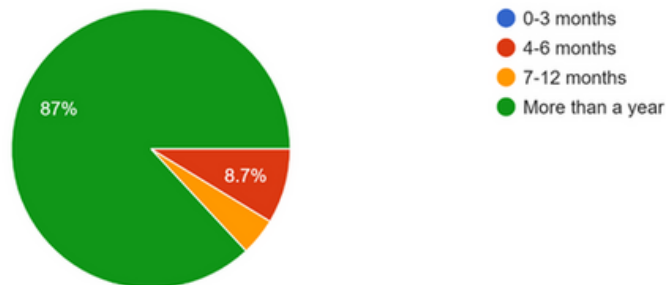
How old is your child?

23 responses



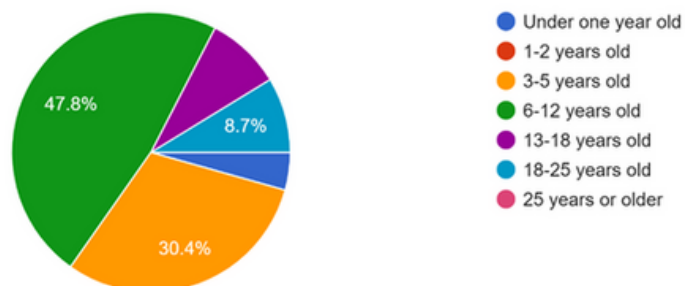
How long did it take to get your child's diagnosis?

23 responses



What age was your child when they were diagnosed?

23 responses

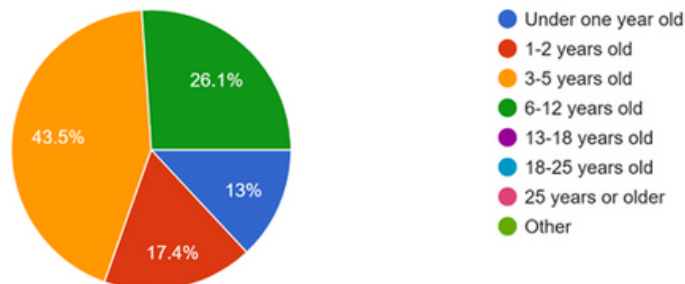




Symptoms

When did you first notice that something was wrong?

23 responses



What symptoms did you notice? (i.e. stumbling, falling, hand-eye coordination, fine motor skills)

- Not meeting milestones
- Stumbling, falling
- Fine motor skills, low muscle tone, delayed development
- Foot turning inward when standing, stumbling, stuttering
- All of the above and speech
- Viel gestolpert und viel hingefallen, unsportlich, Gleichgewichtsstörung (translation: tripping and falling a lot, unathletic, balance disorder)
- Speech, balance disorders
- He often fell, his movements were jerky rather than fluid, his speech development was delayed, and he walked awkwardly.
- Stumbling, falling, slurred speech
- Floppy muscle tone
- Stuttering
- Nonverbal and motor movement difficulties
- Stumbling, speech, fine motor skills
- Speech stuttering
- Lack of progression in learning; verbal and motor skills loss; regression of balance; and everyday skills
- Regression of motor skills, hand tremor, and trouble with fine motor tasks, inadequate balance
- Stumbling slower speech balance issues
- Speech issues, coordination issues
- Calf cramps, difficulty running fast, balance problems, ADS
- ·Er könnte sich nicht mehr selbstständig anziehen und die rechte und die linke Hand koordinieren. (translation: He could no longer dress himself independently and coordinate his right and left hand.)
- Tremor in hands, balance problems, fine motor skills, grob Problems Motorik (translation: gross motor problems), falling, hypotonia in the body
- She couldn't draw pictures in kindergarten. When she started school, she found it very difficult to learn. She couldn't retain anything. Learning to read took much longer. We held her back a year... the learning process was always difficult and time-consuming. However, once she had learned the material, she was able to apply it well.
- Muskelschwäche, Entwicklungsverzögerung (translation: muscle weakness, developmental delay)

What symptoms are most difficult to manage?

- Breathing, GI
- Speech difficulties
- Delayed development and cerebral palsy due to illness and nonverbal
- Inability to stand and transferrequires overhead lift to get her out of bed and into wheelchair and back into bed at end of day
- Incontinence, speech, stumbling
- Aufstehen, Laufen, Treppe gehen (translation: standing up, walking, taking the stairs)
- Speech, stumbling, and fine motor skills
- His unclear and heavily slurred speech and his motor impairments
- Falling
- Seizures
- Not walking
- Nonverbal
- Speech, Mood swings, Balance Problems
- Behavior
- Seizures and muscle spasms
- Cognition and motor decline
- Lack of sleep, regressions, moods
- Eating and drinking, speech
- The ADS problems
- Die Tatsache, dass er immer schlechter läuft, kaut, dass er nicht mehr spricht und allgemeine nicht mehr mit seiner Umwelt kommunizieren, Inter agieren kann (Translation: The fact that he is walking worse and worse, chewing, that he no longer speaks and generally can no longer communicate with his environment, interact)
- The hand tremor
- The logical thinking, the retention. She was avoided and excluded by other children.
- Epilepsy





How do their symptoms impact their daily life?

- Every aspect
- Isolation and frustration
- Exhausted, frustrated with trying to figure out what he wants, getting him around
- requires 24/7 caretotally dependent for everything
- Not being able to communicate, delayed academically, difficulty walking... impacted his entire life
- Aufstehen, Laufen, Treppe gehen, Sprechen, Schluckstörungen, der motorischen Fähigkeiten, psychische und neurologische Störungen (translation: Standing up, walking, going up stairs, speaking, swallowing disorders, motor skills, mental and neurological disorders)
- Speech problems make her communication so difficult that her social contacts are very limited. Fine motor problems make it difficult to carry out daily activities as personal hygiene, schoolwork, eating Balance problems prevent her from moving freely, going up stairs and performing typical activities of children of her age, running, jumping, climbing, riding a bicycle, swimming....
- He needs help with almost everything in everyday life.
- She cannot speak fluently and is unable to live normally like her peers, requiring external assistance.
- Completely
- Requires 24/7 assistance with almost everything
- She can't express herself or tell me what's wrong.
- Loss of social contacts and autonomy
- His behavior disrupts our whole house because of the temper tantrums.
- He falls quite often and injures himself. He can still walk, but it's a risk at times. Also his eating is going downhill.
- He falls often and requires help with all daily activities. He must be watched closely for choking and seizure activity.
- My child can't do anything for herself anymore. It's all affecting her.
- Needs help with most daily living tasks and now help with safely doing stairs
- Difficult to be successful in some sports, school problems caused by ADS
- Es hat eine große Auswirkung. Er hat 100-prozentige Schwerbehinderung Pflege Grad fünf (translation: It has a major impact. He has 100 percent severe disability, care level five)
- He can't write in school; eating is very difficult; often I must give him the meal.
- It took her a long time to learn to ride a bike; she is weak in sports. She was developmentally delayed, and she was often excluded in school.
- Große Sorge, er könnte sich bei einem Anfall verletzen. (translation: Very worried that he might injure himself during a seizure.)





How are you currently managing your child's symptoms?

- Full time nursing
- Several therapies, tangamil, miglustat
- He has medication, wheelchair, walker, AAC device, school OT, PT, and APE along with Outside PT
- My husband and I both quit our regular jobs to become her full-time caregivers.
- Palliative care
- Fährt teilweise noch mit Rollator, längere Strecken mit dem Rollstuhl, der geschoben wird, sie wohnt in einer Einrichtung für Behinderte, Hilfe beim Dusche/Baden/Körperpflege
(translation: Partly still uses a walker, longer distances are covered in a wheelchair, which is pushed, she lives in a facility for the disabled, assistance with showering/bathing/personal care)
- With accompaniment, aids and improvement of the living environment. With therapies, physiotherapy, speech therapy and occupational therapy. With electronic communicator
- He has a variety of therapies every week.
- Conduct some rehabilitation training for her, such as strength training, to improve her balance, and help her correct pronunciation in daily life.
- Drugs against the seizures, but often there is a deep sadness
- Some with medications. Some by adapting.
- Reassurance
- Improvement of the living environment, therapies in the areas of language, physio and ergo. Constant accompaniment.
- Gaufacine
- My child is in hospice care and therapies, and we are trying to keep him active and walking.
- OT, PT, speech therapy
- Therapies, lots of them, cough assist, cvt shake vest, equine, speech, occupational, physical and feeding therapy
- With medications, therapies, and frequent advice from doctors
- He needs to use a wheelchair; meanwhile, mental problems by medicine
- Comme je peux (Translation: As I can)
- I help him every time. He goes in a special school for kids with motorik disability
- We've changed schools. We go to speech therapy, occupational therapy, psychotherapy, etc.
- Antikonvulsiva, Betreuung (translation: anticonvulsants, care)





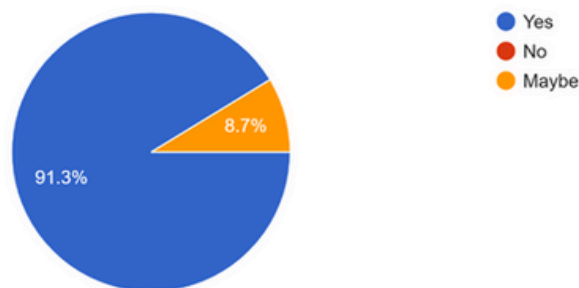
Considerations for a Possible New Treatment

What symptom(s) would you most want a therapy/treatment to address?

- Slowing progression
- speech
- Strengthening him
- Her ability to communicate
- My son will be 36, has a gtube, non-ambulatory, incontinent, non-verbal, Bronchiectasis, complete and total care 24 hours a day. Not much left to cure unfortunately.
- Psychische/Neurologische Symptome, training für Aufstehen, Laufen, Treppe steigen, Sprechen (translation: psychological/neurological symptoms, training for standing up, walking, climbing stairs, speaking)
- Speech, balance problem
- If he could speak clearly, if he had greater learning ability, and if he were more physically fit
- I want to improve her motor skills and balance to help her master more life skills.
- Seizures. Stop the fast progression of the disease.
- Cognitive
- Motor
- Ability to speak, improving balance and the ability to walk safely, improving fine motor skills and concentration and attention, reducing moments of confusion
- Temper tantrums
- Seizures and motor skill regression
- Toxin blocker-to prevent or slow down further accumulation
- Constipation, stiffness, neurological
- Pain management and the dementia
- Balance problems, leg muscle weakness, psychological issues
- Das stehen und laufen (translation: standing and walking)
- All symptoms!
- Psychological support should be provided first and most intensively
- Wachheit, Epilepsie, Aufmerksamkeit (translation: alertness, epilepsy, attention)

Would you still want a therapy even if it didn't completely cure the disease?

23 responses



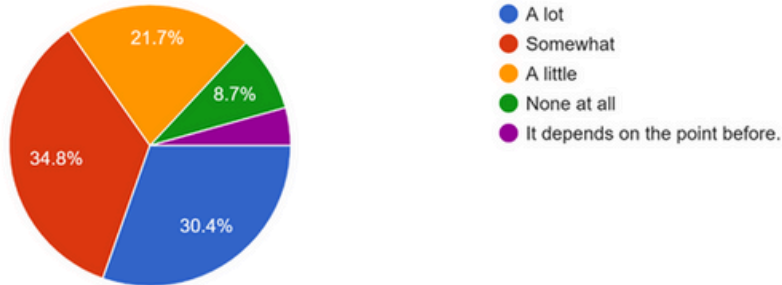


What factors would increase or decrease your willingness to use that treatment?

- Side effects that negatively affect quality of life
- Placebo for a long period of time
- I'm tempted to let the disease run its course so that he doesn't have to suffer long term
- As long as she continues to fight GM1, we will never give up hope.
- Alleviate his spasticity, his pain
- Entfernung zu speziellen Therapeuten zu weit, Mangel an speziellen Therapeuten (translation: distance to special therapists too far, lack of special therapists)
- In case the side effects affect other abilities that decrease the quality of life without the possibility of compensation
- How high the risk of side effects would be
- Excessive risks arising during treatment
- No placebo. Do not discontinue any other medications.
- Oral pill
- The treatment must lead to an improvement. The risk of deterioration in one area for improvement in another area is not a profit for us.
- If we knew it worked
- Risk of making him worse or dangers of treatment also whether or not his happiness/comfort would be compromised
- I would try anything to help my child
- Severe side effects from treatment
- Easy to handle and take by the patient, less side effects
- Dass die Lebens Qualität verbessert wird (translation: that the quality of life is improved)
- Stopping the disease
- We want to help all of our children
- Sicherheit, keine oder wenig Nebenwirkungen (translation: safety, no or few side effects)

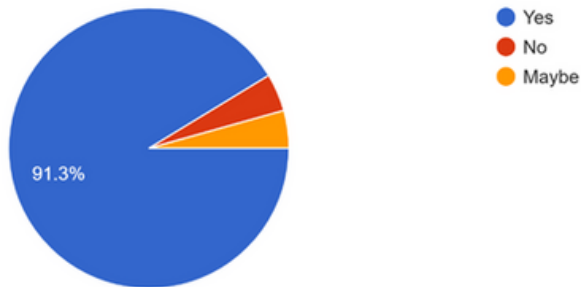
How much risk would you be willing to take with a new treatment?

23 responses



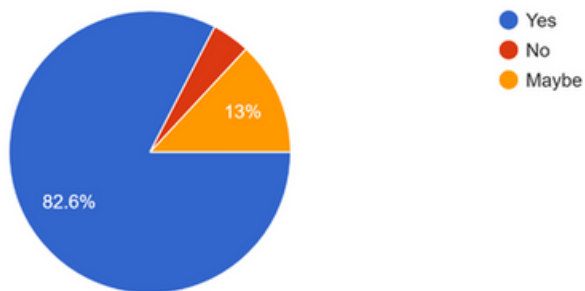
If a therapy slowed down how quickly the disease progresses, would you still be interested in using it?

23 responses



If it did not address all of the symptoms, would you still be interested in using it?

23 responses



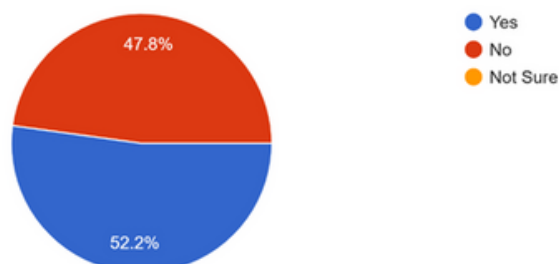
Clinical Trial Preferences

Why has your child participated or not participated in a clinical trial? What are/were the reasons?

- Too young or old, too far progressed
- She wasn't eligible for gene therapy. Other than that, there weren't any more trials available
- Not offered and my son is potential dual diagnosis (Tay-sachs & undiagnosed)
- She was too old for the clinical trial
- Recommended by Dr. Cynthia Tiff
- Studie zur Gleichgewichtsstörung, Schwindel, Motorik bei Tay-Sachs (translation: study on balance disorders, dizziness, motor skills in Tay-Sachs)
- She has participated in two clinical trials because we believe participation is necessary to contribute to the medical advancement in the possible treatments for this horrible disease and we trust in the professional teams that carry them out. Of course, in both cases we have hoped to obtain a personal benefit and help our daughter to have a better quality of life and to improve her symptoms.
- He suffers from a very rare lysosomal storage disorder for which there is no other treatment, and which is fatal.
- Her condition is progressing rapidly and requires timely treatment, but there is currently no cure for her illness.
- He had to stop other drugs for a placebo trial.
- Natural history study. To aggregate facts on symptoms and progression of the disease.
- None are open
- We are convinced that only scientific progress can cure our children's illness, and we are ready to do our part as long as there are no personal disadvantages.
- Not participated
- My child has not participated in a trial because there has not been one available to him since getting the diagnosis.
- There has not been any available.
- She was never accepted into any; we keep trying.
- To try to help slow down the disease progression
- Because of the balance issues
- Die Verbesserung der Lebensqualität (translation: improving the quality of life)
- There was no possibilities
- We would help my and other children.
- Alles versuchen, die Krankheit zu besiegen (translation: try everything to defeat the disease)

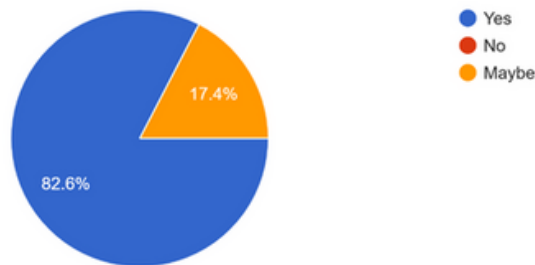
Has your child ever participated in a clinical trial?

23 responses



Would you want your child to be enrolled in a trial?

23 responses



What should researchers, companies, or regulators know about your child's diagnosis?

- As the years go by, one observes how the disease inevitably progresses, degrading every aspect of our children. No matter how much effort they put into therapy, the available medications, or the diet, the disease advances, mobility decreases, and speech becomes almost nonexistent. We know that recovering what has already been lost is very difficult, but it is extremely important to be able to stop the deterioration.
- He's complex because he doesn't fit the "normal."
- As long as these children regardless of age are battling and not giving up, they deserve all of us to support them with whatever we have available.
- It is fatal. Destroys your body, you lose every function needed for normal daily life.
- Sollten das volle Diagnosebild kennen (translation: should know the full diagnostic picture)
- I do not understand the question at all.
- Yes
- It is fatal.
- It's devastating to the whole family.
- It's hard to watch the children regress and lose their smiles. We just wish we could help them.
- Researchers, companies, and regulators should know about the certain type and individual course of the disease.
- Behavior is something no one talks about.
- Most parents dealing with children with this disease are very willing to try and help their quality of life.
- As a parent of a child diagnosed with a terminal condition, for which there is currently no cure or effective treatment...time is not on our side. With every passing day, my child's condition worsens—toxins continue to build up in his brain, causing him to regress and lose the abilities he once had. This steady decline is heartbreaking to witness, and it makes the waiting and red tape associated with clinical trials and treatments even more unbearable. The extended timelines and constant hurdles are very discouraging. I urge you to prioritize swift action and flexible solutions that can give our children the chance they so desperately deserve.
- That we need the placebo thing to go away our children don't have time to waste
- It's devastating and a horrible thing to live with
- The mental problem of bipolar symptoms
- All about the diagnosis.
- Many doctors lack basic knowledge of this disease. It affects their entire lives, including their mental and physical ability. It's very stressful for the entire family.
- Morbus Sandhoff (translation: Sandhoff disease)

**If your child might receive a placebo instead of the therapy being tested, would you still enroll your child in the trial? Why or why?**

- Maybe
- Yes because there's almost no other choice
- Yes because I would be watching more carefully to see if there are improvements that are noticeable.
- Not sure we but it is better then option we have now of nothing
- Solange die aktuell gegebenen Medikamente nicht abgesetzt werden, gegebenenfalls muss es abgesprochen werden. (translation: as long as the medication currently being administered is not discontinued, if necessary, it must be discussed.)
- Yes, because my daughter does not currently take any other medication and entering the study does not mean giving up any treatment and offers us the possibility in the future of having a medicine that helps her.
- Being part of a clinical trial is very challenging for the patient's entire family, both financially and emotionally. I want to know that a drug is being tested on him and not a placebo.
- It probably won't, because a placebo has no therapeutic effect.
- No. It is ethically unacceptable.
- No. We don't have time for that.
- Yes- the risk is better than not trying at all.
- We would also participate in a placebo study, as it guarantees a higher level of scientific accuracy.
- I would still enroll my child because the risk is worth the potential to cure or slow down the progression of this disease
- Yes. I understand that placebos are an essential tool in evaluating the efficacy of new treatments, allowing for clear comparisons and helping to establish whether a treatment is genuinely effective. However, I find it deeply disheartening that extended placebo timelines are applied to children, especially those with shortened life spans. For these children, every moment counts, and withholding potentially beneficial treatments for the sake of scientific rigor can feel particularly cruel and unjust.
- I am on the fence as my child is progressing.
- Possibly but think that is irresponsible considering most families would deserve to try anything to help
- No
- Vielleicht. Die Frage ist die Frage der Verabreichung. (translation: Perhaps. The question is the question of administration.)
- Yes, it's a possibility.
- I would include my child in the study. It's not just about my child, but also about many other children.
- Nur wenn er dafür keines seiner Medikamente absetzen muss (translation: only if he does not have to stop taking any of his medication)



If your child had to stop all current treatments to participate in a trial, would you still want your child to participate? Why or why not?



- Yes, because there's almost no other choice.
- Potentially depending on the type of trial being done. (Ex. Testing medicine or a therapy treatment)
- Yes, because there are no current treatments, we are just managing issues
- Maybe
- Nein, das Risiko der psychischen Beeinträchtigungen könnte sich stark steigern, damit eine Verschlechterung des derzeitigen Zustands eintreten könnte. (translation: No, the risk of mental impairment could increase significantly, causing the current condition to worsen.)
- I do not know. It is Not the case at the moment.
- Since there are no very effective medications for some diseases, yes.
- Yes, because all current treatment methods are only attempts at a cure.
- No. It is ethically unacceptable
- Maybe
- Yes
- We don't use other treatments currently, so probably yes.
- Yes, he doesn't really take anything other than 1mg of gaufacine.
- I would because the treatments for this disease only helped the quality of life. It doesn't cure or slow down the disease.
- Yes, because we have no other real option to save our little boy.
- Depends on what the potential gain is and if there is a chance of a placebo I might be reluctant
- Depends on the trial potential
- No, because the psychiatric medicine could not be cancelled
- Oui il prend en ce moment, pas de médicaments (translation: Yes, he is taking it at the moment, no medication.)
- He has no current treatments.
- I can't answer that. The question is why I should stop with speech and occupational therapy. It would have to be reasonable.
- Nein! Ohne seine Antikonvulsiva kann er nicht leben! (translation: No! He can't live without his anticonvulsants.)



Quality of Life: Living with the Diagnosis

What does a typical day look like for your child and your family?

- Busy. Constant care
- In the mornings, she goes to school (special education), and in the afternoons, she does various therapies. She needs help with dressing, hygiene, and eating, and requires a companion at all times.
- Get him up, give meds and feed through g tube, diaper change, get him dressed, put on his AFOs. Then pick him up, get him to TRY and eat and drink (takes a looong time), pick him up to settle him on the couch or table to play or watch TV (if NOT a school day). Attempt to get him lunch and drink. Change him. Settle him somewhere.... Evening time: Go for a walk in his wheelchair, sit him down to eat dinner (sometimes he does, sometime he doesn't) Hang out & watch a movie on the couch. Bedtime: diaper change, meds and feed through Gtube, put on his leg straighteners.
- My husband and I have devoted our lives to caring for our daughter. We make every attempt to give her as much enjoyment as possible with no regrets but in that effort we have no time for anything besides that. We never do anything that does not include the 3 of us by choice.
- [He] has no quality of life. Two care givers on a daily basis. He has to be bathed, changed, gtube fed. Short of breath, in a wheelchair, aspiration pneumonias, dysphagia, arthritist
- Früh aufstehen, Unterstützung bei Körperpflege, arbeiten in einer Behindertenwerkstatt, (wird gefahren), nachmittags in der Einrichtung Freizeit, Mahlzeiten werden gemeinsam mit anderen Mitbewohnern eingenommen, Telefonieren mit der Familie, an Wochenenden Besuche mit/bei Familie (translation: getting up early, assistance with personal care, working in a workshop for people with disabilities (driven), free time in the afternoon at the facility, meals are taken together with other residents, phone calls with family, visits with/to family on weekends)
- My daughter needs 80 percent of the day to do almost all daily activities, get dressed, wash, eat, free time, social contacts...
- We wake him up, help him eat and get dressed, brush his teeth, drive him to school and pick him up again after six hours. In the afternoon, we go to therapy sessions or spend time with him, then we have dinner and help him wash, brush his teeth together with him and read him a story.
- I go to work during the day, and my child goes to school to study. After we return home in the evening and have dinner, I help my child with some homework, followed by some recreational activities. Around 9:30 PM, I make sure my child goes to bed.
- Full of hard work.
- Trying to stay busy to provide as much quality of life as possible
- Hectic. 2 children with disease makes like very stressful. Knowing both children have no chance of survival makes it very depressing.
- We accompany our child through all phases of the day and actively help with the daily challenges, such as personal hygiene, dressing, transport, etc., as the child can only act alone in a few activities.
- Now that its summer, swimming driving 4wheelsers and dirt bikes around



What does a typical day look like for your child and your family? (cont'd)

- Hectic and stressful. Two children with this disease in one household, makes it very depressing.
- We tend to our son's needs every day, all day. He requires assistance with all basic living activities. He has to be watched closely due to choking, seizures, and lack of safety awareness. He falls often and has poor motor control. He finds contentment in only short spurts and can be very emotional. Taking care of our son is very taxing emotionally, mentally, and physically.
- Exhausting! Therapies, medications, medical equipment, lack of help with nursing care! Constantly watching 24/7 to keep my child safe
- Nighttime wakings, helping child with everything, it's hard
- Due to psychiatric problems it is difficult to steadily work, also due to the wheelchair.
- das kranke Kind muss auf Hilfe angewiesen, muss auf Toilette hingesetzt, werden, gefuttert angezogen ausgezogen, bespaßt Er kann sich selbst nicht beschäftigen (translation: The sick child needs help, has to be put on the toilet, fed, dressed, undressed, entertained. He cannot entertain himself.)
- Getting up in the morning, helping with things (brushing teeth), helping with getting dressed, preparing and partially serving breakfast, getting dressed, taking the child to the school bus and picking them up again, afternoon therapy (ergo, physio, speech), preparing and possibly serving dinner in the evening. Helping with personal hygiene, helping with pajamas. Then going to bed.
- In the morning, my husband drives my daughter to school. She stays there until 3:00 p.m. We usually have various therapy sessions afterward. As her mother, I pick her up and accompany her to all treatments. She can continue to pursue some hobbies, live horseback riding. The day is always very long then. In the evening, we do our training sessions at home. I always have to help with homework. I often get up early in the morning to mark und write homework
- Viel Zeit für Essen und Pflege (translation: plenty of time for eating and care)



What specific activities is your child unable to participate in or have difficulty with? Include the activities you enjoy or could enjoy as a family? What adaptations have you made?

- She has lost the ability to socialize on her own, and the inability to communicate prevents her from forming connections during family gatherings or when we're with friends. Her motor difficulties keep us from going on walks and limit our access to certain places—we always have to consider distances and the accessibility of the places we plan to visit.
- Walking, talking, having friends, being able to go on rides & experiences. We want to go camping, etc. but so often the roads are rough, and wheelchair and equipment needed are sometimes too much.
- She used to love to ride horses but no longer has the balance to safely do that. She used to love to ride her bike but also can no longer do that.....she loves the feeling of wind in her hair so we bought a convertible and use a Hoyer lift to put her in and out and ride her around in that.
- Drive to the beach, stroll the mall, visit family.
- Rad fahren, Schwimmen, sportliche Aktivitäten, Familienfeiern, Rollator, Rollstuhl, Duschstuhl, Sessel mit Aufstehhilfe als Hilfsmittel angeschafft (translation: cycling, swimming, sporting activities, family celebrations, walker, wheelchair, shower chair, armchair with stand-up aid purchased as aids)
- Dressing, washing, eating, free time activities, social contacts
- He cannot go to his friends' houses alone to play with them, he does not go to training alone, and he does not do his homework alone.
- My child is unable to participate in the various outdoor activities organized by the school, nor can she go hiking or climbing with the family. So, if she really wants to take part in a school-organized outdoor activity, I have to apply to the school to accompany her.
- Hiking. Use a wheelchair on flat or accessible trails.
- Arts and crafts
- Establishing and maintaining social contacts is difficult or impossible. Electronic language aids are used.
- He can't drive them anymore so we got a UTV, and he is a passenger now.
- My child can do almost nothing without my help.
- He is unable to participate in any age-appropriate activities. We can't go on hikes or play sports or engage in play with other children. We can barely go to the grocery store.
- Outdoor activities, traveling
- Hiking, biking, even just a long walk. Family games. Eating. We've made modifications to most of our daily life activities and participate in adaptive programming such as skiing.
- Completing an apprenticeship was not possible, concentration problems, hand tremor. He likes to paint, bike with his electric recumbent bike, but needs a person to help getting off.
- My child cannot take part in any sporting activities (football, gymnastics, handball, etc.) due to balance and coordination problems and an increased risk of falls.
- She can't participate in the pleasure of everyday life. She can't go on school trips. She is often excluded. This is a huge burden for her. She has difficulty understanding others in her family. There are arguments. As a family, we have little time for friends...
- Leider wird alles immer schwerer, weil die Krankheit schreitet voran! (translation: Unfortunately, everything is getting more and more difficult because the disease is progressing!)



What would you like the FDA to know about your child and living with their diagnosis that could be important to know when reviewing potential therapies or clinical trial designs?

- I understand that the trial periods for this disease are long, but I do not agree with the use of placebo groups, especially in Phase 3. I insist—we don't have much to lose, but we are losing valuable time, especially if the medication can at least slow the progression of the disease
- Our kids suffer in pain and so many of them can't tell us. They rely on us to understand them and help them.
- These disorders progress fast and so trial with a placebo in their case seems unfair and cruel in most cases.
- No child or family should live through this horrible disease, takes your entire life away slowly. He can't even be changed without using oxygen, he is so short of breath.
- Müsste in einem Gespräch geklärt werden (translation: would have to be clarified in a conversation)
- For us it is very important to find as quickly as possible a safe medicine that can stop the development of this disease that in less than two years stole my daughter's voice and independence and that every day that passes makes her more and more dependent.
- It is also important to keep an eye on the patient's mental health, and if an examination or a series of examinations represents too great a hurdle for the patient, to change it.
- I hope the FDA can understand my child's condition related to the disease before receiving treatment, as well as the recovery after receiving treatment. I believe this information can help improve research aimed at curing the disease.
- My son lost the ability to walk, to talk, to eat and to laugh. We and all the other children have no time.
- We need help NOW.
- Our child has, in a juvenile course of illness, a certain quality of life, which must be preserved as long as possible.
- He is fully functioning just is delayed.
- Children deserve a fighting chance.
- We don't have time to waste. Daily life is enough of a challenge as it is, and the longer successful treatment is delayed the more challenging it will become.
- I would like them to know as a parent I am doing everything I can for my child, and we need help getting better access to trials and these placebos to be reconsidered.
- They are slowly and some painfully dying. Treatment options, even if risky are needed ASAP!!!!
- How hard it is to treat the psychiatric and physical problems, and the medication for the psychiatric issues have very bad impact on the physical issues.
- mein Kind ist in allem langsamer als andere Kinder und ist daher ein Ausenseiter, er wird von anderen ausgeschlossen da er nicht an Aktivitäten teilnehmen kann die andere Kinder in seinem Alter machen. Auch ist mein Kind sehr zurückhaltend, hat ein reduziertes Selbstwertgefühl und Selbstbewusstsein durch seine körperlichen Zustand/ Einschränkungen. Kognitiv ist mein Kind auf normalem Level. Auch hatte er im März ein psychologisches Gutachten im SPZ Freiburg da kamen Konzentrationsproblem heraus, er hat ein sehr heterogenes Intelligenzprofil. Kognitiv fit, aber körperlich Stark eingeschränkt. (translation: My child is slower than other children in everything and is therefore an outsider. He is excluded by others because he cannot take part in activities that other children his age do. My child is also very reserved and has low self-esteem and self-confidence due to his physical condition/limitations. Cognitively, my child is at a normal level. He also had a psychological assessment at the SPZ Freiburg in March, which revealed concentration problems. He has a very heterogeneous intelligence profile. Cognitively fit, but severely physically limited.)
- You need time for these perplex and attention. Stress and pressure are very detrimental.
- Dass das Leben immer mehr eingeschränkt wird in nahezu allen Bereichen! (translation: That life is becoming more and more restricted in almost all areas!)

What would you like the FDA to know about your most important goals for a treatment?

- Stop progression of the disease
- Better quality of life
- While a cure would of course be wonderfulslowing the progress would be life-altering.
- Treatment as soon as they are diagnosed to stop the disease
- Verbesserung der psychischen, kognitiven und motorischen Fähigkeiten. (translation: improvement of mental, cognitive and motor skills)
- Help improve my daughter's autonomy and quality of life.
- Maintaining independence, quality of life, and longevity
- It's not about a cure. Just a little relief in life.
- We have experienced a lot of disappointments with treatments such as companies not willing to include older children in clinical studies. We need the FDA to advocate for older children being included without the results punishing the companies' opportunity to advance the treatment. We KNOW that the results may not be as significant for children who have had the disease longer but there still might be effect and things could be learned regarding the disease, dosage efficacy etc. We need hope for older patients not just infants.
- We just want hope. They all just want what's best for them.
- A medication or therapy should not bring any worsening.
- He still has time to slow it down.
- Most important goal is to stop giving minors placebo options for trials. They don't deserve that I feel that anyone under the age of 18 should never have to deal with placebos. It shouldn't even be an option.
- To stop wasting time and stop further regression
- To help slow or stop regression asap because we can't get back what we lose
- Giving better quality of life
- See answer above the question before
- I would like the disease to be stopped or rather slowed down. I would like the existing symptoms to be reduced and maintained at a healthy level.
- The most important goals should be to improve the targeting of this disease, to slow down the physical and mental deterioration and to improve the quality of life
- Etwas mehr Lebensqualität und mehr Zeit mit meinem Sohn, weil sein Leben verlängert werden könnte! (translation: a little more quality of life and more time with my son because his life could be extended)

**What would you like the FDA to know about the risks you are willing to accept for a treatment?**

- GM1 is an incurable and degenerative disease. Personally, I prefer to take the risk of trying a medication. Unfortunately, we already know how it ends—and it's the outcome no parent ever wants for their child: death. Only by stopping the progression of the disease—which we already know the medication can do—can we make a difference. I do not agree with the use of a placebo
- A lot of these diseases progress so quickly we don't have a lot of time to waste
- We already know how the story ends with our treatment so its worth risk to change that ending
- If he were younger, a lot of risk, risk it all
- Keins (translation: none)
- Once the risks of a significant worsening in the short and medium term of my daughter's quality of life have been ruled out, I would be willing to take the risks of trying a new medicine under medical observation.
- The subsequent recovery.
- No placebo.
- Because we know this disease is fatal, we are willing to accept more risks than other populations. Give us, as parents, the chance to say yes or no.
- We know the outcome of our children- risk is worth it for a potential better quality of life.
- A medication or therapy should not bring any worsening.
- I'm willing to try something as long as it not to invasive
- Parents are willing to do just about anything to help their children
- Once safety protocols are established, there's not much of a risk that we are not willing to accept.
- I'm willing to take a risk but I'm not willing to risk years of being on a placebo.
- At a certain point in the disease, many would risk losing their child to them having a longer more painful life.
- My son suffers since many years facing the bad progress of the disease- taking risks is not easy to face.
- I am willing to take some risks if I have been informed about them.
- It is a balancing act. I can't answer that so easily. It is a question of what complications might arise.
- Kein Placebo und kein Absetzen wichtiger Medikamente (translation: no placebo and no discontinuation of important medications)



Finally, what is your ask of the FDA? What should they consider when it comes to evaluating rare disease drugs and therapies?

- Taking part in a trial involves physical and emotional strain for both the patient and the family. We already live with that every day. It's not right that our only option is to accept a trial with a placebo, going through all of this while also facing the possibility of not even receiving the medication.
- In our cases these diseases are terminal and/or crippling. In so many ways what do we have to lose if we try new drugs /therapies that may or may not work?
- Just because these individuals are rare and not as common as some diseases they are just as valued and deserve just as much in the line of trials and chances.
- Make it accessible and affordable
- Wenig Nebenwirkungen, keine Verschlechterung des derzeitigen Zustandes, Größe der Medikamente beachten, da Erstickungsgefahr/ Schluckstörung Speziell geschulte Therapeuten für seltene Erkrankungen (translation: Few side effects, no worsening of the current condition, pay attention to the size of the medication, as there is a risk of suffocation/swallowing difficulties, specially trained therapists for rare diseases)
- If there is a safe, proven medicine that can be used to improve my daughter's symptoms and quality of life, its use should be approved automatically even if it has not been authorized for her disease.
- They give patients and their families hope in a hopeless situation.
- Encourage flexibility in risk assessment — for rare diseases that are fatal or have no effective treatment, the FDA could consider accepting a higher level of uncertainty.
- Who decides which life is worth living and when everything should be done to save it?
- It's not ONLY about the money. Using that as the only criteria restricts scientific knowledge and prevents the potential for treatments that could affect real people and real families.
- Children deserve a fighting chance! These are innocent children that have no idea what's really going on and they deserve a fighting chance. Placebo should not even be a question for anyone under 18. Minors should not get placebos.
- The course of rare diseases is very rapid in many cases. Therapies and medications that have been successfully tested for their safety should be able to be approved more quickly. Already approved drugs for similar diseases with the same symptoms should be approved immediately for the treatment of the same symptoms.
- Consider our community small big they don't have time. I wish we had more funding
- These children need help and a lot of resources. The FDA won't approve. Placebos need to be off the table for minors and there needs to be more chances for people to get on the trial not just pick a few but because of this rare disease and that there's not very many people especially in this age bracket I think everyone should have a chance at a trial if they are wanting to.
- 18-month placebos are far too long for trials for children who may not have 18 months left. I understand the need for placebos, especially in the early phases of trials, however when reaching the later phases, it seems completely unnecessary for these children to have to be on a placebo, especially when the safety profile of the drug is very favorable.
- To not use placebos when children's lives are at stake
- Be responsible but very, very efficient. Speed is everything to this disease.
- To take into account the individual mental and physical problems of the patient and his medical history.
- I demand the approval of medications which have already been shown in studies to improve the symptoms of GM2... I demand that the living conditions and changes in family life be taken into account and, above all, that the life changes/restrictions of each individual affected be taken into account!
- Warum kann die Zulassung neuer Medikamente nicht schneller gehen? (translation: why can't the approval of new drugs be faster?)



Speaker Statements in Full

Following are the statements in full shared with permission from each speaker.

KELLY

Hi, my name is Kelly. I'm Kipley's mom, and we live in Conway, Arkansas.

Kipley is the most precious 10-year-old little boy with blonde hair and blue eyes. Kipley was born just as perfect as can be. He was healthy and developing normally. Around age 4 we started noticing some delay in his speech and motor skills. (Kip began therapy and initially made small gains.)

We decided to take Kip to see a neurologist at age 6. Six months after our first visit we started noticing some signs of regression. His regressed speech made the biggest impact. Sometimes he would stare at you for several seconds before he could say what he wanted to say.

He also stopped doing certain tasks that he once would do such as walk down the steps of our front porch. Kip was 7 when we decided to do the brain MRI and genetics testing. I'll never forget the day I read his test results online.

I remember reading the words, Tay Sachs disease and not knowing what that was, but knowing that the word disease was not good. I remember telling myself that maybe it could be a misdiagnosis, but Kipley's symptoms were matching up with everything I was reading.

When we were able to talk to the doctor, I asked him two questions. Are you sure? Is it "always" terminal? He said, yes to both.

Currently, Kip is most affected by cognitive decline, loss of motor skills, and speech regression...in that order. It is interesting though that we detected symptoms in the reverse order. Kipley struggles in all aspects. He requires help with all daily activities and must be closely monitored at all times.

Most recently, we have seen a loss of muscle strength and endurance, lack of coordination and balance, and an increase in seizure and choking activity.

Kipley falls a lot. He requires help walking up or down stairs, even if it's just one step. He now feels timid stepping down even just one step and will become stuck there until help arrives. He has had a few instances where he has gotten choked, even eating soft foods.

Public settings are difficult because he has extreme emotional swings, no regard to his surroundings or safety, and he becomes hyper focused on a desired task and is unable to move beyond that. He often gets upset about wanting to do something unrealistic at the moment, such as go on a vacation.

He is very discontent, which makes it more than challenging to sit down at a restaurant to eat, wait in lines, or even drive across town. He has very small spurts of contentment.

At home Kipley is into everything, much like a toddler is. He doesn't play independently, and he often goes from one thing to the next, not really able to enjoy the moment. On our best days with Kipley he is happy, loving, and energetic without being worried about what's next.

Kipley is experiencing a decline in all of his abilities. The skills that he's maintaining are not growing or strengthening. It's heartbreaking to see him lose the ability to do things that he once could do.



Kelly cont'd

Kipley mostly talks with one-word phrases, which is so sad because I have videos of him speaking clearer and with sentences at a much younger age. Here is a video of him speaking a few years ago where you can hear the beginning of his speech becoming affected and a more recent one that shows how his speech has changed.

Exchanging in conversation with Kip is difficult because he struggles to stay on topic. It feels like he is stuck at age 4. He was meeting milestones and growing, and then he just stopped. Even though Kipley is 10, his interests and skill levels align with children much younger than him.

Kipley struggles more than he should have to. His leg turns in causing him to trip over his own feet. It breaks my heart to see him fall when he's just walking through the house. He is a very active little boy and he wants to run and play. His legs get tired, and we have to carry him or use a stroller quite often. Kipley has trouble navigating uneven terrain and walking long distances.

He is slowly losing interest in playground equipment but still enjoys visiting the park. He requires help for all day-to-day tasks such as basic hygiene, going to the bathroom, getting dressed, opening food packages, and getting in and out of vehicles. Kipley is still working on the same skills he has worked on for the last 4 years, but with no growth.

Finding out that your child has a terminal brain disease and that there's no cure or treatment is something that no parent can ever be prepared for. I am trying to remain hopeful that something is going to become available to save Kip. We've been searching all over the world for someone that can help us.

In terms of clinical trials, we understand the need for placebos and that safety measures must be in place, but we urge the FDA to see that these kids do not have time to spare. Diseases such as Tay Sachs have no good end result. Requiring a lengthy placebo for a clinical trial that has already shown to have positive results just seems so cruel, especially when there is absolutely nothing else available to help these kids. Every day that goes by, we lose a little more of Kip. I fear him regressing further, losing the ability to eat, talk, or walk.

At times, I feel his personality fading, and that may be the hardest of them all. The thought of losing him is indescribable. Kipley has always adored holidays, inflatables, animal statues, and hotels. He keeps our yard and porch decorated year-round. He is purely innocent, sweet, and kind. He loves to laugh and be silly. Kipley has such an abundant love for life. We are struggling because we don't know how much time we have left with him, but honestly, we just can't lose him.





JENNIFER

Hello! My name is Jennifer and my daughter, Madelyn, was diagnosed with Juvenile Sandhoff disease (GM2) in August of 2021 when she was just 9 years old. Madelyn, or Maddie as most people call her, began showing symptoms of her disease around age 6. It started with what appeared to be simple clumsiness such as occasionally stumbling and losing her grip on items such as her pencil. That grew into difficulty getting on and off the school bus, slushy speech, along with a persistent tremor that started in her hands and spread throughout her body.

It took us 3 years, and endless visits to specialists in order to get to the point of diagnosis. During this time her symptoms were advancing at a very concerning rate. Today Maddie is 13 and we've been living with the reality of her disease for the past four years.

There are important things I need you to know and the first is the reality and the speed of Maddie's decline.

One of the scariest things for me, as her mother, is knowing that there is very little I can do to slow down her decline, and absolutely nothing I can do to stop it. Every single day that passes I lose more of my daughter.

Her speech has declined to the point where she is difficult to understand, especially if you aren't around her often. Eventually she will completely lose her ability to speak, and I will no longer hear her sweet little voice telling me she loves me. Instead, her mind will be trapped inside her dying body. Unable to express her thoughts or her feelings.

Her little arms that used to so easily wrap around and hug me tightly, now shake and tremor. Her grip has become weaker, and hugs don't happen as often as they used to. They come now with more effort, but they are cherished just as much as they were when she was squeezing me with all her might.

I use Facebook to keep in touch with friends and family, and there is a feature on there that shows you memories from years past. For most people these memories are wonderful reminders. However, for the parent of a child with a progressive disease like Sandhoff, these memories are sharp, harsh reminders of what's been lost.

[FIRST VIDEO] Just four years ago my daughter could walk on her own, she could write her name or color me a picture. She could even sign my Mother's Day cards. She could eat normally and there was no fear of choking. These things are no longer possible for her.

I want you to understand that Maddie is more than just a number, she's a real, live, little girl, and she's dying.

She loves all the things a typical little girl loves. Dressing up for a night out, reading her favorite books, playing with friends, making crafts, and enjoying video games. Despite the challenges she faces she's a warrior. She fights so hard to "be normal" putting in the time in OT, PT, and speech therapy classes.

[SECOND VIDEO] working to try and hold onto her skills for as long as possible but frustrated because despite her hard work those skills are still being lost. We have explored compassionate use drugs, FDA approved solutions, as well as clinical trials. But navigating these options is extremely challenging.

Jennifer cont'd

There is a large investment in both time and money to navigate the options. We have to weigh risks vs benefits, and we have to do this with very little help or support. We need to be careful which paths we choose because certain drugs may disqualify her from clinical trials or have unintended side effects. Some drugs have astronomical price tags and even after fighting for months to get a prescription we are devastated to realize we may be forced into unrecoverable debt just to try them out. Add in the fact that clinical trials often have placebo-based studies and you can only imagine the level of stress that causes.

To give you an example, we've been attempting to get into a clinical trial for over a year now. Praying that we could have a shot at getting her on a new drug. Waiting for the trial to open has been tough but even tougher is knowing that in order for her to get that shot, she can't be on other possible life saving experimental drugs. If we get past the first hurdle of enrollment, the next is the hurdle of a placebo. If she is off all other experimental drugs and ends up having to take a placebo for 18 months, she will continue to decline, and I will lose more of my daughter before I'm even given the opportunity to save her. She still has so much left to save, if only she could be given the live saving drugs as soon as possible. Although I am terrified of what abilities she may lose, I hold on to hope that after the 18 months pass that she will be guaranteed to try the drug.

Considering how aggressive these diseases are, I'd like to ask the FDA to allow more non-placebo-based studies. The harsh reality of these types of studies is that our children may die before even getting a shot at life. While I understand the reason placebo-based studies exist, I truly believe in the case of our children there should be a way to get these drugs to them sooner. If not, our children cannot even be saved by the drugs that are being developed to save them.

These are the kinds of choices each of us are forced to face. We don't know if we are making the right choices all of the time, but with so little research on these diseases we are forced to be the pioneers that will pave the path for others. My daughter may die in order for someone's daughter to live. As a mother I'm willing to do anything to save my child, but at the end of the day, if she can't be saved, my hope is that her legacy will help save someone else's child.

I have so much more that I wish I could say, but with limited time I can only hope that I was able to convey a fraction of what our life is like, living with Sandhoff disease.





YASMINA

Hello, my name is Yasmina. I am the mother of two daughters: Emma, who is 16 and healthy, and Lily, my 12-year-old daughter who is living with juvenile Tay-Sachs disease. I am Lily's full-time caregiver.

Lily was diagnosed at age 7. At the time, she was a vibrant, happy child who lit up every room. She loved ballet, singing at the top of her lungs, running across playgrounds, and making everyone laugh with her sass and wit. She adored arts and crafts and had a deep love for slime—she could spend hours creating and squishing it, giggling at the textures and colors. But as the disease progressed, we watched all of that slowly fade.

It has been over two years since I last heard her say “Mommy.” This video – for example – is Lily singing her ABCs.

Today, she can no longer speak, walk, eat by mouth, or play like she once did. Her sadness shows in her eyes as I try to guess what she needs or wants, because she can no longer tell me.

Now, her daily life is centered around medical routines – cough assist and chest vest therapy twice a day, feeding through a G-tube, and rotating sessions of physical, occupational, speech, and equine therapy.

She is homeschooled because she is too fragile for any outside setting, and it would be emotionally devastating for her to watch other children doing all the things she no longer can.

Caring for Lily is the greatest honor of my life. But it's also mentally, physically, and emotionally exhausting. I am not just her mother. I am her respiratory therapist, pharmacist, nurse, educator, and entertainment. I'm also an advocate who supports other families facing this same nightmare.

After a 3-year battle with our state's Medicaid system, I finally became a paid caregiver because I couldn't hold down a traditional job, especially as a single parent providing care 24/7.

This diagnosis didn't just change Lily's life—it shattered mine and Emma's life as well. My 20-year marriage ended. I was left to raise my children alone, without consistent support.

The emotional toll on my healthy daughter Emma is profound. She is an unsung hero. She has watched her sister deteriorate and faces anticipatory grief no teenager should have to carry. Our family lives in constant mourning and grieving the life Lily will never live and the joy we've lost along the way.

Economically, we are trapped. I cannot save for retirement or even build a financial cushion, because I must remain eligible for Medicaid. I don't get paid when Lily is in the hospital, or if I'm sick. Nursing care is nearly nonexistent, and even when available, it's emotionally jarring. Children like Lily need routine and familiarity. Having different nurses cycle in and out only adds to her distress.

I don't have a social life. My only sense of community comes from other parents I've met online and scattered across the country, holding each other up from a distance.

My world revolves around keeping my daughters alive, safe, and loved.

Yasmina cont'd

The future terrifies me. I cannot even begin to process the reality of losing my child, let alone make final arrangements. The thought of selecting a burial site for my 12-year-old daughter sends me into a panic. No parent should ever have to do that.

Finding doctors and treatments is another full-time job. Every time a clinical trial opens, we get our hopes up, only to be crushed by endless red tape and impossible hurdles. And then there are the placebo ratios. Being told that your terminally ill child may be randomized into an 18-month placebo arm, where they receive no treatment while their disease progresses is gut-wrenching.

Lily may have only a few years left. Asking parents in our situation to watch their child decline while “on placebo” is cruel. These aren’t hypothetical outcomes. We’re watching our children regress in real time. Every lost skill is permanent. Every delay in treatment is a sentence of further suffering. I cannot express how devastating it is to have even a glimmer of hope extinguished by a random assignment.

So, I ask you: why are terminally ill children not treated with greater urgency? Where is the compassion in this process? I urge the FDA to reconsider the use and structure of placebo-controlled trials for fatal pediatric diseases. The goal should be to give every child a chance not to risk wasting what little time they have left. It should be my choice as Lily’s parent and advocate whether I would take the risk of not having a placebo. You may have time we do not. My child does not have time.

Slowing Lily’s regression would mean everything. It would give her moments of comfort, dignity, and peace. It would ease the unbearable tension we live with every day. And it would allow families like mine to hope again.

On behalf of my daughter, and every child like her, I implore the FDA to see our children, not just their charts. Please let them be more than data points in a clinical equation. Their lives matter. Their time matters. They deserve access to treatment, not a coin toss.

Thank you for listening. I am grateful for the opportunity to share our story.



**RYAN**

Thank you for the opportunity to speak today. My name is Ryan. I live in the United Kingdom with my wife Karen and our two daughters, Nella, who is 10, and Savannah, who is 7.

We always wanted a family, and the day Nella was born was the happiest day of our lives. She was a healthy, happy baby. She walked early, spoke in full sentences, and was always engaging with the world around her. For two years, she reached every milestone with ease.

Then things began to change.

We first noticed her right foot turning inwards when she walked, and around the same time, she began drooling more frequently. By age three, Nella had begun walking on her tiptoes and falling more often. Her speech had lost clarity, and she was diagnosed with glue ear. She had her tonsils and adenoids removed, and grommets fitted. The drooling did improve slightly but did not stop.

When she was four years old, a single blood test result changed everything. Nella was diagnosed with GM1 gangliosidosis, type 2 — a rare, degenerative disease that destroys nerve cells in the brain and spinal cord. We were told to expect a slow and cruel decline, with no approved treatment and no cure. That she would gradually lose all the abilities she had worked so hard to develop. That her life would be shortened.

This was the moment our world crumbled. We were terrified. All the hopes and dreams we had for our daughter collapsed in a single sentence.

Although we were lucky to have a dedicated team of doctors, they could only tell us that her symptoms would be managed as best they could. There was nothing else they could offer. And so, we began searching — reading everything we could, reaching out to others, looking for any trial, any treatment — anywhere in the world — that might offer hope.

In July 2021, Nella became the first child in the world to be enrolled in a small molecule clinical trial at Manchester's Children's Hospital — part of a larger investigational study that also included adult patients with late-onset Tay Sachs. This drug is a substrate reduction therapy designed to slow disease progression. We knew it was experimental. We knew there were risks. But we also knew the cost of doing nothing. So, we made the decision to proceed.

Within a month of her first dose, we began seeing changes. Nella began walking with flatter feet. Her speech became clearer. The drooling stopped. We tried to stay grounded — the most we had hoped for was a slowing of progression — but what we were seeing felt like something more.

Over the following months, the improvements continued. Her confidence grew. Her personality shone brighter than ever. Teachers and family began commenting on how much stronger she seemed. She completed her walk and peg tests more quickly and with greater control. Her doctors were amazed. There were no obvious side effects. And for the first time since her diagnosis, the disease appeared to have stopped progressing.

Yet despite everything we have seen — and everything her clinicians and therapists have recorded — the adult arm of the trial was shut down in late 2024. Because the adult arm was the primary focus of the study, its closure triggered the automatic shutdown of the entire basket trial — including the paediatric arm.



Ryan cont'd

It was marked a failure. Not because the drug did not work, but because the trial design could not capture what real-world benefit looked like.

In the paediatric arm, all seven children — including Nella — showed visible and measurable benefit. Yet there is no new trial planned. And the path to approval remains uncertain.

Four years on, Nella is now 10. Thanks to continued access via a post-trial access programme, she continues to thrive. She attends school, makes friends, and takes part in weekly activities including horse riding, art, choir, and swimming. She is loving, funny, full of imagination and ambition. She talks about what she wants to be when she grows up. She is living with GM1 — not defined by it.

So today, we remain in a fragile position. There is no long-term guarantee. No regulatory approval. No certainty that what is helping our daughter today will still be there for her tomorrow. This is where the system is failing. If regulatory frameworks cannot adapt to the specific realities of rare disease — where trials are small and progression varies — then therapies that work will continue to be lost, not because they are ineffective, but because the system is not equipped to recognise when they are making a difference.

And so, I speak to you not as a data expert or a policy lead, but as a father who knows — with absolute clarity — that this drug has changed our daughter's life.

She was fading in front of our eyes. Now she is living. Learning. Laughing. And still progressing.

We are not asking for shortcuts. We are asking for balance. We need a regulatory environment that can evaluate therapies based on totality of evidence, on real-world data, and on the stories that emerge from small but meaningful samples. One that can measure what matters, even when the numbers are small.

In closing, I want to thank the FDA for your commitment to listening to rare disease families. I know how hard these decisions are. But I ask you to look beyond the limitations of the data and see what is right in front of us.

Because without this drug, our story would look hugely different today. Our daughter is living proof that this therapy works. Please do not let that progress slip away. Thank you.





MERLIE

Imagine for a moment you have an itch you know the kind that makes your nose just need a gentle rubbing that reminds you of I Dream of Jeannie. Things are suddenly all better and you are ready to continue your day without a second thought afterwards. No Worries.

Sadly, that is not the reality of life for our daughter Jessie. She is soon to be 34 years old and when and if her nose itches she not only is not able to rub It she cannot even use her voice to ask for help. She is nonverbal. She has Juvenile GM 1 Gangliosidosis. She is locked inside a body that is progressively shutting down, taking her ability to walk, her ability to talk, her ability to move, her ability to eat and eventually her life.

Hello, I am Merlie, parent to three grown children. Amber, our oldest, is a teacher and mother to two amazing children. Casey, our son is our middle child and father to three adorable little ones. Jessie is our youngest, but she will never marry or have children. She will forever live with her father and I and depend on us for all her care. She is an amazing young lady that continues to beat the odds and has far exceeded the age the doctors projected for her.

As young child, Standing still did not happen often for Jessie at that age as she was a very active, joyful and delightful little girl. She was full of life and constantly talking about her plans for the future. At six years old she proudly announced her career goals with determination! She was going to "raise and train whales"! Not sure how a young girl in the mountains of North Carolina came up with that career option but she was determined! She would explain to us how she could raise her whales in the swimming pool she would build in the front yard. She made us all believe in her dream! She was the poster child for determination!

It is that same determination that has kept her on the journey none of us saw coming for her.

Jessie started showing signs in kindergarten at around age 5 that gave her family and her doctors concern. It started as simple motor skill issues and stuttering. We noticed Jessie seemed clumsy and would fall or trip when walking or running. Her balance seemed weirdly off when she would swing on her swing set. In fact, she simply quit attempting to swing after falling out of the swing a few times. When we asked her about it, she said her feet and hands weren't listening to her.

We now know she was right ...her brain wasn't able to send the correct signals, and simple tasks were becoming more difficult for her. We noticed that her foot turned inward; we thought she needed corrective shoes and therapy.... we were wrong.

Here is a video of Jessie walking across the living room about 14 years ago...one of the last times she would do that.

As Jessie continued to decline and lose skills, we spent 13 years of endless doctor appts, hospitals and medical testing to learn our future whale trainer had GM 1 Gangliosidosis ... a disorder with no treatment and no cure. She was not going to get better she was not going to improve. She was 18 years old, and we were told she had an incurable life ending disorder. She was diagnosed at the NIH as part of the Undiagnosed Clinic. We had an answer for years of unanswered questions but no hopeno treatmentno cure.

We made a decision that day to do all we could to give our Jessie the life she deserved while we waited and prayed for a clinical trial, a treatment or a cure. She had a life to live and we would find a way to give that to her! And we have for the last 15 years and will continue to do so for as long as God allows.



Merlie cont'd

This life we have been given isn't an easy one. We are averaging about five hours sleep on a good night since it takes every minute of the day to care for Jessie. She requires all the care that a newborn baby would except our baby is 110 lbs!! In addition to her medical needs, we also battle daily to make sure she has the supplies and equipment she needs. That she sees the doctors she needs. That they see her as more than a silent young lady in a wheelchair.

She is Jessie she is a person, and she desires all of us to do whatever we can to fight this disorder as fiercely as she is! Are you doing everything in your power to fight for her and others?

We had to have an overhead lift system installed to move her around our home because it was getting impossible for us to lift her on our own any longer. Our den has become a medical supply room to store all the equipment and necessities she requires to live day to day. My Jeep that I loved dearly became impossible for Jessie to get into years ago and was traded in on a not so cool wheelchair accessible minivan.

Our day is planned 100% around Jessie and sometimes that means our plans with our other children and grandchildren get cancelled at the very last minute.

In fact, there are still Christmas presents sitting on my living room floor for our grandchildren because our Christmas with them was cancelled because Jessie was airlifted to the hospital on December 22 this past year. So, Christmas was cancelled.

It is just the reality of the world our family lives in..... everything can change in a moment, and we have to always be prepared for that.

This past Christmas morning was spent in ICU no tree, no presents, no Christmas!

Our entire lives revolve around Jessie and her needs and no I am not complaining I love my daughter dearly, but this is not the life I thought I would be living.

While we are very blessed, we also realize the sacrifices we are making and some of those things have had a negative effect on our relationship with each other as well as our other friends and family. Some have chosen to walk away because of the sadness they see in our lives. This life can be very isolating for families. This is not an easy life; it's 24/7 stress that if not careful will consume your spirit so that is why after almost 34 years, I have taught myself to find the positive energy even on days when that seems impossible.... for my own sanity. Some days the positive for the day is a smile from Jessie some days the positive for the day is that we all survived to try again tomorrow.

Jessie is now in a wheelchair -time, nonverbal, tube-fed and totally dependent on others for all her needs. She requires constant 24/7 care, and both her father and I have given up our jobs to care for her. We had to sell the home our children grew up in and relocate to a new town because it was a better climate for Jessie and our old home was not wheelchair friendly. We now all live in a wheelchair-accessible home that we have renamed Jessieville, and we continue to make the best of life none of us asked for. We continue to keep the promise we made to her to support her and allow her to live her life to the best of her abilities at whatever cost.... we are her parentsit is our job to care for her. No one is going to do that as well as we are since, to them, they won't see the bright-eyed tom boy we once knew. They won't see that spirit alive and well locked in a body that is failing her.



Merlie cont'd

While her life journey has not been what we planned. She has had an amazing adventurous life. She has been in a four-seater airplane, tubed down the New River, rode in a hot air balloon, rode a Harley Davidson, rode horses, been to Disney World, and countless live music events she is LIVING the life she was given. That same determination that had us all convinced you could raise whales in the mountains of North Carolina has convinced us "impossible" really reads I AM POSSIBLE. We just have to be creative and think outside the box and make things happen.

So while Jessie is out living life we ask that people such as yourselves do your part for the Jessies of the world and work together to give those so bravely fighting what the rest of us cannot imagine a chance to someday hear the words "there is a treatment available" We ask that you give every possible opportunity for a clinical trial or a potential treatment to Jessie and the othersgive them HOPE.

Given the opportunity we would allow Jessie to be a part of a clinical trial if it meant a chance to do her part to help herself and others. Of course, with the hopes of a cure but the simple ability to regain her speech or ability to rub an itchy nose would be life altering for her.

Thank you for your time and for hearing Jessie's story. This is not the life we dreamed of for her on the day she was born. We never expected to be special needs parents or full-time care givers. Jessie has taught us more about determination and what it means to LIVE life then we ever dreamed of so many years ago. Have a blessed day.

Thank you.



**KAREN**

Hello, my name is Karen. I am honored to speak to you today as someone who wears many hats....retired Registered Nurse of over 30 years, Director of Camp Snuggle and Camp Active at the yearly NTSAD Family Conference, and most importantly I am Mimi to my grandson, Sweet Baby James, who passed away April 3, 2019 from Infantile Tay-Sachs at the age of just 27 months old. In my career as a Labor and Delivery Nurse, I witnessed countless births and had the pleasure to participate in the birth of my own grandchildren. And then I had the heartbreaking task of watching MY child watch HER child slowly slip away and die.



As you know, children with the juvenile onset of these illnesses may appear healthy and active early in life, only to begin a heartbreaking and irreversible decline in motor and cognitive function. In just four years of running Camp Active at the Family Conference, I have witnessed kids walk independently into camp one year, only to return year after year with increasing physical limitations until mobility is lost entirely and they are confined to wheelchairs. In addition to motor function decline, there is also a significant impact on their speech. My grandson never spoke a word, but children with juvenile onset learn to say, “I love you, Mommy”, then over time they lose this ability and become unable to speak. This regression is emotionally crushing—not just for the child, but for the entire family. One of the hallmark symptoms of these diseases is spasticity (severe tightening of muscles) which is painful but also interferes with purposeful movement. Basic tasks like feeding oneself, playing with toys, or hugging a loved one become difficult or impossible. These children may understand what they want to do but be unable to control their bodies to accomplish it. Imagine watching your child decline to the point where they want to hug you but can no longer do it. Imagine knowing your child wants to tell you they love you, but they can’t speak with words.

The impact extends far beyond the child who is diagnosed. The entire family becomes immersed in the caregiving process. Parents often leave their jobs or dramatically alter their careers to provide full-time care. My husband and I quit our jobs and moved across the country to help our daughter and her husband care for my grandson James. Siblings can feel neglected and often times they become young caregivers themselves. Simple family outings require extensive planning and equipment. The weight of responsibility never lifts.

Yet, among this challenging journey, there are moments of beauty, community and shared understanding. For many families, the only “vacation” they get is attending conferences designed specifically for families affected by Tay-Sachs and related disorders. These gatherings are more than educational events—they are lifelines. In these spaces, parents meet others who deeply understand their fears, frustrations and grief without explanation. These aren’t the kind of conferences with golf outings and fancy dinners at expensive restaurants. The men don’t gather at the bar to talk sports... these Dads are talking about handicap accessibility, wheelchair modifications, feeding tubes, grief and the impending death of their child. The Moms don’t have spa days and go shopping...they spend their days attending sessions to learn how to better care for their affected child and their evenings together with other families supporting each other. Children see others like themselves and are able to build friendships without barriers as it is the only place where they don’t feel different.

Traditional summer camps are often inaccessible due to medical needs, but at Camp Active we provide adapted camp activities where they engage with volunteers who understand their condition and enjoy moments of independence, fun...and LOTS of laughter! It’s the best family that you never wanted to be a part of!



Juvenile onset Tay-Sachs and related illnesses are relentless diseases with no cure and limited treatment options. Yet, within our community there is remarkable strength, love and resilience. These families face unimaginable challenges with grace and determination. Their stories highlight the urgent need for continued research, better support systems, and greater public awareness.

As a mom, Mimi and volunteer whose life has been forever changed by this horrible disease I am asking for some hope. **YOU CAN DO THAT!** By prioritizing research, allowing more flexibility in clinical trials for rare diseases, and advocating for improved support and services for these families, you will be making a difference for generations to come. I dream of the day where no parent has to get “the D-day call”, where no parent has to experience the suffering and grief of losing a child to these awful diseases. Please help us make that dream come true. Thank you.

**Sara Scaparotti | NTSAD Board President - CLOSING REMARKS**

Sara, a rare mom to a child who had the infantile onset of GM1 gangliosidosis, delivered the closing remarks and the themes and messages shared by families. Following are her closing remarks that summarized what the FDA heard from families during the session:



Thank you for listening today. The stories we've heard are heartbreaking, but they also shine a light on what must change.

Kelly reminded us that these children do not have time to spare. For diseases like GM1 and GM2, requiring a lengthy placebo when there is nothing else available feels unbearably cruel.

Yasmina shared how [her daughter] can no longer walk, speak, or eat by mouth — and how caring for her has become a full-time job as her mother, nurse, therapist, and advocate. The prospect of being randomized into a placebo arm while the disease takes more from [her] is gut-wrenching.

Merlie described [her adult daughter], trapped in a body shutting down, and how even small improvements — regaining speech or the ability to scratch her own nose — would be life-changing.

Jennifer spoke about the hurdles to access off-label drugs, and the fear of losing her daughter to 18 months on placebo while her disease continues to progress.

Ryan, on the other hand, showed us what's possible when access is granted. His daughter is thriving thanks to an investigational therapy, but their family lives with the fear that what helps her today could be gone tomorrow if the system doesn't adapt.

And Karen, who directs our camp, has witnessed children walk into camp one summer, only to return the next year in wheelchairs. She reminded us that this isn't just about the child diagnosed — the entire family's life is transformed by the weight of caregiving.

What we hear from these families is clear: lengthy placebo-controlled trials are not just impractical — they are unfair and cruel for children with terminal, fast-progressing diseases. Compassionate access is not a luxury; it is a necessity. Families need regulatory change that allows children to stay on therapies that are working for them, even if they do not work for all participants, and parents must have options to try more than one approach while there is still time to save their child.

As a member of the NTSAD community, and as Joey's mom — who lost his life to GM1 before treatments could reach him — Sara shared that she knows too well the cost of waiting.

These families are pleading for the chance to save their children, to hold on to the futures that these diseases are trying to steal.

Sara urged the FDA to work with the patient community— to create a regulatory environment that can measure what matters, even when the numbers are small. And to act with the compassion and urgency that these children and families so desperately need.

Thank you.