

# VOICE OF THE PATIENT REPORT

## Krabbe Disease

Externally-Led Patient-Focused  
Drug Development Meeting

Meeting Date: October 29, 2020

Report Date: March 15, 2021



**NORD**<sup>®</sup>  
National Organization  
for Rare Disorders

## VOICE OF THE PATIENT REPORT: KRABBE DISEASE

This report represents the summary composed by the National Organization for Rare Disorders (NORD®) as a result of an externally-led Patient-Focused Drug Development meeting held virtually on October 29, 2020. This report reflects the host organization's account of the perspectives of patients and caregivers who participated in the public meeting.

**Submission:** This report is submitted as patient experience data for consideration pursuant to section 69C of the Federal Food, Drug, and Cosmetic Act to:

- Center for Drug Evaluation and Research (CDER)
- Center for Biologics Evaluation and Research (CBER)
- US Food and Drug Administration (FDA)

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## A MESSAGE OF THANKS

NOTE FROM THE OCTOBER 29, 2020 MEETING

Welcome to today's externally-led Patient-Focused Drug Development (EL-PFDD) meeting on Krabbe disease. On behalf of NORD, KrabbeConnect, The Legacy of Angels Foundation, Partners for Krabbe Research, Hunters Hope, Gain Therapeutics, Magenta Therapeutics, PassageBio and Neurogene, we thank you for joining us. If you are a patient, family member or caregiver affected by Krabbe disease, this is an important opportunity to have your voice heard.

NORD and our meeting supporters believe that Krabbe is a disease with an unmet need, one that imposes a severe burden on patients and their families, especially among the pediatric population. Through today's meeting, we will strive to provide researchers, drug developers and FDA with a robust understanding of patients' and caregivers' experiences with Krabbe disease. The ultimate goal of the meeting is to produce a Voice of the Patient report that will help to inform the development of potential therapeutics that can improve the lives of patients impacted by Krabbe disease.

We appreciate your participation and valuable input on this rare, severe neurological disorder, and look forward to sharing the insights gathered from today's discussions.

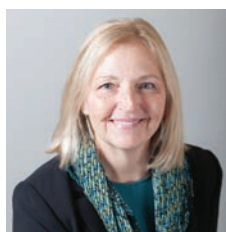
Sincerely,



Peter L. Saltonstall  
President and CEO, NORD



## OPENING REMARKS



**Pamela Gavin, Chief Strategy Officer, NORD**

*"Good afternoon, everyone. I'm Pam Gavin. I head strategic program development and operations at NORD, and it's my great pleasure to welcome you to today's externally-led Patient-Focused Drug Development meeting on Krabbe disease, also known as globoid cell leukodystrophy. The leukodystrophy community is near and dear to my heart as I've experienced loss in my own family to these rare, progressive metabolic genetic diseases*

*that affect the brain, spinal cord and often peripheral nerves. So, I'm honored to help start us off today on this important collaborative journey with the Krabbe disease community and the US Food and Drug Administration.*

*It's also critically important to get the input of patients and caregivers on potential treatments. What do you hope these therapies achieve and what medical risks might you be willing to take for the benefit of these future treatments or what these future treatments may offer? Your voice, your experience, and your courage to participate and contribute make it possible for us to embark upon this very important dialogue today. This is why we are here, to discuss what is meaningful for the Krabbe disease community and the context of developing and approving therapies.*

*What you share in this meeting will be integrated in a Voice of the Patient report, which will serve as a guide for bringing the voice of the Krabbe disease community into every decision that the FDA makes as they weigh the risks and benefits of new treatments for your community. This special report will also be read by researchers and biopharmaceutical industry drug developers that are designing research programs and or clinical trials for Krabbe."*



**Stacy Pike-Langenfeld, President, KrabbeConnect**

*"I am Stacy Pike-Langenfeld, mother to this beautiful little girl right here, Mikayla Pike, who lost her life to Krabbe disease. I'm also the co-founder and president of KrabbeConnect.*

*The focus of this meeting is to hear from many resilient families who want you to learn from their Krabbe disease journey. I urge you to listen carefully as our community continues to battle the following:*

- *Our families have great barriers accessing transplant because of delays in diagnosis, and because 49 States do not currently screen for Krabbe disease at birth.*
- *Number two, our families experienced insurance delays to transplant being a standard of care, but not an FDA-approved treatment for Krabbe disease.*
- *Number three, while we're thankful for transplant and it has the potential to enhance a Krabbe disease patient's quality of life, transplant is not a cure.*
- *And last but not least, number four, even though new treatments are coming in 2021, the treatments targeting early infantile onset will only be available to the states currently testing for Krabbe disease as part of their state's newborn screening panel.*

*In closing, I want to thank the FDA for this meeting as you work hard to ensure the health and safety of our country amidst COVID-19. Krabbe disease patients and families need you more than ever."*

## OPENING REMARKS: US FOOD AND DRUG ADMINISTRATION (FDA)



**Michelle Campbell, Senior Clinical Analyst for Stakeholder Engagement and Clinical Outcomes, Division of Neurology Products, Center for Drug Evaluation and Research, FDA**

*"My name is Michelle Campbell, and I lead stakeholder engagement and clinical outcomes for the Office of Neuroscience in the Center for Drug Evaluation and Research. First, I'm happy to see so many parents, caregivers and advocates on the web today. Thank you for being a part of this meeting and sharing your experiences with us.*

*We share the patient community's commitment to facilitate the development of safe and effective medical products for Krabbe disease. Know when we say medical product development, we mean it in the broader sense of identifying, developing, and evaluating potential therapies or devices that can help manage a patient's condition. We're here to learn from you and your experiences with Krabbe disease.*

*We learn so much from these meetings. We look forward to incorporating what we learn today into the agency's thinking and understanding of how patients view benefits and risks of their therapies and devices for Krabbe disease. We thank you for participating, particularly in these unusual times. We are grateful to each of you for being here today and sharing your personal stories, experiences and perspectives. I look forward to learning from you today."*



**Melanie Blank, MD, Clinical Team Leader, DCEPT, Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, FDA**

*"I am Melanie Blank and I am so honored to be representing FDA today and providing opening remarks for this momentous event. I'm a kidney doctor by training, and after many years in private practice, my path led me to FDA. That was 16 years ago, and now I spend most of my time studying rare diseases like Krabbe and looking into gene therapies.*

*This is an exciting day because it is a chance for you to share your experiences and your unique insights into Krabbe disease to inform other stakeholders, including FDA, about how best to develop safe and effective drugs for Krabbe disease.*

*The FDA has learned that there's no better way to assess what would be clinically meaningful to you than to ask you. We need to listen to you, the patient and caregiver, to better understand your priorities, your concerns and your struggles."*



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## KRABBE DISEASE EXTERNALLY-LED PATIENT-FOCUSED DRUG DEVELOPMENT (EL-PFDD) MEETING: INTRODUCTION

The patient perspective is critical in helping FDA understand the context in which regulatory decisions are made for new drugs. EL-PFDD meetings provide an opportunity for patients, their families and caregivers to share critical information about the impact of their disease on their daily lives and their experiences with currently available treatments. Patients' experiences provide valuable insight for FDA and other key stakeholders, including researchers, medical product developers and health care providers.

NORD and KrabbeConnect, The Legacy of Angels Foundation, Partners for Krabbe Research and Hunters Hope, with additional support from Gain Therapeutics, Magenta Therapeutics, PassageBio and Neurogene, hosted this EL-PFDD meeting on Krabbe disease (pronounced krab-A), a rare genetic disorder also known as globoid cell leukodystrophy, which is caused by a deficiency of the enzyme galactocerebrosidase (GALC).

About 1 in 100,000 individuals in the United States are affected with Krabbe disease, with males and females equally affected; it is seen most in infants, but can also develop later in life. Unfortunately, there is currently no known cure for Krabbe disease and it is commonly fatal. Currently, the only disease-altering treatment available is hematopoietic stem cell transplantation (HSCT), but it must be administered early and is typically only available to patients with a family history or who have been identified through newborn screening. Like many lysosomal storage disorders, there is a wide range of disease symptoms impacting the age of onset and disease severity. Since Krabbe disease damages a person's central and peripheral nervous systems, complications include feeding difficulties, blindness, deafness, seizures, spasticity, severe loss of muscle tone and respiratory failure.

## KRABBE DISEASE EXTERNALLY-LED PFDD MEETING DESIGN

EL-PFDD meetings are organized and led by patient organizations and FDA personnel are invited to attend. The Voice of the Patient report, generated after the meeting, is an essential resource for the FDA to review beyond the mandatory safety and efficacy data. NORD applied to the FDA and was granted approval to host an EL-PFDD meeting focused on Krabbe disease. This EL-PFDD meeting provided a place for the Krabbe disease community to relay to FDA officials, medical experts and other stakeholders their daily burdens and preferences for potential treatments. These patient insights will provide the FDA additional information in order to assess the benefit-risk balance of treatment options, severity of the disease, and the urgency of unmet medical needs.

Krabbe disease is a rare condition with no FDA-approved treatment currently available. NORD believes this rare disorder is one with an unmet need and a severe disease burden for patients and caregivers.

### ***The goals of this meeting were as follows:***

- Obtain patients' and caregivers' perspectives on living with Krabbe disease. Specifically, which burdens and symptoms impact the quality of life of patients and caregivers.
- Learn patients' and caregivers' preferences regarding current and future treatments as well as experiences and preferences for clinical trial, in order to help FDA understand: their hopes for future treatments, treatment side effects they are willing to tolerate, the medical risks they are willing to take in clinical trials, and their interests and challenges in participating in clinical trials.

The EL-PFDD meeting included panelists that represented patients with various types of Krabbe disease as well as caregivers.

The voice of Krabbe disease patients and caregivers was heard through brave patient and caregiver testimonies, open discussions with meeting attendees, live polling of the broader audience and post-meeting commentary.

For those who would like to view the entire meeting, a recording is available at the NORD website:

[Krabbe Disease EL-PFDD Meeting.](#)



## BACKGROUND ON KRABBE DISEASE

### What is Krabbe disease?

Krabbe disease, also known as globoid cell leukodystrophy, is a rare inherited lysosomal storage disorder caused by deficiency of an enzyme called GALC. GALC is required to maintain myelin, the protective covering of nerves. GALC deficiency causes severe damage to the peripheral and central nervous system due to degeneration of the myelin sheath that surrounds all of the nerves in the body including the brain.

### What causes Krabbe disease?

Krabbe disease is a genetic disease caused by a mutation in the gene encoding GALC. Inheritance of Krabbe disease is autosomal recessive. Krabbe primarily affects infants; however, the disease does impact a small percentage of older children, juveniles and adults. We are finding a significant diagnostic odyssey exists for adult Krabbe disease patients.

### How is Krabbe disease diagnosed?

Early diagnosis of Krabbe disease is critical in order for patients to be potentially eligible for treatment with HSCT. Patients who qualify for HSCT should be transplanted before they are 30 days old in order to improve clinical outcomes.

Newborn screening has been implemented for Krabbe disease; however, it is not approved in most states. Only nine states currently screen for Krabbe, though several other states have plans to implement screening soon. In addition, there is now a test for an important biomarker in Krabbe disease called psychosine which should be used as the reflex or second tier test for babies who screen positive on the initial enzyme screen. With the implementation of improved screening and the application of psychosine testing, it is now feasible to rapidly identify all infants with the early form of Krabbe disease. Newborn screening can also identify most infants with the later onset-infantile forms of Krabbe disease.

### What are the symptoms of Krabbe disease?

There are various types of Krabbe disease. The symptoms may vary depending on the type and may present differently by patient.

#### **Early-infantile onset:**

Symptoms generally start anywhere from birth to six months of age. Many babies have cortical thumbs at birth and develop severe acid reflux in the first few weeks of life. They also experience feeding problems, which are often initially mistaken or misdiagnosed as colic by parents and pediatricians. Other common symptoms are stiffness, arching, abnormal tone, spasticity and poor head control. Some developmental milestones may initially be achieved, but then they are lost, and later, by generally six to nine months of age, babies develop seizures, vision loss and other symptoms.

#### **Late-infantile onset:**

The Late-Infantile Krabbe disease (LIKD) generally occurs in children 1-3 years of age. Those babies and toddlers commonly present with loss of developmental milestones and gait disturbances.

#### **Juvenile-onset:**

Patients in this age group are 4-18 years of age and present with one or more of the following symptoms: visual defects, memory deficits and deteriorating motor symptoms particularly with their gait.

#### **Adult-onset:**

Krabbe is rare in adults. Generally, it may cause gross motor disease manifested by gait disturbances. Many patients also have frontal lobe syndromes. Peripheral neuropathy may be the presenting sign of Krabbe disease in adult patients.

### How is Krabbe disease currently treated and managed?

All Krabbe patients, regardless of how their disease is managed and treated, require supportive care and palliative care.

Currently, the only available therapy is HSCT. While disease progression is slowed, life is extended and quality of life is improved with HSCT, Krabbe disease is not completely corrected. Peripheral nerve disease usually progresses over the first two decades of life. However, it is possible for HSCT to favorably change the clinical course of babies who are transplanted early in the course of their disease. To achieve this goal, early diagnosis is critical. Newborns or fetuses are diagnosed with early-infantile onset, who qualify for HSCT should be transplanted before they are 30 days of age in order to significantly improve clinical outcomes.

Dr. Joanne Kurtzberg, a leading Krabbe disease expert, and her team at Duke Children's Hospital, Durham, NC use unrelated umbilical cord blood transplantation to treat children and babies with inherited metabolic diseases. The transplant provides cross-correction of the patient's cells through the engrafting donor cells. Unrelated donor cord blood transplantation is an aggressive and risky therapy and involves myeloablative or very high dose chemotherapy, an average stay of two months in the hospital, and a recovery of 12 to 18 months. The risks include dying from a complication of the procedure or a late complication called graft versus host disease.

We learned early on that children who come to transplant with significant symptoms of disease have about a 20% chance of survival and that surviving children have significant impairment. For this reason transplant therapy is not recommended for children who present with significant symptoms of the disease.

### What research is currently being conducted to develop new therapies for Krabbe disease?

Currently, there are multiple research studies being conducted to find new therapies for Krabbe disease.

Gene therapy is in development by multiple companies and clinical trial screening will begin in 2021. Preclinical gene therapy research in animal models of Krabbe disease is promising with successful results.

There are now drugs which may be able to enhance engraftment of the cells from the transplant into the brain more quickly, shortening the time to engraftment and earlier correction of disease.

*“The FDA has learned that there’s no better way to assess what would be clinically meaningful to you than to ask you. We need to listen to you, the patient and caregiver, to better understand your priorities, your concerns, and your struggles.”*

Melanie Blank, MD, Clinical Team Leader, DCEPT, Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, FDA

Novel cellular therapies are emerging, which have the ability to remyelinate the brain or reduce inflammation in the brain while engraftment is occurring.

In addition, there is also ongoing research for enzyme therapies, substrate reduction therapy, in-utero transplant and combination therapies. The goal of any new therapy holds hope of correcting the disease further than transplant alone can do today.

The following themes were mentioned by multiple patients during the meeting. These themes express many of the challenges that patients and caregivers face while living with Krabbe disease. Throughout the patient panel stories, call-in comments and comments submitted in the form, the following struggles/issues were mentioned often:

**Early diagnosis of Krabbe disease is extremely critical:**

- Newborn screening (NBS) is critical, and most states do not currently screen for Krabbe at birth. At the time this meeting was conducted, nine states provide NBS for Krabbe.
- If a patient is diagnosed too late, then he/she will not be eligible to receive a stem-cell transplant.
- When Krabbe is diagnosed too late, patients have limited treatment options.

**Patients with Krabbe disease suffer from life-altering symptoms which include:**

- Neurological difficulties
  - Developmental delays and regression
  - Seizures
  - Spasticity
  - Muscle weakness
- Gastrointestinal issues
  - Swallowing problems
  - Reflux
  - Constipation
- Body temperature regulation and/or fever
- Inability to speak
- Inability to stand or walk
- Inability to move or to attend to ADLs independently

**Patients with Krabbe disease take multiple medications including:**

- Baclofen (Lioresal, Ozobax, Gablofen)
- Gabapentin (Neurontin)
- Albuterol (Proventil, Ventolin)
- Budesonide (Pulmicort)
- Seizure medications
- Metamucil
- Ativan

**Most caregivers have multiple pieces of medical equipment at home and must know how to use it all including:**

- CPAP machine
- Suction machine
- Supplemental oxygen
- Pulse oximeter
- G-tube
- Vest treatment
- Walker
- Wheelchair
- Nebulizer
- Stander

**Most patients with Krabbe require assistance with personal care including:**

- Feedings
- Medication administration
- Bathing
- Dressing
- Moving
- Communicating

**Multiple medical experts/specialists are involved with the care of Krabbe patients:**

- Physical therapists
- Speech therapists
- Occupational therapists
- Neurologists
- Orthopedics
- Gastroenterologists
- Dieticians
- Pulmonologists
- Home health care support teams
- Durable medical equipment providers

**Caregivers are exhausted by additional, multiple roles they assume to help loved ones:**

- Health care coordinator
- Patient advocate, especially in geographic areas where resources are limited
- Nurse/health care provider
- Patient transporter (to multiple doctor/health care appointments, multiple times per week)
- Medication and medical supply manager



**Caregivers of Krabbe patients experience significant negative impacts to their quality of life:**

- They often lose hours of sleep and feel extreme fatigue.
- They are unable to focus at work.
- They often feel socially isolated from friends and family.
- They often experience many challenges in their marriage.
- They feel uncertain and stressed when deciding whether to have additional children knowing they may pass this genetic mutation onto future children.
- They struggle to travel with all the patient's medical equipment needs:
  - They are rarely able to go on vacation alone and feel guilty if they do.
  - They struggle with providing care for their child with Krabbe disease and the other neurotypical children in the family
  - They worry about caring for their child if they are no longer able to.

**Caregivers also experience a high level of financial and emotional stress:**

- Some caregivers need to reduce employment hours and/or resign to care for the patient.
- Medications and medical equipment are expensive, causing families to reconfigure their budgets.
- Costs of traveling and relocating to be near a Krabbe disease expert are high.
- Families are separated temporarily (sometimes months) so patient can receive diagnosis, transplant or other treatment; part of family moves near treatment city while the other part of family stays at home with the other parent.

**Caregivers suffer mental anguish watching patient suffer:**

- It seems like the patient is 'trapped' in his/her own body.
- Patient is unable to verbally communicate.
- Caregiver struggles to understand or know the patient.
- Caregivers are overwhelmed with the constant 24/7 caregiving required to keep his/her patient alive.
- Caregivers feel hopeless as they are only able to help the patient with basic living functions.

**Clinical trial opportunities are limited or unknown to patients:**

- Some caregivers reported the patient did not qualify (meet inclusion criteria) for a clinical trial.
- Some caregivers and patients reported never being told of clinical trial opportunities.

**Patients and caregivers have treatment requests:**

- They would love for a cure to be found.
- They prefer a drug which reduces the severity of symptoms instead of a drug that will extend life but not improve symptoms.
- They would like access to drugs which improve muscle tone/improve mobility, reduce pain, and improve verbal communication skills.

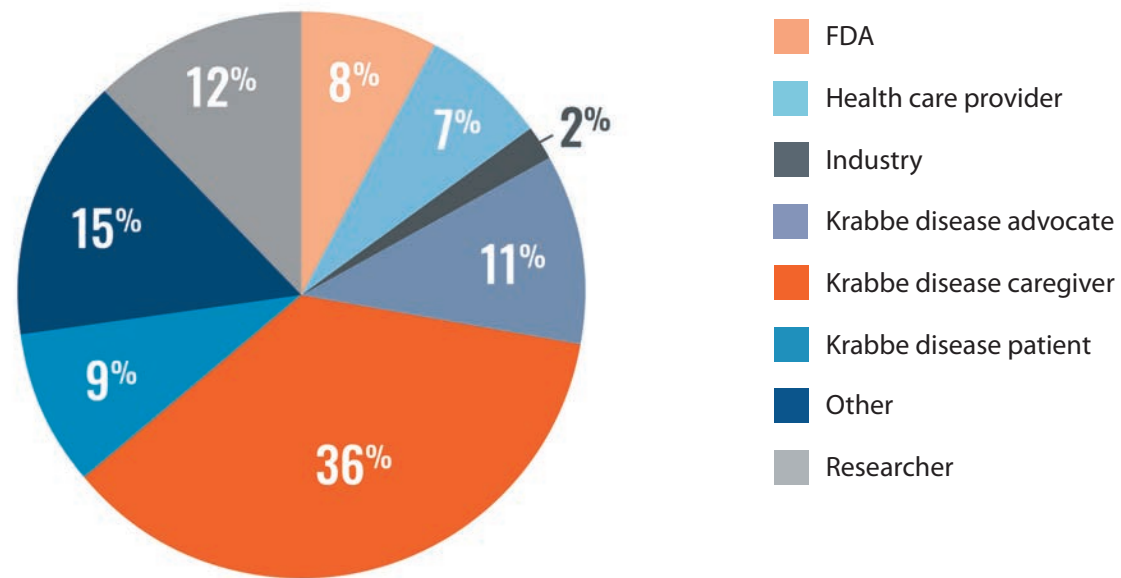
**Many patients and caregivers are open to learning about clinical trials:**

- They have an interest in learning about clinical trial options.
- They would need to know more about side effects.
- They want to see evidence that a drug reduces symptoms.



## MEETING PARTICIPANT DEMOGRAPHICS

This EL-PFDD meeting was attended by 226 participants via a live webcast, including:



All patients and caregivers were invited to answer the polling questions and 46 participated.

### Demographic Polling Questions

#### Where do you live?

The majority of participants were from the US: Eastern time zone (41%) and Central time zone (24%). The United Kingdom and EU countries (Italy, Germany, France and Spain) were represented at 14%, while remaining participants (21%) were from other parts of the US, Mexico and other regions (not specified).

#### What is the current age of the patient?

Many age groups were represented: 3% were 13-18 months old, 3% were 19-23 months old, 25% were 2-9 years old, 6% were 10-18 years old, 3% were 19-29 years old; and 6% were 30-45 years old.

Caregivers represented the majority (56%) of patients who are deceased.

#### Does the patient identify as female, male, non-binary/prefer not to say?

The majority (57%) of patients identified as female, 40% identified as male and 3% identified as non-binary or prefer not to say.

#### What form of Krabbe disease do you or your loved one have?

The following forms of Krabbe were represented: early-infantile onset (68%), late-infantile onset (26%), juvenile-onset (6%) and adult-onset (0%).

#### At what age did the onset of symptoms begin?

The onset of symptoms began early in life for all participants: 97% reported their symptoms began at 0-1 years of age and 3% of participants reported their symptoms began at 2-5 years of age.

#### At what age did you or your loved one receive a correct diagnosis?

The majority of participants (88%) received a correct diagnosis at age 1 or younger, 9% received a correct Krabbe diagnosis at 2-5 years of age and 3% were correctly diagnosed at 12-18 years of age.

#### How were you or your loved one diagnosed with Krabbe disease? (Patients were able to select multiple answers, if applicable)

Participants reported various ways he/she received a diagnosis: 38% were given a clinical diagnosis, 36% were diagnosed through genetic testing, 20% had enzyme level testing, 3% were diagnosed at newborn screening, and 3% had neonatal testing.



NORD's Director of Education Programs Rebecca Aune (left) and Director of Membership Services Debbie Drell



## VOICE OF THE PATIENT, TOPIC 1: LIVING WITH KRABBE DISEASE - BURDENS AND SYMPTOMS

The focus of this session was to hear directly from patients and caregivers regarding their struggles with the most severe symptoms and most impactful burdens of Krabbe disease. This session began with a panel of patients and caregivers who shared their stories, specifically about the daily impacts symptoms and burdens have on quality of life, including financial, emotional and mental effects. Following the panel stories, there was a moderated discussion. All participants had the option to call in or submit comments online in the comment form.

During the moderated discussion, polling questions were administered for patients and caregivers to answer. For those who were unable to complete the polling questions live, the poll was available until November 30, 2020.

### Topic 1: Patient and Caregiver Testimonies\*

This section includes highlights from each of the panel members. To read the full story of each patient or caregiver, please refer to Appendix 2.

#### Natasha (Parent/Caregiver):

"In 2011, our son, Kenan Witczak, was diagnosed at the age of eight months with early infantile Krabbe disease. Because he was symptomatically diagnosed, rather than being identified through newborn screening, we missed our opportunity to intervene with the stem cell transplant. The first two years of Kenan's life were riddled with rapid neurological deterioration, including painful muscle spasms, excruciating nerve pain, and an insupportable irritability in the form of a high pitch scream caused by the swelling of his brain, as the myelin of his white matter deteriorated.

My first mental twist as a parent was seeing my nine-month-old baby stoned after giving him a dose of clonazepam, a sedative used to treat anxiety by reducing the electrical activity of the brain. And my rationale to cope with having just drugged my son, seeing his little body slouched against the side of his stroller, his eyelids heavy, and his pupils glazed over. If anyone deserves to check out on life right now, it's Kenan."



#### Kevin (Parent/Caregiver):

"On December 19th, 2010, my wife Judy gave birth to our first child, Collin John Cushman, and I became a dad. At 13 months of age, Collin was diagnosed with Krabbe leukodystrophy, that had a life expectancy of 13 months to two years. There is no cure, and because Wisconsin is not yet screening for Krabbe, it was too late for any treatment that could have given him a better quality of life than what he was in for.

Krabbe had started robbing Collin of everything. He never walked, never talked, or even sat up on his own. He lost his eyesight, and he had little to no muscle strength, so whenever we would pick him up or hold him, we had to be aware of and support every single part of his body. Collin was a prisoner to Krabbe and dependent on us for everything."



#### Kirsten (Parent/Caregiver, Wife of Tom):

"Today, we wanted to focus mainly on the biggest challenge we face as parents and caregivers of a child with a life-threatening disease. We live in a state with a massive workforce shortage and do not have access to private, duty, shift, and nursing. We moved back to Vermont the summer of 2008, shortly after receiving a dire diagnosis for our daughter. Sylvie has this rare hereditary, degenerative, neurological condition that is typically fatal by age three. Feeling overwhelmed by this news, we decided to return to Vermont after living in Massachusetts for the last eight years so that we could be closer to friends and a teaching hospital.

We love the extremes in the weather, the beauty of the Green Mountain State, but living in a predominantly rural state has some very serious systemic infrastructure challenges, such as a lack of consistent access to broadband, poor cell phone reception, few hospitals, low pay, and inadequate nursing care.

We spent many nights without sleep so that we can care for our child and like many parents of children with disabilities, we have chosen not to geographically relocate based on the current medical team we have here in Vermont. Which means we have forgone possible career opportunities. And many parents ended up quitting their jobs to make sure their child has the care they desperately need. And in our case, Tom has spent the last 10 years, essentially out of the paid workforce to provide consistent in-home care."



\*The testimonies in this report was transcribed from the live event. Any omissions or errors are unintended.



**Tom (Parent/Caregiver, Husband of Kirsten):**

“We have twin girls, one living with Krabbe disease and the other is a carrier. Our daughters are 14 years old. Sylvie, our daughter with Krabbe, was diagnosed in January of 2008 with a late infantile form of this disease. She has frequent seizures, is unable to move or speak, and has a feeding tube that she was fitted with seven years ago.

And we’ve set up a mini-hospital in our house. We have ventilator, oxygen tanks, suction machines, monitors. Cold and flu season brings reasonable fears that our daughter will be hospitalized or perhaps even die. We don’t have medical degrees, but we are responsible for monitoring our daughter’s oxygen, monitoring her fluctuating body temperature, and administering respiration therapy.”



**Tammy (Parent/Caregiver):**

“Our third child, Marshall, had reached his first birthday, just as normal as any one-year-old does. About 12 to 13 months of age, he began to regress in milestones, losing his ability to walk, talk, stand, and hold his head. He was even having spasms. We were also encouraged to have Michael tested for the same disease. So, on November 19th of that year, 2010, Marshall received his diagnosis of Krabbe disease. And one month later to the date, we had received devastating news that Michael also had Krabbe disease.

I will never forget that day or any of those ‘D’ days, diagnosis and death days. They both come with their own level of unbearable and agonizing grief. After evaluations with Dr. Maria Luisa Escolar in December of 2010, it was recommended to transplant Michael. Michael received his transplant on February 10th of 2011 here in Oregon.

When Michael came home, we added to the schedule with his rehabilitation, speech therapy, occupational therapy, physical therapy and clinic visits. We rode this rollercoaster for almost six years. When Marshall passed away on March 5th of 2016, Krabbe disease did not die with Marshall. He is free from Krabbe disease, but we are still prisoners.”



**Jhyrve Sears (Patient):**

“By 18 months, they noticed walking problems that presented as an odd gait with tripping and falling a lot. At 12-years-old, I began falling more because my hip and leg would just give out. This was the first time I was put on crutches. By 14-years-old, I was permanently on crutches due to chronic falling.

I have balance problems, spatial awareness issues. I fall, I walk into walls and I have minimal coordination. Most of the time, I cannot feel my feet. For me walking, it’s a combination of watching the ground where I am about to step, and how I feel the nerves firing up my legs. When I can feel my feet, the sensations include pins and needles, burning, icy, prickly, and a pulsating throb. The most common sensations together are burning and icy.”



**Topic 1: Moderated Discussion**

During the discussion, the panel members answered questions presented by NORD and questions submitted by attendees. Participants were able to call in and/or enter comments online in the comment form. The following includes some of the questions and comments discussed. A selected list of additional comments were submitted during the meeting or during the 30-day open comment period, and can be found in Appendix 4.

**Discussion Question for Natasha: You had mentioned that your son had three to four breaths per minute. How was that medically significant? Or why were you guys scared to hear that?**

**Natasha:** “One of his first sleep studies where he had to qualify for CPAP, it was recorded that he had 900 central apneas during the course of the sleep study. And I don’t remember whether that was a six-hour or eight-hour period of time, but 900 central apneas. That’s not an apnea caused by a physical obstruction. That’s caused by his central nervous system, his brainstem. That number was incredibly shocking. So that gives perspective when we say that he dropped down from the toddler’s average to four to eight breaths per minute. That gives you a concrete example of what that means, how our children breathe.

And on top of that, because of his low tone, he’s using his accessory muscles to breathe. And with the loss of tone, his jaw is open. So, if you imagine going to the doctor’s office and they say, “Take a deep breath,” you know how hard you have to work at that deep breath. Now, try doing that with your jaw dropped open, and that’s a tremendous amount of labor just to do something that we all do involuntarily and don’t think about. So, the burden of this is just incredible.”



**Discussion Question for Jhyrve:** *You mentioned recurring infections and then also subsequently having to take antibiotics regularly. How long have you been taking antibiotics, and has it affected your gut microbiome? Has it affected your GI system? As a quick follow up, for probiotics, are you using prescription probiotics or over the counter probiotics?*

**Jhyrve:** “I don’t know that it’s affected my gut system, only because it’s so irregular to begin with. So, I do so much intake of probiotics and fiber. I don’t notice a difference because it’s so irregular. I’ve been taking antibiotics while getting sick for the past 16 years since transplant.

Over the counter, I use Yakult. I also tend to do a lot of yogurt. Also what helps a lot is I’ve found a hemp-based fiber product that I can use in shakes. Also, I use that psyllium husk.”

**Discussion Question for Jhyrve:** *You had mentioned that you have some workarounds for daily activities, but there’s some things you just can’t work around because of your Krabbe. What are those things that you can’t do that you actually wish you could?*

**Jhyrve:** “Driving would be nice to get myself from point A to point B. I can’t guarantee my legs is going to work, so it’s not safe for me to drive. There’s a lot of stuff I can’t guarantee is going to work, so I just don’t do it. Mostly, it revolves around my legs and their daily function. I do tend to throw things on occasion accidentally because my hand doesn’t realize it’s still holding it and just lets go.”

**Discussion Question for Tammy:** *Have we said anything, or have you looked at the polls or anything that you’ve heard so far that has made you think about Michael, about your experience with Marshall? Anything you want to share, Tammy?*

**Tammy:** “Well, obviously, as a family of two, with having two Krabbe children, one affected and one transplanted, they’re really so opposite of one another. I had a son that was fully affected with Krabbe and saw all of the symptoms that Krabbe causes. Whereas Michael, we were very fortunate to catch or to have transplant before any symptoms presented itself, and that was the advantage of having late infantile. So yeah, we saw both worlds. We saw the affected side that was just absolutely excruciating to watch your child die for six years, and then see one after rehabilitation thriving.”

**Discussion Question for Kirsten:** *You mentioned chronic stress, depression, isolation, weight gain, sleep deprivation. Did you find a way to cope? And how are you doing now?*

**Kirsten:** “Well, one of the things I just want to acknowledge is that Kevin and Tammy and Natasha were all part of our cohort, and so are a couple of the families you’re going to hear in the afternoon. We’re one of two families that I know of that we had met early on where our daughter is still alive. And so I don’t feel like we have survivor guilt, but there’s definitely the added stress of watching other people go through what we know is down the pike for us.

Tom is an avid cyclist, that’s one of the ways he’s coped. I think having connections with other families has been sort of a mixed bag. It’s both useful and also heartbreaking. And just because you have a common disease, doesn’t necessarily mean you’re necessarily friend material. I know some people when they were listening to what we talked about were like, “Why the hell don’t you just move out of Vermont if there’s no nursing and you don’t have it?” Because it’s beautiful here, and we wanted to stay here and we love hiking.”

**Discussion Question for Tammy from an audience member:** *Does Michael have any ongoing issues from the transplant? Has Michael witnessed any peripheral nerve disease?*

**Tammy:** “Michael has not experienced any nerve complications of any kind that’s noticeable and he doesn’t complain of any pain. I think the only thing that we’re really seeing, and it was just a result of chemotherapy is we’re starting on a path of dental repair. And then we closely watch Marshall, or sorry, Michael’s kidneys and liver, just because of complications from the chemotherapy. So, he sees those specialties every six months.”

**Discussion Question for panel from an audience member:** *Amanda wants to know about the effect on siblings. Can you speak to the impact of siblings and other family members? How did this affect them? Anybody want to weigh in on that? Tammy?*

**Tammy:** “Both Michael and Marshall have three other siblings. And during Marshall’s lifespan, we actually fostered another child. My oldest daughter, she wanted to be a caretaker and wanted to be a part of both Michael and Marshall’s care. However, with that being said, the way she handled her grief actually manifested in her being worried about weather. And I also saw how it matured her a lot faster in her years and how she also became a caring person. But for several years, she was very fearful of any kind of rainstorm or thunderstorm or anything like that. So that was a significant impact. And it really took her just growing and aging and maturing more to not have issues.

And even still once in a while, she’ll be like, “Mom, can I hang out with you during the thunderstorm?” That was how her grief and her struggles manifested. And then my boys, I didn’t see anything drastic other than... I think a significant thing was we’re a very open-door policy type family within limits. And the fear was that I think my children really limited their socializing and didn’t want to bring that home a lot, which was very unfortunate. So, I think they felt isolated in some fashion as well.”

**Jhyrve:** “My brother basically felt abandoned. We’ve done years of counseling together to move past a lot of the trauma that has happened.”

**Discussion Question for Kevin:** *What kind of communication did you have with your son Collin?*

**Kevin:** “Collin never spoke verbally, so it was all body language. Sighs was a big thing. Eye rolls was something I got a lot. With making funny comments or jokes, I would typically get an eye roll. With smooching grandma, whenever we were telling [him] that smooching grandma was coming, he’d always let out a big sigh and roll his eyes because he knew that that meant grandma’s coming and he was going to get smothered with kisses. So, it was really just that. The body language was the biggest way that we were able to communicate.”

**Kirsten and Tom added:** “We offered choices, which she has enough head control that she can actually look at different options. We’ll give her a choice between alternatives, and then she can look and engage with her eyes with her preference, which is very useful. And then she also can communicate non-verbally in some very interesting ways. She can signal when she needs personal care through...She knows that we’re responsive to coughing or any sign that she might be uncomfortable. So, I know that she needs to be changed when she coughs and there’s no reason for her to cough. She does that because she knows she’ll get my attention.”



Collin John Cushman

## Topic 1: Polling Questions and Results

The following polling questions were presented during the moderated discussion for Topic 1. Below the question is a summary of results. A full list of questions and answers is located in Appendix 3.

### ***Has the patient experienced any of the following difficulties? (Select all that apply)***

The most common difficulties selected were gastrointestinal issues at 12%, neurological difficulties at 12% and body temperature regulation and/or fever at 11%. Other reported common difficulties were respiratory infection at 10%, peripheral nerve disease at 9% and apnea at 9%.

### ***Which three of the following symptoms most negatively impact the patient's daily life?***

This poll revealed that the three symptoms which most negatively impact the patient's daily life are neurological difficulties at 27%, respiratory infection at 14% and peripheral nerve disease at 13%.

### ***Which of the following statements are true for primary caregivers? (Select all that apply)***

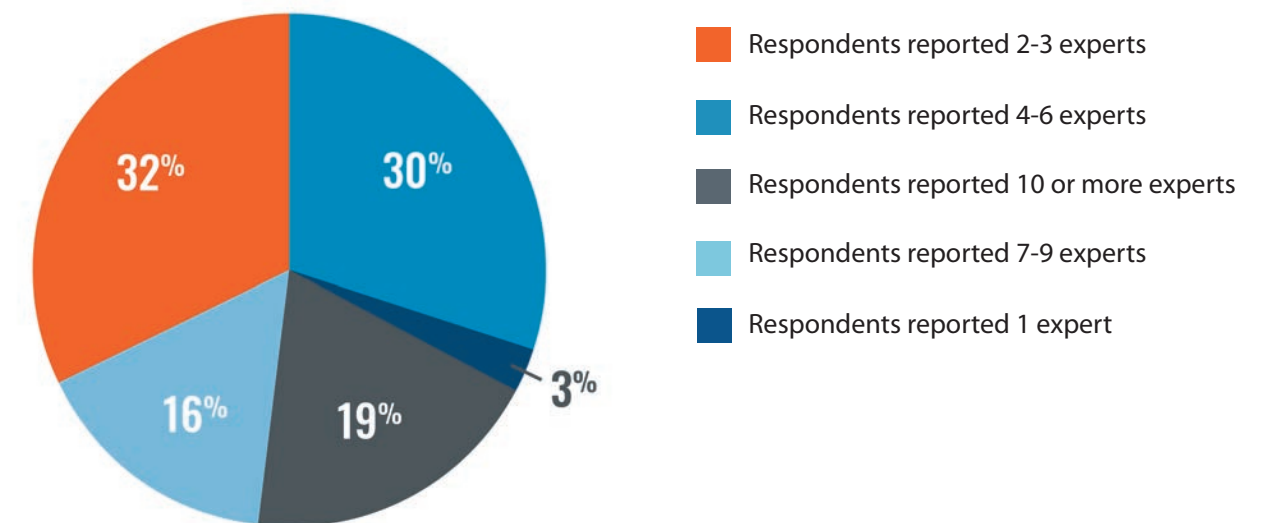
In response to this question, several statements were selected including: commonly feel stress in my family life (29%), feel isolated because others don't know what it's like to live with Krabbe disease (24%), had to quit or modify my work/school schedule (21%), miss work or school and it negatively affects my life (13%) and had to step down from prior job or schedule because of Krabbe disease (13%).

### ***What assisted medical equipment or devices does the patient use on a daily basis? (Select all that apply)***

In response to this question, several assistive medical equipment or devices were selected: adaptive stroller/cane/foot braces/Kid Kart/walker/wheelchair (19%), feeding machine (18%), chest therapy machine/nebulizer/smart vest/suction machine (16%), orthotics/braces (15%), mobility devices (12%), hospital bed/positioning devices for sleeping (11%), BiPAP machine (5%), communication devices (5%) and hoist/lift (1%).

### ***How many physicians and medical experts have taken an active role in the patient's care? Experts include cardiologists, geneticists, ophthalmologists, Krabbe specialists, etc.***

The poll showed multiple physicians and medical experts commonly play an active role in the patient's care:





## VOICE OF THE PATIENT, TOPIC 2: CURRENT & FUTURE TREATMENTS

The focus of this session was to hear directly from patients and caregivers regarding their preferences for future Krabbe disease treatments and their perspectives about clinical trial participation. This session began with a panel of patients and caregivers who shared their treatment preferences and thoughts related to clinical trials. Following the panel stories, there was a moderated discussion. All participants had the option to call in or submit comments online in the comment form.

During the moderated discussion, polling questions were administered for patients and caregivers to answer. For those who were unable to complete the polling questions live, the poll was available until November 30, 2020.

### Topic 2: Patient and Caregiver Testimonies

This section includes highlights from each of the panel members who shared their stories about treatment and clinical trials. To read the full story of each patient or caregiver, please refer to Appendix 2.

#### Christin (Parent/Caregiver)

"And I am the mother of two beautiful children. One whom you've already met, Owen, and Mabry, both of whom are affected by Krabbe disease. While my focus today will be on our son Owen and his treatment, it is impossible to tell his story without acknowledging his sister Mabry. Mabry's short 11-month life with Krabbe made us aware of this horrific disease. She was unable to receive treatment, because she was too far progressed. She is the reason we knew to test Owen, once we unexpectedly found out we were pregnant again, when she was just six months old.



We have never regretted our decision to move forward with this additional therapy. The transplant process Owen underwent, including a very aggressive chemotherapy regimen was a wild rollercoaster ride. During the process we tried to remain hopefully optimistic. We had to take one day at a time as things change daily. Some of the major side effects Owen experienced was mucositis, which is painful inflammation and ulceration of the mucus membranes lining the digestive track, which led to breathing issues that required three trips to the ICU.

We are so thankful for the opportunity he was given. It's a true night and day difference between Mabry and Owen. If only we could have given her this amazing gift too."

#### Anne (Parent/Caregiver)

"My son, Nick, was diagnosed at seven months old, with Krabbe disease and passed away at one year of age. When my daughter Gina was born, we had her tested as a newborn for the disease. As a family, we were devastated that we would be facing this horrible disease again, and potentially losing another child as an infant. Both Nick and Gina were diagnosed with the early infantile form of Krabbe.

I reached out to one of two facilities that had done experimental treatments for Krabbe disease, Duke University Medical Center, where I immediately spoke with Dr. Joanne Kurtzberg, and it was explained to me that Gina was eligible for a stem-cell transplant. Our family traveled to Duke from Cincinnati where Gina received a battery of tests to determine how advanced her disease was. It was explained to our family that Gina would be the youngest patient to receive chemotherapy at Duke and to have a transplant for Krabbe. It was emotionally challenging to make a decision with little or no prior history of long-term outcomes of other patients.

The last few years of Gina's life, she was on oxygen 24 hours a day to help her breathe. She lost her battle to Krabbe disease at the age of 15. Her brain and tissues were donated for research, where it was discovered there was no progression of Krabbe disease in the brain. The transplant had successfully corrected the enzyme deficiency in this part of her nervous system. My son Nick, was diagnosed too late for treatment, but we had the gift of 15 years with Gina, because her Krabbe was diagnosed very early, and she was able to receive a rapid intervention with the transplant."



#### Karlita (Parent/Caregiver)

"In October of 2016, my husband and I welcomed our first child, a son named Ezra, into the world. After about two weeks of being home, my husband had returned to work and I received an unexpected call from the geneticist. I still remember exactly where I was standing in the kitchen and reaching for the post-it as he spelled out the words for me, K-R-A-B-B-E. I was told that Ezra's newborn screening indicated that he had Krabbe disease, but that is essentially where the conversation ended.

At that time, Dr. Kurtzberg shared with us how critical it was that we started the blood stem-cell transplant process as early as possible, whether it be at Duke or a local hospital. For the transplant to be most effective, she shared that they want it to take place within the first 30 days of life, and that Krabbe





disease can start causing damage while still in-utero. While he may never lead a completely normal life, she shared that a transplant could greatly extend his lifespan and stop the progression of the disease, allowing him to preserve his abilities. She shared with us the risks of transplant, such as Graft-versus-host disease, mucositis, seizures, organ damage, and a host of other things. But honestly, the only thing that I could think of was the ultimate risk of him dying without it. And hearing those risks was a blur to me.

We had already decided the night before, if we were to do the transplant, we wanted to go to Duke and have him be treated by the best specialists in this disease. So, our decision was already made. We never considered not doing the transplant. We wanted to give him any and every chance at life that we could. I knew that if challenges arose, we would fight for him. Within 48 hours of receiving the diagnosis, we left our home, family and friends to travel to a state we had never been, with no idea when we will be coming back."

### **Laura (Parent/Caregiver)**

"There are a million considerations for us when it comes to whether or not we would enroll Quinton, diagnosed through newborn screening, in a clinical trial, but it really boils down to whether or not we need to. We would move mountains to ensure that he never faces the burdens that come with Krabbe disease. But as we've said, we've been blessed with that gift of time. We aren't going to put Quinton in a place of high risk for an experimental therapy, unless we're told we're running out of disease-free time.

More minor on the list of concerns when deciding if we would enroll in a clinical trial would be finding out where we need to move to participate in the clinical trial, and we would move anywhere. How long has the clinical trial expected to last? We would need to make arrangements so that we could be where we need to be for as long as we need to be and we would, of course do that. We would like to know what the expected outcome of the trial is. Is Quinton expected to be fully cured of Krabbe disease, or will this slow the progression, make the disease affect him more mildly? And what are the expected adverse effects?

We know the horror that Krabbe does to a child's body, but what can we expect Quinton to experience with an experimental therapy? Ultimately, we know that there is nothing minor at all about deciding to enroll in a clinical trial because we would need to uproot our lives and put everything on hold, but there is no question at all we would do that if Krabbe disease is starting in Quinton's brain."



### **Scarlett (Patient)**

"My family was told to take me home and keep me comfortable as my body would deteriorate and leaving me in a vegetative state until eventually, I died. I was 17 years old. And October 1997, when my family and I were informed that a bone marrow transplant could possibly stop the progression of Krabbe disease, the doctors told me that I was a good candidate for success of that. And my family and I then we discussed the pros and the cons. We knew that it was my only chance, so I underwent bone marrow transplant in February 1998.



[At] 41 years old today, I see now that I was given 20 plus years at life. Even though, there are side effects and symptoms that a bone marrow transplant leaves you with, like I've had cataract surgery and a total left hip replacement in my twenties. Even though, it has been a blessing.

I have never been offered in the past to do clinical trials, but I would definitely weigh the pros and cons of one and I would take part in it, specifically for my shaky hands, I have tremors. I have a hard time relaxing. I've tried marijuana and I've had success with it helping me relax. But if there could be reversal that would be great."

## **Topic 2: Moderated Discussion**

During the discussion, the panel members were asked questions by NORD and the audience could submit questions/comments as well. Participants were able to call in and/or enter comments online in the comment form. The following includes some of the questions and comments discussed. A selected list of additional comments that were submitted during the meeting or during the 30-day open comment period is available in Appendix 4.

### **Discussion Question for panel: What alternative therapies have helped with symptom management?**

**Christin:** "For Owen, we've used Botox for his spasticity in his muscles. And we did that within the last year for the first time and we were very hesitant and nervous because he's already delicate and we had heard that it can be negative, but we've experienced positive results with it, just loosening up his muscles and allowing him to work harder and gain a little bit more with his gait. So, we've tried that twice and then I think we'll continue to do that as long as it continues to provide a benefit for him."

**Karlita:** "Similarly, we also tried Botox with our son. We kind of had an opposite experience than Christin. I think every child reacts differently. We did three rounds of Botox. The first two, we did see some improvement. And then after the last round, we saw some regression just in his mobility functions. So, we kind of stopped doing that after talking with his neurologist. Anything water-based, he does really well with in loosening up his muscles and giving him more range of motion. And then we also obviously do medications that were listed there, like Baclofen, and we recently added another one to help with his initiation and taking steps forward, just in getting his muscles, initiating those." Karlita clarified water-based means, "so swimming in a pool, he takes steps really well in a pool as well. It's crazy just to see him taking steps in a pool versus in a gait trainer, it's the complete opposite. So, he does really well in the water."

**Discussion Question from FDA: If you were told you ineligible for a trial, what was the reason? And was expanded access ever considered or presented as an option to you?**

**Christin:** “I can’t say that we have been told we couldn’t do a clinical trial, but as far as transplant goes with our daughter, we were told we were unable to do that because her symptoms were too far progressed and the transplant doesn’t reverse symptoms, it only stops progression where it is.”

**Anne:** “With Gina being one of the early pioneers in January 2000 for a transplant, she was part of a clinical trial and eligible to participate. Nick was never eligible for any treatments because he was diagnosed in 1986. So, there weren’t any treatments at that time.”

**Discussion Question for Karlita: What was important to you for treatments?**

**Karlita:** “Severity of symptoms, side effects is obviously a big one. He has enough side effects from Krabbe itself. We really try not to add any additional things to his plate. So, we try to really look at those and go over those with his doctor when we’re looking at medications to add. But we really do trust our team of physicians that we have here. We’re really blessed with the doctors who look after him. So we do trust the medications and they really look to us too. They don’t make any decisions or force anything upon us. It’s really a team effort. So those two would probably be our top two things that we look at and then how well the research shows that they actually work.”

**Discussion Topic for panel: treatment decisions**

**Christin:** “The biggest decision we made was for a transplant, so far, for our son and we had just experienced the complete opposite with our daughter. So just to be able to watch him grow up and hit milestones that she did and then lost, and then wasn’t able to hit herself, just the idea of him living was a huge thing for us. And we sat down and talked with Dr. Kurtzberg. We’re very fully aware of all of the possibilities, but that was really the only choice that we had. So now that he is here and doing well, and I know that there’s future treatments coming down the line, it would just be mostly what Karlita said, but we fully trust Dr. Kurtzberg at Duke and her opinion on what she says we should do with Owen. So that’s where we look to first when we make those decisions.”

**Discussion Topic for panel: Has panel ever heard of expanded access?**

**Panel:** No

**Discussion Topic for broader audience: Why were you ineligible for clinical trial — for those who reported in the polling question?**

**Comment from Nikki (audience participant):** “Emmett was told he was ineligible for transplants, which is a trial, because his symptoms were too advanced. As of now, there are no options and/or trials for children with Krabbe who are not transplanted.”

**Discussion Question for panel: What are your thoughts about future treatments? What would you be willing to risk? Karlita, Christin, your children are living. Your boys are living with this disease. If a drug comes down the pike, would you want it to minimize symptoms, extend life; what if it had to be one or the other?**

**Christin:** “I would say minimize the symptoms. Obviously we would want him to live a long, productive life as anyone expects to, but we’ve seen our daughter suffer and we’ve seen the other side of Krabbe and definitely to reduce those symptoms, reduce the side effects would be huge because I think that improves their quality of life. And in the time that he’s here, however long that is, we want his quality of life to be significant.”

**Discussion Question for Laura and Ryan: Do you all want to weigh in on clinical trials and what would your experience be if you had to go in that direction?**

**Ryan:** “Yeah. So, for us, I mean, again, we’re in a little bit of a different boat than most of the other parents here where we have a son with the juvenile late-onset version. And so, he doesn’t have symptoms yet, so for as far as clinical trials, I mean the biggest thing that we would move mountains, we would move anywhere, we would do what we needed to do to participate in a trial if it’s time. And that’s the big thing. And again, different from most of the community here. But if it’s time and we have that luxury. So really the biggest thing is we work with our medical team, the doctors at UPMC and just take from their cues. If they say it’s time, we’re ready to do it.”

**Discussion Question for Anne: Do you have feedback on what we were talking about or anything that we talked about before with trials and treatments?**

**Anne:** “It was always my hope when Gina was alive that knowing that her peripheral nerve disease progression was happening, that there would be some kind of trial that came about to help her with that because cognitively she was age appropriate. She was attending school. She was very active in her community. I would’ve considered a trial for her to help with that peripheral nerve disease progression, had one been available.”

**Discussion Question for Anne: “You talked about Nicholas and Gina passing away from this disease, this terrible disease, but that Gina, because you had that experience of Nicholas being diagnosed and passing, she was transplanted and stabilized for 10 years and she was the first to receive experimental treatment. Can you share what was the trial like? What was that experience?”**

**Anne:** “She was actually the third newborn at Duke, so she was the youngest patient to receive chemotherapy. We had to make a decision quick because this disease was rapidly progressing. At two weeks ago of age, she already had the demyelization going on in her brain and in her peripheral nervous system. You don’t have time. And we wanted to give her the opportunity to get the disease stabilized and to see what the future held. And she lived 14 years longer than Nick. It was remarkable. And the things that we’ve learned from her, what the clinicians, what researchers, what the community has learned from Nick and Gina’s experience is hopefully going to propel us into new treatments and new therapies that we can fix the deficiencies that the transplant just isn’t able to sustain over a long period of time.”



## Topic 2: Polling Questions and Results

The following polling questions were presented during the moderated discussion for Topic 2. Below the question is a summary of results. A full list of questions and answers is located in Appendix 3.

### **What is your loved one's experience in clinical trials for a new Krabbe disease drug?**

In response to this question, 37% did not participate because they did not know about it, 30% did not participate because he/she was not eligible, 13% did participate and would do so again, 10% are not sure, 7% have not participated although he/she was aware and eligible, and 3% chose not to participate.

### **Select the top three reasons that would deter you from participating in a clinical trial**

The top three reasons selected were (1) due to potential side effects from a new drug (24%), (2) due to if the drug is administered in a way that is painful, difficult, or inconvenient in other ways (20%); and (3) whether the drug is supposed to treat symptoms or the underlying cause of the disease (14%).

### **Have you or the patient considered or undergone... (Select all that apply):**

Respondents reported that they have considered or have undergone muscle spasticity/irritability medications (18%), nutritional support such as a gastric tube (17%), oxygen (17%), respiratory support for breathing monitoring (15%), cough assist equipment (13%), shaky vests for respiratory support (11%), and Botox (9%).

### **Select the medications you use or have used for Krabbe disease (Select all that apply)**

The most common answers included baclofen (16%), gabapentin (15%), other (13%), albuterol (12%), anticonvulsants (11%), and pulmicort (7%).

### **Select the supportive treatments you use or have used for Krabbe disease (Select all that apply)**

Respondents reported using or having used supportive treatments such as physical therapy (15%), occupational therapy (14%), oxygen (13%), gastric tube (12%), massage therapy (11%), speech therapy (9%), swallow therapy (6%), other (6%), nissen fundoplication (5%), bone marrow or stem cell transplant (5%), IEP (5%), and VP shunt (2%).

### **How well does your current treatment regimen reduce the most significant Krabbe disease symptoms?**

Forty-eight percent of respondents reported moderately well, 17% reported poorly, 17% reported do not currently take any treatments, 10% reported very well, and 7% reported not at all.

### **Which three factors are most important to you when deciding to select a new treatment or drug for your loved one?**

The three factors selected as most important are (1) evidence that a drug reduces my worst symptoms (26%), (2) whether the drug directly targets the disease and its progression (22%); and (3) severity of side effects known for the drug (19%).

### **Without considering side effects, which one of the following would be most important to you in a future Krabbe disease therapy?**

The majority of participants (73%) responded that a drug that does not extend life but will reduce the severity of symptoms is the most important, while the remaining participants (27%) consider a drug which lets him/her live a longer life, but his/her symptoms remain the same or worsen to be most important.

### **Short of a cure, what specific things would you look for in an ideal treatment? (Select top three)**

The top three specific things selected included improve muscle tone/improve mobility (18%), reduce pain (17%), and improve verbal communication skills (13%).

## PRELIMINARY BENEFIT-RISK FRAMEWORK PROPOSAL FOR KRABBE DISEASE

Benefit-risk assessment is the foundation for the FDA's regulatory review of human drugs and biologics. The assessments capture the agency's evidence, uncertainties and reasoning used to arrive at its final determination for specific regulatory decisions. Additionally, they serve as a tool for communicating information to those who wish to better understand the FDA's thinking. For background and guidance on benefit-risk assessments, please follow this link:

[fda.gov/industry/prescription-drug-user-fee-amendments/enhancing-benefit-risk-assessment-regulatory-decision-making](https://www.fda.gov/industry/prescription-drug-user-fee-amendments/enhancing-benefit-risk-assessment-regulatory-decision-making)

The input provided by patients with Krabbe disease and their caregivers at the EL-PFDD meeting was used to prepare the preliminary benefit-risk table on the next page. This framework provides an overview of the benefit-risk aspects for two of the key decision factors, analysis of condition and current treatment options. Both of these factors are considered in the benefit-risk assessment. This framework will likely develop further over time and may be included into a benefit-risk assessment framework for a drug or biologic product under FDA review.



Jhyrve Sears and Dr. Kurtzberg



*“We learn so much from these meetings. We look forward to incorporating what we learn today into the agency’s thinking and understanding of how patients view benefits and risks of their therapies and devices for Krabbe disease. We thank you for participating, particularly in these unusual times. We are grateful to each of you for being here today and sharing your personal stories, experiences and perspectives.”*

Michelle Campbell, Senior Clinical Analyst for Stakeholder Engagement and Clinical Outcomes, Division of Neurology Products, Center for Drug Evaluation and Research, FDA

## Sample Benefit-Risk Framework for Krabbe Disease

DIMENSION	EVIDENCE AND UNCERTAINTIES	CONCLUSIONS AND REASONS
Analysis of Condition	<p>Patients with Krabbe disease constantly suffer from life-altering symptoms:</p> <ul style="list-style-type: none"> <li>• Neurological difficulties</li> <li>• Gastrointestinal issues</li> <li>• Body temperature regulation and/or fever</li> <li>• Inability to speak</li> <li>• Inability to walk</li> </ul> <p>Patients with Krabbe disease are most impacted by:</p> <ul style="list-style-type: none"> <li>• Neurological difficulties</li> <li>• Respiratory infections</li> <li>• Peripheral nerve disease</li> </ul> <p>Patients with Krabbe disease must have multiple medical experts/specialists involved in their care:</p> <ul style="list-style-type: none"> <li>• Physical therapists</li> <li>• Speech therapists</li> <li>• Occupational therapists</li> <li>• Neurologists</li> <li>• Pulmonologists</li> <li>• Gastroenterologists</li> </ul> <p>Caregivers of patients with Krabbe disease are significantly impacted:</p> <ul style="list-style-type: none"> <li>• They often feel socially isolated from friends and family</li> <li>• They are unable to focus at work</li> <li>• They often lose hours of sleep and feel extreme fatigue</li> <li>• They often experience challenges in their marriage</li> </ul>	<p>Krabbe disease is a genetic disease which causes severe damage to the peripheral and central nervous system. There are various types of Krabbe disease with severe symptoms that must be constantly managed by visiting multiple medical experts and taking multiple medications:</p> <ul style="list-style-type: none"> <li>• Seizures</li> <li>• Vision loss</li> <li>• Gait disturbances</li> <li>• Deteriorating motor symptoms</li> </ul> <p>Impacts of Krabbe disease on the quality of life of patients and caregivers is present throughout life. Since there is no cure, patients and caregivers must manage the symptoms and burdens of Krabbe on a daily basis with no relief.</p> <p>Early diagnosis is critical in order for patients to be potentially eligible for treatment with HSCT.</p> <ul style="list-style-type: none"> <li>• Patients who qualify for HSCT should be transplanted before they are 30 days old, in order to improve clinical outcomes.</li> <li>• Newborn screening has been implemented for Krabbe disease; however, it is not approved in all states.</li> <li>• A psychosine test is available for babies who screen positive on the initial enzyme screen. Psychosine can rapidly identify babies with early infantile Krabbe Disease enabling emergent referral for HSCT under 30 days of age.</li> </ul>
Current Treatment Options	<p>Currently, the only available therapy is HSCT. While life is extended and quality of life is improved with HSCT, Krabbe disease is not completely corrected.</p> <p>Unrelated umbilical cord transplantation is used to treat children and babies with inherited metabolic diseases. This is an aggressive and risky therapy. Children who come to transplant with significant symptoms of disease have about a 20% chance of survival.</p>	<p>Of the participants in this EL-PFDD meeting, 10% reported their current treatment regimen reduces the most significant Krabbe disease symptoms ‘very well’, 48% reported moderately well and 17% reported poorly.</p> <p>The majority of participants, 73%, would prefer a future therapy which does not extend life but will reduce the severity of symptoms, while 27% would prefer a drug which lets him/her live longer but symptoms remain the same or worsen.</p> <p>In an ideal treatment, 18% of participants would look for one which improves muscle tone/improves motility; 17% would look for a treatment which reduces pain; and 13% would look for a treatment which improves verbal communication skills.</p>

## CONCLUSIONS

The Krabbe Disease EL-PFDD Meeting hosted by NORD, KrabbeConnect, The Legacy of Angels Foundation, Partners for Krabbe Research and Hunters Hope, and supported by Gain Therapeutics, Magenta Therapeutics, PassageBio and Neurogene occurred on October 29, 2020.

This meeting provided patients and caregivers an opportunity to share how the symptoms and burdens of Krabbe disease impacts their daily lives. Patients and caregivers also provided feedback regarding their experiences with treatments and clinical trials. These perspectives are significant in helping the FDA make critical regulatory decisions related to new drugs and other treatments. In addition, patients' experiences provide valuable insight for other key stakeholders, including researchers, medical product developers and health care providers.

### **Post-meeting survey feedback included the following comments:**

"I thought it was a well-organized and high quality production. I was happy to be able to share our family's story and advocate for Krabbe."

"I called in during the live event and was able to give a brief story of both of my boys' journey with Krabbe Disease."



## APPENDIX 1: REFERENCES AND RESOURCE MATERIALS

The full recording of the Krabbe disease EL-PFDD meeting can be found at the following link to the NORD website:

[Krabbe Disease EL-PFDD Meeting](#)

For more information on Krabbe Disease, please see the information posted in the Rare Disease Database on the NORD website:

[rarediseases.org/rare-diseases/leukodystrophy-krabbes](https://rarediseases.org/rare-diseases/leukodystrophy-krabbes)

National Institutes of Health, Genetic and Rare Disease Information Center (GARD):

[rarediseases.info.nih.gov/diseases/6844/krabbe-disease](https://rarediseases.info.nih.gov/diseases/6844/krabbe-disease)

Dr. Joanne Kurtzberg provided a clinical overview of Krabbe disease, including diagnosis information, cause, symptoms, treatment options and current research in development.



Joanne Kurtzberg, MD  
Department of Pediatrics,  
Duke University School of Medicine



## APPENDIX 2: FULL PATIENT AND CAREGIVER TESTIMONIES

### Topic 1: Living with Krabbe Disease — Burdens and Symptoms

#### Natasha:

“Hi, my name Natasha Spencer and I live in Chicago, Illinois. In 2011, our son, Kenan Witczak, was diagnosed at the age of eight months with early infantile Krabbe disease. Because he was symptomatically diagnosed, rather than being identified through newborn screening, we missed our opportunity to intervene with the stem cell transplant. The first two years of Kenan’s life were riddled with rapid neurological deterioration, including painful muscle spasms, excruciating nerve pain, and an inconsolable irritability in the form of a high pitch scream caused by the swelling of his brain, as the myelin of his white matter deteriorated. My first mental twist as a parent was seeing my nine-month-old baby stoned after giving him a dose of clonazepam, a sedative used to treat anxiety by reducing the electrical activity of the brain. And my rationale to cope with having just drugged my son, seeing his little body slouched against the side of his stroller, his eyelids heavy, and his pupils glazed over. If anyone deserves to check out on life right now, it’s Kenan. His first baby’s Christmas was spent screaming from Clonazepam withdrawal before the new medications, the Baclofen for his muscle spasms, and the Neurontin for his nerve pain reached therapeutic levels. Finally, relief for some of his pain, but the peripheral nerve damage continued. Kenan lost the tone in his muscles and the ability to move his body voluntarily, including his smile. He lost his function to swallow and was fitted with a g-tube for nourishment, while I was handed a suction machine to help manage his secretions. He lost his means to vocalize before forming his first words. His pupils stopped dilating according to the light in the room, blowing out his vision. Kenan was just beginning to understand the world around him when one by one, Krabbe disease shut his senses down. The most struggling symptom was his respiration rate, he went from a toddler’s average of 20 to 30 breaths per minute, down to four to eight breaths per minute, while still maintaining his oxygen levels near a 100%. His body had amazing ability to physiologically adapt and compensate.

Without the guidance of the only Krabbe specialist, Dr. Maria Escolar, at the children’s hospital in Pittsburgh, where we annually visited to participate in her natural history study, I would not have been prepared for this shocking drop. Even with her accredited insight, Kenan’s breathing made everyone around him nervous, his local doctors, nurses, numerous specialists, and therapists. Because Krabbe is a rare disease filled with nuances that are equally rare and therefore misunderstood, and because I knew Kenan better than anyone, I became the unacknowledged lead in his care.

This role that I assumed and its growing responsibility backfired on me, seven years later, when I was confronted with his end of life. I was not equipped for the conflict between the rational doctor in me who knew we had reached the end and the symbiotic mother in denial, or perhaps it was the opposite.



The doctor whose job it was to protect and endure and the mother who knew it was time to say goodbye. Either way, I suffered the mental health consequences of simultaneously being both while trying to navigate Kenan’s death.

Living in a major urban city, put us at an advantage over most of Kenan’s Krabbe peers. We had a tremendous care team, a hospice nurse that visited our home once a week, a children’s rehab hospital within walking distance where Kenan received his therapies, and two major children’s hospital, one now with an established leukodystrophy care center. When Kenan needed to be rushed to the ER, his hospice nurse would call ahead, prepping the team about his condition and baselines, so that they wouldn’t overreact, potentially doing him more harm. When Kenan needed his tonsils and adenoids removed because they were interfering with his ability to breathe, the head of the PICU came to our home to witness Kenan relaxed, comfortable and at his baselines so that she could prepare her team accordingly. This is extraordinary and evidence of a truly integrated medical support system.

Looking back at the tight regime of around the clock meds, the baclofen, Neurontin, Bactrim, omeprazole, Valium, Onfi, Ativan, and towards the end of his life, pushing morphine and methadone. The treatments: albuterol, vest, suction, CPAP, chest PT, supplemental oxygen, and time in his stander. The therapies: physical, developmental, speech and swallow. The appointments: neurology, orthopedics, GI, pulmonology, ENT, sleep studies and radiology. The coordinating: getting to and from all of the above, ordering supplies, refilling and picking up medications. The advocating: hours spent on the phone with Blue Cross and Blue Shield, and Medicaid. Honestly, it felt like this is all I did. And to remedy my guilt of not playing with Kenan more and having fun, or even teaching him his math and ABC fundamentals, I had to remind myself that following through on all of the above is what it meant to parent Kenan.

For as much as these interventions were ingrained into my vocabulary, my autopilot, essential to sustaining and elongating his life for seven years, it all left me almost the second he did. He died on May 31, 2018. In that moment, I was relieved of my duties as his doctor, his nurse, his therapist, his social worker and his case manager. I attended to his body as a grief ridden mother would. It took Kenan dying, for me to resume my original role.

What remains and what I reflect upon now, is the emotional residence of everything we went through. We all know and understand how completely dependent on us a newborn is. With each physical and developmental milestone, they separate from us gaining more independence and autonomy in the world. This is the normal healthy trajectory, not the case however, when you have a medically complex child, it is the opposite. The older Kenan became the further into the disease he went. The more compromised his brainstem, the greater the pressure on our parent/caregiver, child relationship.

The irony is, within his extreme need of me, our symbiotic attachment, and the intimacy of our non-verbal communication, I had little understanding of who he really was. What was his favorite color? What music did he like? What story did he want to hear next? What did the disease really feel like? All those little pieces of information that collectively distinguish his personality, were locked inside him.

It got to the point where I dreaded his birthday and Christmas each year. Everyone asked me what they should get him? What should we get him? What should Santa bring him? There is great pain for me in not ever knowing. Although altruistic, it is depressing to choose fundraising for disease over fulfilling your child’s desires. We got creative and found ways around it. For his sixth birthday, we sat Kenan up with his own



phone line, using an app. Everyone called wishing him a happy birthday directly instead of going through me. His eyes lit up and beamed at all the voices and their accents. We were great at inputting into Kenan. What we needed craved and desired, was his output.

I still get jealous when I see a transplanted child, one capable of laughing into the world, engaging it with yes and no responses, using their eyes to control an eye-gaze device with the adult programming phrases that they can string together. Imagine me getting to know the boy inside my son like that. Imagine giving him the means to separate from me, even if just a little, and the emotional room and mental space it would have allowed both of us. In those last few months of Kenan's life, I could have asked and known if he was done, if he was just too tired, or if he wanted to keep fighting? I could've asked him if he was afraid to die? I could have actively validated him throughout his life rather than passively soothing the unknown. What's necessary for a newborn, will never be enough for a seven-year-old boy, regardless of the circumstances. Kenan's been gone for two and a half years now and without him here, my greatest sadness is knowing and understanding more about Krabbe disease than I ever did about him. Thank you."

**Kevin:**

"Hello. My name is Kevin Cushman and I'm from Wisconsin Rapids, Wisconsin. And becoming a dad was something that I had always wanted to do. And on December 19th, 2010, my wife Judy gave birth to our first child, Collin John Cushman, and I became a dad. He was handsome and perfect in every way. I could hardly wait to watch him grow, learn to crawl, and then walk. I couldn't wait to teach him so many things, to take him fishing, hunting or play catch in the yard. But all those hopes and dreams were shattered on January 6, 2012. At 13 months of age, Collin was diagnosed with Krabbe leukodystrophy that had a life expectancy of 13 months to two years. There is no cure, and because Wisconsin is not yet screening for Krabbe, it was too late for any treatment that could have given him a better quality of life than what he was in for.



I was in disbelief. I was sad and I became angry with God. And I turned my back on Him. Now, it was difficult for me to be angry with God because I was in charge of the youth ministry program at church. So, I had to teach about God and how wonderfully loving and caring He was, when inside, I was screaming, "BS! If He was so wonderfully loving and caring, why didn't He fix my son? How could He let this happen?"

Caring for our son and learning about Krabbe and everything we would need to do to care for him became our number one focus. Krabbe had started robbing Collin of everything. He never walked, never talked, or even sat up on his own. He lost his eyesight, and he had little to no muscle strength, so whenever we would pick him up or hold him, we had to be aware of, and support, every single part of his body. Collin was a prisoner to Krabbe and dependent on us for everything.

Everything else in our life took a back seat, including our social lives. When Judy was pregnant with our second child, we knew that we would need help caring for our boy. So, we started getting nurses to help us out, even though one of us was always at home. It was over five years after Collin's diagnosis before Judy and I went away for the weekend, just the two of us. It was the first time that we both were away from Collin, and I didn't want to go. I was worried that something would happen and that Collin would pass while we were away, and I didn't want to live with that, but I also knew that we needed it, and I gave in. It was good to go and I'm glad that we went, but I was very glad to get home.

Collin was eight years and 18 days old when he passed. And I believe that he outlived the odds, due in large part to his daily treatments, nursing care, and close family contact. Collin's daily routine was the same each day, and his nursing staff was invaluable. There was so much care that Collin needed, like feeds throughout the day, meds three times a day, range of motion exercises, oxygen, bathing, school projects, massages to feet, legs, back, arms, hands, and so much more. Like I said before, Collin depended on us for everything.

Because Collin never moved on his own, the risk of fluid building up in his lungs was a constant worry. To deal with this, he received a vest treatment three times a day to loosen any fluid in his lungs. After the vest treatment, Collin would get the cough assist. This was a mask that was placed over his nose and mouth, it would blow air into his lungs and then suck it up very quickly, just like when you and I would cough. The idea here was to bring up anything that the vest treatment had loosened. Then we would use the suction machine to remove anything that was brought up.

Collin also received nebulizer treatments two times a day to help prevent that fluid buildup. And suctioning was done throughout the day, and whenever he needed the fluid cleared from his mouth. Because Collin had little to no muscle strength, he was not able to stand on his own, so he would spend four plus hours in his stander. This was a very [important] piece of equipment because it not only put pressure on Collin's growth plates, which helped him to grow. In fact, he grew two inches the first month that we started using it, but it also helped with circulation, digestion, and bowel movements.

Traveling with Collin was always a challenge because he didn't have much of an immune system. But when we did travel, we needed to bring all of his equipment, except the stander. It didn't matter if it was a day trip or a weekend trip. Every inch of our van was packed with his equipment. To make things more challenging, we'd have to plan every part of our trip around his feeds and treatments. This wasn't always an easy thing to do and we missed out on things because taking care of Collin was always our first priority.

When we didn't have nursing coverage, my wife, Judy, and I would switch off taking care of our boy. I did the vast majority of the overnights. All those overnights were time with my boy. I would snuggle with him for hours, even if he was having a good night and I was tired, I kept holding him, because I knew I wouldn't get to do that for long. Doing most of the overnights with Collin took a toll on me, both mentally and physically. It became more and more difficult for me to stay focused at work, and I struggled to do even the bare minimum of things—of what I needed or wanted to do. And every day was a constant struggle to keep focused. I used to go fishing on a weekly basis. Sometimes daily basis. It might be for only 20 minutes, but it was 20 minutes that I could completely disconnect from the world and feel better.

But I gave that all up because it was 20 minutes that I could spend at home with my son, or help out with my daughter. Truth be told, I just didn't have the energy to do it, even for 20 minutes. Looking back on my time with Collin, I find that there are times that are blurry, times that I have difficulty remembering. And I'm sure that this is due to my lack of sleep. But Collin was my life, and I don't regret one minute of sleep that I passed up on.

It's been over a year and a half since Collin has passed, and I feel like I still have not recovered. But again, I don't regret one second that I spent holding my boy, or the sleep that I passed up on. I would do it all over again in a heartbeat. I miss my boy, but I promised him that daddy would be okay. And I will, someday, somehow, I will be okay. Thank you."

**Kirsten and Tom:**

"We have twin girls, one living with Krabbe disease and the other is a carrier. Our daughters are 14 years old. Sylvie, our daughter with Krabbe, was diagnosed in January of 2008 with a late infantile form of this disease. She has frequent seizures, is unable to move or speak, and has a feeding tube that she was fitted with seven years ago. Despite some of these disabilities, she appears to be developmentally age appropriate in many ways. She's learning to use an augmentative, alternative communication device and attends public school when she's healthy. Under the current pandemic, she's doing her learning online, keeping her safe and stable. She likes chocolate pudding, Creamies, maple syrup, being read to, listening to music, being outside, and engaging with her peers, and of course, knowing the love of her family and caregivers.

Today, we wanted to focus mainly on the biggest challenge we face as parents and caregivers of a child with a life-threatening disease. We live in a state with a massive workforce shortage and do not have access to private-duty or shift nursing. We moved back to Vermont the summer of 2008, shortly after receiving a dire diagnosis for our daughter. Sylvie has this rare hereditary, degenerative, neurological condition that is typically fatal by age three. Feeling overwhelmed by this news, we decided to return to Vermont after living in Massachusetts for the last eight years so that we could be closer to friends and a teaching hospital.

For those of you unfamiliar with Vermont, the entire state has a population of slightly more than 600,000 people. We currently live in Burlington, Vermont, the largest city with a population of about 60,000. By comparison, there's only six states in the United States that have less than one million people and Vermont ranks 49th. We love the extremes in the weather, the beauty of the Green Mountain State, but living in a predominantly rural state has some very serious systemic infrastructure challenges, such as a lack of consistent access to broadband, poor cell phone reception, few hospitals, low pay and inadequate nursing care.

Even with our daughter's condition, we don't qualify for high technology nursing. The problem is, in Vermont there's no agency that provides nursing for individuals who are under 18 and are not enrolled in the Medicaid High Tech Program. Children and adults who are medically fragile, often need up to 120 hours a week of skilled nursing care. This means that regular home health visits of one or two hours a few days a week is not enough. For minors, like Sylvie, need nurses who can work full shifts for up to eight hours at a time. And that might seem like a lot, but it's a lot less expensive to Medicaid and the private insurers than hospital stays, and people can end up hospitalized all the time when there's a shortage of home care. And right now, only half the medically necessary hours for nursing are being fulfilled in Vermont.

Well, the reasons for nursing shortages, they're so multifaceted, the responsibility of her care and hiring all respite staff, falls entirely on our shoulders. Because of Sylvie's Krabbe disease and her medical needs, Tom and I essentially act as health coordinators, medical experts, systems, advocates, personal ambassadors and representatives. We've experienced chronic stress, depression, weight fluctuation and unrelenting fatigue. We experienced physical and social isolation. We've had some serious economic hardships and a lack of social services and support.

As our daughter's caregivers, we experience anticipatory grief and the feelings of ambiguous loss, sort of ebbing and flowing in our lives. We spent many nights without sleep so that we can care for our child and like many parents of children with disabilities, we have chosen not to geographically relocate based on the current medicals team we have here in Vermont. Which means we have forgone possible career opportunities. And many parents ended up quitting their jobs to make sure their child has the care they desperately need. And in our case, Tom has spent the last 10 years, essentially out of the paid workforce to provide consistent in-home care.

And we've set up a mini-hospital in our house. We have a ventilator, oxygen tanks, suction machines and monitors. Cold and flu season brings reasonable fears that our daughter will be hospitalized or perhaps even die. We don't have medical degrees, but we are responsible for monitoring our daughter's oxygen, monitoring her fluctuating body temperature and administering respiration therapy.

We have a solid medical team that would be hard to replicate quickly if we were to move. With time in one place, we've established a rapport and a relationship centered-communication with many of our providers.

One of the key mantras of the Disability Rights Movement is 'Nothing About Us Without Us'. As parents of a non-verbal child, we've been thrust into a constant state of advocacy for a daughter to be included in a biased world. We've learned much about patient and family-centered care and collaborative decision-making. And while the isolation and financial strain of caring for our daughter in a rural state with little services has been challenging, at the moment, it's one of the safest states in the country for avoiding COVID-19."

**Tammy:**

"Hi, my name is Tammy Wilson. We are the Wilson family. We live in Oregon. We are a family of six. 11 years ago, we were introduced to Krabbe disease in a very direct and invasive way. Our third child Marshall had reached his first birthday, just as normal as any one-year-old does. About 12 to 13 months of age, he began to regress in milestones, losing his ability to walk, talk, stand and hold his head. He was even having spasms.

It was in my last trimester of pregnancy with Michael that we began testing for Marshall's diagnosis. Those five months from July 2010 to December of 2010, were a roller coaster of events that I wouldn't wish on my worst enemy. Doctor visit after doctor visit forced our family from a two-income family to one. There was no other choice, but for me to be at home to meet the needs of our new journey that we knew nothing about.

I remember early on sitting in our living room in a recliner holding Marshall because at the time that was his only level of comfort. I would not leave him or put him down. I needed to ensure his security, his safety, and any discomfort he was experiencing. I remember not eating and drinking for over 10 hours, just so I could limit any discomfort he was having.





My mind raced that day [there was] a lot of thinking, and I asked myself, "How is my family going to survive this?" That day I decided we were going to live that we weren't going to just sit by and watch our son die. Marshall was going to live, and we were going to live a life and not wait and wonder. And it was my goal that all my children were going to live very decent and normal lives because my biggest fear was them resenting the family, or even me or even Marshall.

In September of 2010, we had kids going to school, my husband was working. I was seeking assistance for additional care for Marshall and hospice. Lots of ER trips with Marshall, they became more and more frequent for anything and everything. Marshall would go to the ER for his first seizure and those never stopped, we learned to live with them. And he was often in the hospital for breathing difficulties, sometimes unexplained breathing and even low heart rate. Eventually with each ER trip, Marshall taught us to do most everything at home and those trips became less frequent.

We were also encouraged to have Michael tested for the same disease. So, on November 19th of that year, 2010, Marshall received his diagnosis of Krabbe disease. And one month later to the date, we had received devastating news that Michael also had Krabbe disease.

I will never forget that day or any of those D days, diagnosis and death days. They both come with their own level of unbearable and agonizing grief. After evaluations with Dr. Maria Luisa Escolar in December of 2010, it was recommended to transplant Michael. We went home to weigh all of our options, and in January of 2011, we began a month long of tests and preparation for Michael's transplant.

Michael received his transplant on February 10th of 2011 here in Oregon. My husband and I saw each other in passing for 200 days. He worked weekends, and I managed our family with Krabbe. Every Thursday, we would trade shifts at the hospital. So, someone was always with Michael at the hospital, and then a parent was always at home with Marshall and our other children.

I was at the hospital on the weekends, and he was there on the weekdays. Family also helped with Marshall and the other children, getting them to inform their school events and sport events. While Marshall was home regressing, as the disease continued to take over his body, Michael was in the hospital, fighting for the disease not to take over his body.

Marshall also had hospice. Hospice offered relief in the sense of all necessary medications. They would order medications and supplies and come into our home for weekly checkups. Marshall would have massages and music therapy. Marshall had 24/7 routine care as he was completely dependent on others for medications, therapies, position changes, bathing, appointments and schooling.

When Michael came home, we added to the schedule with his rehabilitation, speech therapy, occupational therapy, physical therapy and clinic visits. We rode this rollercoaster for almost six years. When Marshall passed away on March 5th of 2016, Krabbe disease did not die with Marshall. He is free from Krabbe disease, but we are still prisoners.

Michael has yearly follow-ups and as he gets older, he will always have a visit of some sort related to Krabbe disease. My other children, if they even think about starting their own family, they will have a series of doctor visits related to Krabbe disease. My husband and I were trying to find our way back to each other in our marriage. The grief that we have absolutely suffocates us sometimes. We are truly not free from Krabbe disease in this mortal life. Thank you for hearing our story. Have an awesome day.

### **Jhyrve:**

Hi, my name is Jhyrve. I'm 33 years old, and I have Krabbe. I would like to take you through some of the ways Krabbe has affected my life. From birth to one year old, life was a struggle. I would not latch or suckle, and I liked to permanently stay in the fetal position. My mom had to do a lot of PT with me multiple times a day for the first three months.

I had excessive spit up to projectile vomit up to half my intake. I was an extremely irritable baby, I never crawled. By 18 months, they noticed walking problems that presented as an odd gait with tripping and falling a lot. At 12 years old, I began falling more because my hip and leg would just give out. This was the first time I was put on crutches. By 14 years old, I was permanently on crutches due to chronic falling.

At 16, I had right side tremor and twitches start. Six months later, I started myoclonic jerks, trouble putting thoughts together, and slight vision degradation. I received a cord blood stem cell transplant at 16 years and 9 months old. It's hard to talk about one specific symptom or another because a lot of them can happen in conjunction with other symptoms. They also can be hard to differentiate, let alone, put into words.

Some of my symptoms are constant, but the intensity fluctuates while other symptoms come and go. In order for me to have a functional day, I need at least eight to 12 hours of sleep at night and ideally a two-hour nap. On bad days however, I can sleep up to 22 hours a day. On those days, I cannot put my thoughts together, I have no balance and I'm in a lot of pain. Basically, I struggle to function.

I have balance problems, spatial awareness issues. I fall, I walk into walls and I have minimal coordination. Most of the time, I cannot feel my feet. For me walking, it's a combination of watching the ground where I am about to step, and how I feel the nerves firing up my legs. When I can feel my feet, the sensations include pins and needles, burning, icy, prickly, and a pulsating throb. The most common sensations together are burning and icy.

Sometimes you can divide either my feet in half in any direction, and one part will be burning hot while the other half of the same foot is icy cold even to touch. I also have swelling in my feet, ankles and knees. The more I am on my feet, the worse they swell. Elevation for multiple days helps, but that keeps me in bed for days. My right hip feels like it shorts out like an electrical circuit then sends fireworks from my hip to my knee

and back again, after that my leg collapses and I'm on the ground.

This forces me to constantly be aware of my surroundings in case I fall. How could I get up or who can help me up? If I fall in the shower, how am I getting up or who will be able to hear me? I also I have to think about questions like what kind of surface am I walking on? How many stairs are there, how level are the stairs? In all honesty, I avoid stairs whenever possible. I have fallen down then too many times.



Additionally, I have to consider how far I'm walking as well as the overall distance in the day. The further I walk and the faster I walk, both seem to be factors in causing my hip to short out. Those speeds seem to be the most influential. My nervous system feels like sitting on a subwoofer with ants crawling on me.

On a good day, it's a three or four on a scale of zero to 10. On a bad day, it's cranked to 10. I can always feel my nervous system. In less than a second. I can go from a three to a 10. On a good day, I only have a slight tremor, that's nearly unnoticeable. So I try to avoid things that can trigger my nervous system.

On a bad day, it's a fight to control the tremor. Some triggers include flashing lights, loud sounds and light touch on my skin. If it's a good day, I can handle some triggers and it's not too bad. On a bad day, I avoid anything that might act as a trigger. Flashing lights are always bad. I can handle one or two pictures, with a flash, but that's about it. By the second flash, my right hand will be shaking and quickly get worse if they continue. Around the fourth flash, the room will start to spin and I will have to lay down for a nap.

I have trouble using anything electrical. Heating pads are painful and a blow dryer gives me hot flashes. Touching me has to be a firm touch. Light touches cause immense pain, not just for the moment of contact, but for several minutes to hours afterwards. It can take my nerves a long time to calm back down. If someone rubs back and forth across my spine, I feel fireworks that shoot pain.

It explodes and radiates from my spine to my limbs. My legs can become weak, and my body vibrates. It also plays havoc with my internal temperature. Usually, I become hot and break out in sweats, but sometimes I can become freezing cold. Anywhere from a couple of times a month to a couple of times a week, I can get ocular migraines manifesting as fireflies in my vision. It can last from a couple minutes to a few hours before disappearing.

When this occurs, there is no accompanying headache or dizziness. I also can get migraines that make me light sensitive and dizzy. Additionally, when I'm tired, my left eye has a tendency to become lazy, making it very hard to focus my vision.

In 2012, I came out of an MRI tube with the ptosis of my left eye. Now it is permanently drooping, and fatigue can exacerbate the problem. Every illness I have, especially a sinus infection, seems to end up in my lungs. I usually am sick anywhere from three to six weeks, and I tend to have to take an antibiotic for about 20 days. I also have a rash on my chest and arms that comes and goes. It has constant pins and needles sensation with a pulsating burning throb. It's currently under control with CBDs, which I take orally and I have a bong I can use.

My memory is frustrating. This becomes apparent when I'm taking classes or doing cognitive testing. If I read a paragraph or someone reads a paragraph to me, then asks me to recall a specific paragraph I can, most of the time, remember the main idea, but I struggle to recall specifics. Although, I can have trouble retrieving words. I know the word I'm looking for and can tell you similar words, but it sometimes takes me a while to figure out what word it is that I want.

For me for the most part, I acknowledge what my body is doing, then try to ignore it. It's just there. I've found workarounds for some things I can't do, but other things I avoid altogether. Fatigue plays a big part of my daily life and will determine how much I can do in a day. Thank you for letting me share a little of my story."

## Topic 2: Current & Future Treatments

### *Christin with her son, Owen*

"Hi. My name is Christin Webb and this is Owen, and he's going to talk. And we're from Knoxville.

Can you put your paper lower so they can see your beautiful smile? And I am the mother of two beautiful children. One whom you've already met, Owen, and Mabry, both of whom are affected by Krabbe disease. While my focus today will be on our son Owen and his treatment, it is impossible to tell his story without acknowledging his sister Mabry. Mabry's short 11-month life with Krabbe made us aware of this horrific disease. She was unable to receive treatment because she was too far progressed. She is the reason we knew to test Owen, once we unexpectedly found out we were pregnant again, when she was just six months old. Owen, who was tested in-utero first through chorionic villus sampling at CBS, which is a prenatal test that is used to detect birth defects. We did this with the hope to receive results in time to consider possible participation in a trial for in-utero treatment.

This didn't work out because after three weeks of waiting for results, they came back inconclusive. I then underwent an amniocentesis as another means of detecting Krabbe. It was another long, grueling wait. On December 19th, 2014, exactly three months to the day after our daughter's diagnosis, we received the same news for our son. I was six months pregnant when we learned he had Krabbe. We experienced a range of emotions from sheer devastation and anger, to fear and guilt that we were unable to provide our daughter the same opportunity. However, beneath these emotions was just a small glimmer of light, treatment. We knew it wasn't a cure, but it was better than the alternative. Fast forward a few months to March of 2015, just weeks after our daughter, Mabry, had passed away in February.

In order for Owen to get the best care for Krabbe after he was born, my husband and I had to put our lives on pause, pack everything up and move five hours away from our family and friends in preparation for Owen's arrival and treatment at Duke University Hospital. I had to take unpaid leave from my job as a teacher, while my husband was able to transfer the location of his job with UPS, from Knoxville to Raleigh. Upon arrival, we sat down with Dr. Kurtzberg and her team, prior to Owen's delivery. She presented us with the opportunity to enter into a clinical trial called DUOC-01, a cell therapy done in conjunction with blood stem-cell transplant. He would be second in the world, first with Krabbe to partake. The unknowns made us a little uneasy, but Ashley explained more in-depth, the purpose of this therapy. We saw no reason not to participate.

The major benefit behind it was, it could prevent disease progression. And it does this through the acceleration of delivery of donor cells, to the central nervous system. With Owen having a massive new mutation of Krabbe, this slowing down of progression was definitely ideal. The way this was done was he was given 80% of the donor stem cells on transplant day, while the other 20% was sent to the lab where they reproduce as many more healthy cells as possible in a 28-day timeframe. On the 20th day, Owen received a second dose of stem cells through a lumbar puncture. We have never regretted our decision to move forward with this additional therapy. The transplant process Owen underwent, including a very aggressive chemotherapy regimen was a wild rollercoaster ride. During the process we tried to remain hopefully optimistic. We had to take one day at a time as things change daily. Some of the major side effects Owen experienced was mucositis, which is painful inflammation and ulceration of the mucus membranes lining the digestive track, which led to breathing issues that required three trips to the ICU.



He received countless blood and platelet transfusions and was placed on an exhaustive list of medications. He also experienced severe burns on his bottoms due to chemo in his urine. The burn team came and taught us a routine we used with each diaper change to help the healing process of these burns. He spent his first 110 days of life in the hospital and an additional four months living just outside the hospital, once discharged. We were finally able to take Owen home to Tennessee at the end of November in 2015. As far as lasting side effects, the major ones we see today are low muscle tone and dental issues. The chemotherapy he received has caused weakened enamel, resulting in many cavities and thinning roots. He does not have any permanent teeth from canine-to-canine tooth on the bottom and top. He has had several dental procedures, including the removal of six teeth on top, which were replaced with a partial just recently.

Can you smile and show them your beautiful teeth? Yeah. He will receive implants when he is fully grown. As excruciating as the process was, and despite the side effects that seem to pale in comparison to the alternative, this treatment works. We would do it all over again to make sure Owen has the chance at life he deserves. Today he is... How old are you? He's five years old. He attends preschool. He loves to tell jokes and hit golf balls with his own set of clubs. While he still requires a walker to get around, he doesn't let anything get in his way. He is stubborn and strong-willed, which has served him well. He's the biggest cuddle bug and tells us a hundred times a day that he loves us, which we soak up each time as this is a miracle in and of itself. We are so thankful for the opportunity he was given. It's a true night and day difference between Mabry and Owen. If only we could have given her this amazing gift too."



**Anne:**

"My son, Nick, was diagnosed at seven months old, with Krabbe disease and passed away at a year of age. When my daughter Gina was born, we had her tested as a newborn for the disease. As a family, we were devastated that we would be facing this horrible disease again, and potentially losing another child as an infant. Both Nick and Gina were diagnosed with the early infantile form of Krabbe. I reached out to one of two facilities that had done experimental treatments for Krabbe disease, Duke University Medical Center, where I immediately spoke with Dr. Joanne Kurtzberg, and it was explained to me that Gina was eligible for a stem-cell transplant. Our family traveled to Duke from Cincinnati where Gina received a battery of tests to determine how advanced her disease was. It was

explained to our family that Gina would be the youngest patient to receive chemotherapy at Duke and to have a transplant for Krabbe.

Prior to Gina, there had only been two other newborn transplants at Duke University Medical Center. Gina's pre-transplant evaluation showed that her central peripheral nervous systems were already compromised and that the nerves were demyelinating, even at two weeks of age. Without treatment, her body would continue to deteriorate rapidly. It was difficult as a mom to look at your perfectly two-week-old infant, holding her in your arms, knowing that she had a raging terminal disease going on inside of her, Gina would be a part of a pioneer research study. It was emotionally challenging to make a decision with little or no prior

history of long-term outcomes of other patients. Early infantile Krabbe disease is rapid, devastating, and a neurologic disease that [gives you] no time to weigh in on a decision. Gina began her chemotherapy and transplant journey at three weeks of life. Our oldest son Philip was 15 years old and in school in Cincinnati. My husband stayed home with Phillip, and I stayed in-patient with Gina for five weeks during her treatment, then four months in Durham for outpatient treatment.

The separation from the family was difficult, but we needed to divide and conquer in order to try to save Gina from any further deterioration of Krabbe disease. The transplant initially stabilized the enzyme deficiency for the first eight to 10 years of Gina's life. She thrived and gained a number of milestones that her brother Nick never achieved. Gina had a bubbly personality and seemed to flourish and develop physically. Although she did have some physical limitations, Gina was never able to walk independently, but she was able to walk in a walker in her early years. From early progression of her disease prior to transplant, Gina had challenges with her speech and used a communication device to help her to communicate her wants and needs. She had some verbal skills, but her muscles around her mouth and throat were weak and she was not able to speak clearly or to eat efficiently. Because of the compromises with her oral motor functions, Gina took a long time to chew her food and swallow liquids. So, she was not getting her proper sustenance.

Gina required a feeding tube to supplement her nutrition and hydration in order to live. Gina was on a number of medications for muscle tightness, known as spasticity. She was in constant need of stretching to help loosen and lengthen her muscles. As she grew, her muscles were not always able to keep up with the bone growth due to the early damage of the nerves in the peripheral nervous system. Gina wore braces on her legs, hand splints, received Botox injections routinely in different nerves in her arms and legs to stop muscle contractions. She had surgery to lengthen her hamstrings and went through serial casting a number of times to help the bones to develop normally and to stretch the muscles in her legs. Gina was dependent on others for all of her daily needs, including nutrition, hydration, bathing, dressing, administering multiple medications throughout the day. As a caregiver, and now single parent for Gina, it was a full-time job to manage her emotional, physical, medical prescription drug and medical supply needs.

On a weekly basis, we typically spent a minimum of three days a week at multiple doctor and therapy appointments. Gina's medical team consisted of a number of medical professionals in multiple specialties, two Krabbe disease experts, and a home health care support team. Her team also included service technicians for her wheelchair and communication equipment, durable medical equipment providers, school nurses, educational assistance, along with caregivers and nursing staff in the home to support Gina's overnight needs. Gina was able to attend school, drive a power wheelchair and was cognitively age-appropriate throughout her life. She began declining significantly around the age of 10, losing functions of her hands, arms and legs. She developed severe scoliosis in her back due to the weakening muscles. Her internal organs, including her lungs were compromised, all of which were from progression of Krabbe disease in the peripheral and autonomic nervous systems.

The last few years of Gina's life, she was on oxygen 24 hours a day to help her breathe. She lost her battle to Krabbe disease at the age of 15. Her brain and tissues were donated for research, where it was discovered there was no progression of Krabbe disease in the brain. The transplant had successfully corrected the enzyme deficiency in this part of her nervous system. My son Nick, was diagnosed too late for treatment, but we had the gift of 15 years with Gina because her Krabbe was diagnosed very early and she was able to receive a rapid intervention with the transplant."

**Karlita:**

“Hi. My name is Karlita Blackwell, and I’m from St. Louis, Missouri. In October of 2016, my husband and I welcomed our first child, a son named Ezra, into the world. I know that all parents say this, but we truly could not have felt a more instant love and bond with our little boy. We soaked up the next several weeks with early morning snuggles, first baths and settling into our new routine, as a family of three. After about two weeks of being home, my husband had returned to work and I received an unexpected call from the geneticist. I still remember exactly where I was standing in the kitchen and reaching for the post-it as he spelled out the words for me, K-R-A-B-B-E. I was told the Ezra’s newborn screening indicated that he had Krabbe disease, but that is essentially where the conversation ended.

I Googled it and my heart dropped, my throat closed, and my eyes welled up with tears. I read that my healthy newborn baby boy would likely die by the age of two. And that’s as far as I could let myself read in that moment. Immediately, I called my husband to return home from work. We cried together and wondered how this happened. I refused to have anything to do with the internet at that point, but my husband found the Hunter’s Hope Foundation and we were in contact with them within an hour. They put us in contact with Dr. Kurtzberg at Duke University Hospital, and she kindly contacted us in that evening, despite being late at night, to discuss Krabbe disease more in-depth and talk about stem-cell transplant as an option for treatment. She contacted our local pediatrician to have additional testing run the next day to confirm Krabbe disease and determine whether or not it was the early infantile form, which it was determined to be.

At that time, Dr. Kurtzberg shared with us how critical it was that we started the blood stem-cell transplant process as early as possible, whether it be at Duke or a local hospital. For the transplant to be most effective, she shared that they want it to take place within the first 30 days of life, and that Krabbe disease can start causing damage while still in-utero. While he may never lead a completely normal life, she shared that a transplant could greatly extend his lifespan and stop the progression of the disease, allowing him to preserve his abilities. She shared with us the risks of transplant, such as graft-versus-host disease, mucositis, seizures, organ damage, and a host of other things. But honestly, the only thing that I could think of was the ultimate risk of him dying without it. And hearing those risks was a blur to me.

We had already decided the night before, if we were to do the transplant, we wanted to go to Duke and have him be treated by the best specialists in this disease. So, our decision was already made. We never considered not doing the transplant. We wanted to give him any and every chance at life that we could. I knew that if challenges arose, we would fight for him. Within 48 hours of receiving the diagnosis, we left our home, family and friends to travel to a state we had never been, with no idea when we will be coming



back. And when we came back with, would our son be with us? Ezra was transplanted on November 17th, 2016. He spent a little over three months in-patient at Duke, and then we spent an additional two and a half months outpatient living at their Ronald McDonald house, where he had weekly follow-up appointments.

One of us slept at the hospital with him every night, and the other one of us slept at the Ronald McDonald house. It has now been almost four years post-transplant and Ezra has done remarkably well. He is in preschool four days a week, and absolutely loves it. He is incredibly social, knows all of his body parts, colors, and letters of his name. We are truly amazed every day at all of the things he accomplishes. However, there are still struggles that he has due to Krabbe disease. Ezra receives physical therapy, occupational therapy, and speech therapy weekly through the Special School District. In addition, he participates in outpatient physical therapy once a week, and occupational and speech therapy twice a month. The main area of defect for Ezra is motor, as he cannot yet sit up or walk on his own for extended periods of time. This doesn’t stop him as he’s very innovative. He has an array of different devices to assist him, including a gait trainer, a walker, an augmentative communication device, orthotics, a trunk support vest, thumb braces, elbow braces, immobilizers for nighttime and night ankle braces. Some of these are used in rotation, and some of these are used all the time. Obviously, all of the above therapies and equipment do not come without cost. When Ezra received his diagnosis, we made the decision for me to switch to a part-time, as-needed position at my job. It’s a job I love and did not want to fully give up. And we knew that any source of additional income would still be handy with all of Ezra’s additional expenses. However, going from working full-time to working approximately five hours a week while having additional medical expenses has been challenging at times. We’ve had to cut back in certain areas and be creative in others. However, we’ve also been very grateful to have a strong support system, that’s come forward to help without ever being asked.

Thank you for allowing me to share our family’s journey with Krabbe disease.”

**Laura with her husband, Ryan:**

“Hi, my name is Laura Nitahara. And my husband, Ryan and I welcomed our son Quinton to this world on August 11th, 2018, so we just celebrated his second birthday. Thus far, he’s been happy, healthy, but we are painfully aware that healthy won’t always be our reality because Quinton was diagnosed at three weeks old with late-onset Krabbe disease. We’re lucky enough to live in Illinois, a state that has Krabbe disease on its newborn screening panel. So, we don’t know when Quinton’s Krabbe disease will manifest, we’re just watching and waiting. While we have been blessed with the gift of time, which isn’t the case for most families affected by Krabbe disease, the waiting comes with its own emotional burden. We do a lot of comparing Quinton to kids his age, constantly questioning if there’s a delay. While most kids get a grace period for a normal timeline to hit milestones, we’re more anxious for those milestones to arrive.





It's very frustrating as a parent to wish for time to just slow down so the disease never shows up, while also willing to go faster to prove that we had another day with no signs of disease. Anytime he shows the slightest symptom of an illness, we're on high alert to monitor and make sure it isn't something else. Each day with Quinton is an absolute blessing, however, his diagnosis weighs heavy on us. When the bad thoughts come to mind, we take solace in the fact that we know what we're up against. We can proactively take steps to stay prepared and ready to take on what the future holds. For Quinton's routine assessments, we are seen at the University of Pittsburgh Medical Center Children's Hospital. He's seen through the program for the study of neurodevelopment and rare diseases run by Dr. Maria Escolar. We enrolled Quinton and a natural history study in order to utilize the data collected for a better understanding of Krabbe disease.

Quinton is a little boy that has thus far lived in normal, healthy two years. If enrolling him in a natural history study can help unlock answers for the next family who gets a call that their child's newborn screening revealed they have Krabbe disease, that's what's important to us. We traveled to Pittsburgh every six months for Quinton to be monitored and data to be collected. The emotional toll that these visits take on us is obvious because each visit could bring the news that our child's brain has started to be affected by Krabbe disease, but also the anxieties that come with traveling across the country with a baby. The emotional stress of the visit isn't isolated at the time we're present for the visit, it's the anticipation for a month prior and the decompression for the month after, it's overwhelming and consuming. Each visit Quinton undergoes blood draws, he goes under anesthesia for a brain MRI.

He's had a lumbar puncture. He sees an eye doctor, an ear doctor, a physical therapist, a speech therapist. He undergoes nerve conduction testing and cognitive testing. It's a very intense few days, especially for a child. You can't explain the reasoning behind all the testing. Through all the fear, all the sadness, all the anxiety, we remain incredibly hopeful for the future though. We know a cure can and will be developed, we just don't know what that looks like for our family. There are a million considerations for us when it comes to whether or not we would enroll Quinton in a clinical trial, but it really boils down to whether or not we need to. We would move mountains to ensure that he never faces the disease, burden that comes with Krabbe disease. But as we've said, we've been blessed with that gift of time. We aren't going to put Quinton in a place of high risk for an experimental therapy, unless we're told we're running out of disease-free time.

More minor on the list of concerns when deciding if we would enroll in a clinical trial would be finding out where we need to move to participate in the clinical trial, and we would move anywhere. How long has the clinical trial expected to last? We would need to make arrangements so that we could be where we need to be for as long as we need to be and we would, of course do that. We would like to know what the expected outcome of the trial is. Is Quinton expected to be fully cured of Krabbe disease, or will this slow the progression, make the disease affect him more mildly? And what are the expected adverse effects?

We know the horror that Krabbe does to a child's body, but what can we expect Quinton to experience with an experimental therapy? Ultimately, we know that there is nothing minor at all about deciding to enroll in a clinical trial because we would need to uproot our lives and put everything on hold, but there is no question at all we would do that if Krabbe disease is starting in Quinton's brain. Until then, we're lucky enough not to need to volunteer him for experimental trials."

**Scarlett:**

"Hi, my name is Scarlett, and I have adult form of Krabbe disease. And from the time I was diagnosed in the summer of 1996, I was told that there wasn't a cure for the disease, and I was given five to 10 years left in life. My family was told to take me home and keep me comfortable as my body would deteriorate and leaving me in a vegetative state until eventually, I died. I was 17 years old in October 1997, when my family and I were informed that a bone marrow transplant could possibly stop the progression of Krabbe disease, the doctors told me that I was a good candidate for success of that. And my family and I then we discussed the pros and the cons. We knew that it was my only chance, so I underwent bone marrow transplant in February 1998.

And it was hard, I had to deal with things such as a suggestion of making a living will before I went under the transplant. And then as I went through it, I was in Minnesota and I live in Tennessee. So, it was hard for me emotionally to be away from family and friends. And the transplant itself, it was easy for me because I didn't suffer hardly any side effects and hardship. And I even got out an early discharge day plus 13. And a year later we're told that it was 100% successful in stopping the progression of Krabbe disease. Though I still carry the scars, mentally and emotionally which are harder than that physically. The transplant was worth it, of course, because I stood throughout the whole ceremony of my wedding and then I danced at my reception.

And 41 years old today, I see now that I was given 20 plus years at life. Even though, there are side effects and symptoms that a bone marrow transplant leaves you with, like I've had cataract surgery and a total left hip replacement in my twenties. Even though it has been a blessing, I have never been offered in the past to do clinical trials, but I would definitely weigh the pros and cons of one and I wouldn't take part in it, specifically for... My hands shake, I have tremors. I have a hard time relaxing. I've tried marijuana and I've had success with it helping me relax. But if there could be reversal, that would be great. Thank you."



*Krabbe disease patient Ezra Blackwell*

## APPENDIX 3: POLLING QUESTIONS

### Demographic Polling Questions:

1. Where do you currently reside?
  - a. US Eastern Time
  - b. US Central Time
  - c. US Mountain Time
  - d. US Pacific Time
  - e. US Alaska Time
  - f. US Hawaii Time
  - g. Canada
  - h. Mexico
  - i. EU/UK (Italy, Germany, France, Spain, etc.)
  - j. Middle East
  - k. Asia
  - l. Other
  
2. What is the current age of the patient?
  - a. 0-6 months
  - b. 7-12 months
  - c. 13-18 months
  - d. 19-23 months
  - e. 2-9 years
  - f. 10-18 years
  - g. 19-29 years
  - h. 30-45 years
  - i. 46 years or greater
  - j. Deceased
  
3. Does the patient identify as:
  - a. Female
  - b. Male
  - c. Non-binary/prefer not to say
  
4. What form of Krabbe disease do you or your loved one have?
  - a. Early-infantile onset
  - b. Late-infantile onset
  - c. Juvenile-onset
  - d. Adult-onset



5. At what age did the onset of symptoms begin?
  - a. 0-1 year
  - b. 2-5 years
  - c. 6-11 years
  - d. 12-18 years
  - e. 19-29 years
  - f. 30-39 years
  - g. 40 or greater
6. At what age did you or your loved one receive a correct Krabbe disease diagnosis?
  - a. Age 1 or younger
  - b. 2-5 years
  - c. 6-11 years
  - d. 12-18 years
  - e. 19-29 years
  - f. 30-39 years
  - g. 40 or greater
7. How were you or your loved one diagnosed with Krabbe disease? (Select ALL that apply)
  - a. Newborn screening
  - b. Clinical diagnosis
  - c. Genetic testing
  - d. Neonatal testing
  - e. Enzyme level testing
  - f. Other

### Topic 1 Polling Questions: Living with Krabbe Disease — Burdens and Symptoms

8. Has the patient experienced any of the following difficulties? (Select all that apply)
  - a. Apnea
  - b. Body temperature regulation and/or fever
  - c. Dental issues
  - d. Gastrointestinal issues
  - e. Hydrocephalus
  - f. Loss of hearing
  - g. Loss of speech
  - h. Loss of vision
  - i. Neurological difficulties
  - j. Peripheral nerve disease
  - k. Pulmonary hypertension
  - l. Respiratory infection
  - m. Seizures

9. Which THREE of the following symptoms most negatively impact the patient's daily life?
  - a. Apnea
  - b. Body temperature regulation and/or fever
  - c. Dental issues
  - d. Gastrointestinal difficulties
  - e. Hydrocephalus
  - f. Loss of hearing
  - g. Loss of speech
  - h. Loss of vision
  - i. Neurological difficulties
  - j. Peripheral nerve disease
  - k. Pulmonary hypertension
  - l. Respiratory infection
  - m. Seizures
10. Which of the following statements are true for primary caregivers? (Select all that apply)
  - a. I miss work or school and it negatively affects my life
  - b. I've had to quit or modify my work/school schedule
  - c. I have had to step down from my prior job or schedule because of Krabbe disease
  - d. I commonly feel stress in my family life
  - e. I feel isolated because others don't know what it's like to live with Krabbe disease
  - f. None of the above
11. What assisted medical equipment or devices does the patient use on a daily basis? (Select all that apply)
  - a. Adaptive stroller/cane/foot braces/Kid Kart/walker/wheelchair
  - b. Bipap machine
  - c. Chest therapy machine/nebulizer/smart vest/suction machine
  - d. Communication devices
  - e. Feeding machine
  - f. Hoist/lift
  - g. Hospital bed/positioning devices for sleeping
  - h. Orthotics/braces
  - i. Mobility braces
12. How many physicians and medical experts have taken an active role in the patient's care? Experts include cardiologists, geneticists, ophthalmologists, Krabbe specialists, etc.
  - a. 1 specialist
  - b. 2-3 specialists
  - c. 4-6 specialists
  - d. 7-9 specialists
  - e. 10 or more

## Topic 2 Polling Questions: Current & Future Treatments

13. What is your loved one's experience in clinical trials for a new Krabbe disease drug?
- I am currently participating in a trial
  - I have participated in a trial and would do so again
  - I have participated in a trial and would NOT do so again
  - I have NOT participated in a trial, because we didn't know about it
  - I have NOT participated in a trial, because I was not eligible
  - I have NOT participated in a trial, although I was aware and eligible
  - I chose NOT to participate in clinical trials
  - Not sure
14. Select the top three reasons that would deter you from participating in a clinical trial:
- I do not want to risk it if there's potential for a placebo (sugar pill)
  - Potential side effects from a new drug
  - If the drug is administered in a way that is painful, difficult or inconvenient in other ways
  - If the trial required I stop current disease management and treatment regimen
  - Whether the drug is supposed to treat symptoms or the underlying cause of the disease
  - Frequency of exam appointments
  - Barriers to travel to treatment site
  - Length of trial
  - Negative things my loved one has heard about clinical trials
  - If the clinical trial might impact my eligibility to participate in future studies
  - Other
15. Have you or the patient considered or undergone any of the following for Krabbe treatment? (Select all that apply)
- Botox
  - Cough assist equipment
  - Muscle spasticity/irritability medications
  - Nutritional support (i.e. gastric tube)
  - Oxygen
  - Respiratory support for breathing monitoring
  - Shaky vests for respiratory support
16. Select the medications you use or have used for Krabbe disease. (Select all that apply)
- Albuterol
  - Anticonvulsants
  - Azithromycin MWF
  - Baclofen
  - Benadryl
  - Calcium
  - Chemotherapy



- Cuvposa
- Flonase
- Gabapentin
- Indocin
- Pulmicort
- Other

17. Select the supportive treatments you use or have used for Krabbe disease. (Select all that apply)
- Bone marrow or stem cell transplant
  - G-tube (gastrostomy tube)
  - IEP
  - Massage therapy
  - Nissen fundoplication
  - Occupational therapy
  - Oxygen
  - Physical therapy
  - VP shunt
  - Speech therapy
  - Swallow therapy
  - Other
18. How well does your current treatment regimen reduce the most significant Krabbe disease symptoms?
- Very well
  - Moderately well
  - Poorly
  - Not at all
  - I do not currently take any treatments
19. Which three factors are most important to you when deciding to select a new treatment or drug for your loved one?
- Whether drug is taken by mouth, IV or injections in muscle
  - How often you have to take the drug
  - Evidence that a drug reduces the worst symptoms
  - Whether the drug directly targets the disease and its progression
  - Number of side effects known for the drug
  - Severity of side effects known for the drug
  - Cost and/or whether covered by insurance
  - What your physician recommends



20. Without considering side effects, which one of the following would be most important to you in a future Krabbe disease therapy?
- The drug lets me/them live a longer life, but the symptoms are the same or worsening
  - The drug does not extend life, but will reduce the severity of symptoms
21. Short of a cure, what specific things would you look for in an ideal treatment? (Select top three)
- Ability to eat by mouth
  - Cardiac regulation improvement
  - Fewer side effects of treatment
  - Improve ability to see and hear
  - Improve digestion
  - Improve life expectancy
  - Improve muscle tone/improve mobility
  - Improve verbal communication skills
  - Minimize dental problems
  - Reduce pain
  - Reduce respiratory issues
  - Reduce seizures
  - Temperature regulation improvement

## APPENDIX 4: PATIENT AND CAREGIVER COMMENTS RECEIVED DURING AND AFTER MEETING

### Topic 1 Comments:

#### **Lesia (Caregiver)**

"My daughter Tory died from Krabbe at 20 months of age in 2016. Since then, I have been fighting for change in Pennsylvania, and we are very close to passing legislation that will not only make Krabbe part of the mandatory screening finally, which will implement Hannah's law of 2014, but it will also pave the way for other rare diseases to be added quickly.

We would have done anything to try to save our daughter's life, but we were denied that opportunity because she wasn't screened for it at birth. There isn't much that I can add about life with Krabbe to what has already been said by my fellow Krabbe parents and friends. Krabbe was, and is devastating.

I did want to speak about something else Krabbe parents face, which is the risk of having additional children. Not only did we lose a child, we were told on diagnosis day to not have any more children naturally because of the high risk of a repeated Krabbe diagnosis.

It cost us around \$20,000 to have our identical twin boys. \$6,000 of that was to genetically test the embryos."

#### **Sue (Caregiver)**

"Our daughter had all of her skills. She had quite a vocabulary, no problem with eating. We started noticing her high stepping and sitting in a W, and that didn't take very long. And she started falling down more when she was walking, even though she want[ed] to toddle. It didn't take very long for the neurologist to diagnose her by drawing blood from my spouse, myself and our daughter. And so by this time, she's two years old and the doctor said, "Typically, children don't live about a year past diagnosis." And when she turned three, we started making funeral arrangements because we didn't think she'd live another year. And she rallied, and this pattern went on and on. She never lost her ability to smile or giggle even when she was near death. She lived to be 26 years old, and she was born in '85. So, there was no talk about any kind of treatment or transplantation.

For me, it became a life of close relationships with my children; however, it pained me to know Joseph and Sam lived their entire lives having a sister with an illness they knew she wouldn't survive, yet developed and excelled in their interests."

#### **Nikki (Caregiver)**

"It took 11 months before our son was diagnosed. He has late infantile and is now four and a half years old. He was delayed at one year of age and didn't start regressing until 17 months old. We received an accurate diagnosis at 23 months of age, and he lost his vision two months after his diagnosis. We are thankful to have videos of him laughing, eating, talking, and playing. We often use those videos to share his story so that people see him for who he is rather than what they see physically."

#### **Hedy (Caregiver)**

"Diagnosis of our son took only 10 days from first GP visit to diagnosis in academic center (he was 2.5 months at the time) passed away at 7 months".

#### **Jacque (Caregiver)**

"Severe clinical issues since birth, but not diagnosed until 4 months old. Found out about cord blood transplant with Dr. Kurtzberg at 6 months old, but by then it was too late for treatment. That is why NBS for Krabbe is so important. Hunter went to Heaven in 2005, now healed"

## Topic 2 Comments:

### **Carol (Caregiver):**

"My 21-year-old daughter was transplanted for Krabbe a disease when she was just 19 days old. We knew to have her tested because we lost our son to Krabbe disease when he was two years old. Being treated for Krabbe has improved my daughter's life more than I could ever express. She lives fully, plays power wheelchair soccer, has traveled to Italy, and co-wrote a book with me."

### **Diana (Caregiver)**

"My son lived to be 21 years old and on June 25th, he was confirmed with a stopped progression of Krabbe disease many years ago. However, neurologically there was peripheral nerve damage that caused him to have severe scoliosis because he couldn't have control of his upper trunk and he did not have surgery to correct the spine and which compromised his lungs. And so, he did have issues and on his last few years, he was on oxygen, but he developed a virus unfortunately. I would have to say it was very similar to the COVID-19 right now in June 2018 and spent 10 days in ICU. He told us he was ready to go to heaven."

### **Andrea (Caregiver)**

"My son Bryce was on Omeprazole and another drug to calm him when he was really irritated, which I can't remember the name of."

### **Audrey (Caregiver)**

"I have two babies with Krabbe disease, Angela 4 ½ and Vladimir 5 months. It is very difficult not to be able to offer them anything that improves their quality of life and just be a spectator of how the Krabbe steals everything from us."

### **Allison (Caregiver)**

"My son, Max, had late onset Krabbe disease. He was born on February 6, 2014. Max was right on the borderline of transplant as to whether it would help him in the future or not. We were also told that anything that he had already lost or would lose leading up to transplant day would not be regained with the transplant, and there was a lot of risk. We chose to spend his remaining life keeping him comfortable and trying to live life to the fullest rather than remain in a hospital. If we had found her (Dr. Maria Escolar in Pittsburgh) program a month or two earlier, it would have been a no brainer and we would have participated. Max passed away in his sleep on June 26, 2016.

In terms of medication, Baclofen provided the most help to my son when he was alive (he had early-infantile late onset). It helped him relax but made him VERY sleepy most of the time, which was the tradeoff. Gabapentin also helped along with Albuterol and Morphine when he needed it, which was rare and we tried not to use Morphine (only for extreme pain). He also had a lot of GI issues, so we had to also add MiraLAX to his regimen to help with bowel movements. We also used Pedialyte often to help keep him hydrated. But when Baclofen was mixed incorrectly by apothecary, it would affect him for days, and he would have terrible muscle spasms and complete discomfort."

### **Hedy (Caregiver)**

"Our son already had too much brain damage at 2.5 months (passed away at 7 months). Our pediatrician told us in our country, no treatment (e.g. transplant) is available. However, I would [not] have wanted it for our son, because it can prolong the suffering throughout life and still result in an early death. In my opinion, the treatment options should first improve before adding it to the newborn screening program.

By far, the worst of this disease is to see your child suffer. Therefore, reducing symptoms and increasing comfort is the most important goal."

Hedy provided a list of medications used: Phenobarbital, Nexium, Erythrosine, Ranitidine, Paracetamol, Glycopyrronium, Zofran, Forlax and Nurofen.

### **David (Caregiver)**

"We use lipoic acid, coenzyme Q10, vitamin B12 and iron."

### **Lana (Caregiver)**

"We also give Sulfatrim, MiraLAX, Esomeprazole, and a daily multivitamin."

### **Karen (Caregiver)**

"I would like to talk insurance, as my daughter was transplanted at 16 years and then as she approached 26 years old, insurance became a problem. No one wanted to cover her. After 4 months of no insurance, we finally got her on SSI and then state insurance was gained. I think this needs to be talked about, because this makes life very scary!"

### **Kirsten (Caregiver)**

"Like Dr. K mentioned, the likelihood of our daughter surviving a transplant given the progression of her disease at 1 ½ years old when she was seen at the Mayo Clinic... It didn't seem as if the quality of life would be any better post-transplant. It totally didn't seem worth it!

Albuterol has been the bane of our existence. When our daughter goes into respiratory distress and is in the ICU, it's what is immediately administered. However, it causes epic seizure activity. We have all kinds of warning signs on her medical records NOT to use this drug. Additionally, our insurance really gives us a hard time for alternatives to Albuterol (e.g. Advair and Xopenex).

Because our daughter is now 14 years old (soon to be 15) and non-transplant, she is a total outlier in any of the pending clinical trials."

### **Nikki (Caregiver)**

"It took 11 months before our son was diagnosed. He was late infantile. He is now 4.5 years old. He was delayed at one year of age and didn't start regressing until 17 months old. We received an accurate diagnosis at 23 months of age. At that point, he was too symptomatic for treatment. He lost his vision 2 months after his diagnosis. We are thankful to have videos of him laughing, eating, talking, playing and everything a child should be able to do at that age. We often use it to share his story, so that people see Emmett for who he is rather than what they see physically now.



I really related to Natasha's testimony. My son Emmett has taught us that he communicates with blinking. A positive response is one blink, and two blinks is a negative response. Because of this, we are teaching him Braille and are able to ask yes/no questions. It is very clear that he is cognitively intact. I wish I could know what he is thinking and all his preferences. He is literally trapped in his body.

My hope is that treatment options would also focus on patients not treated with stem cell transplant. If there was a way to integrate therapies for children not diagnosed at birth, we would most likely participate in a trial. Stem therapy is so promising from what I have seen/heard in the medical community. I have a background as a RN/BSN and keep up-to-date constantly. Emmett was told he was ineligible for transplant, which is a trial, because his symptoms were too advanced. As of now, there are no options/trials for children with Krabbe who are not transplanted."

**Stacy (Caregiver)**

"We used alternative therapies such as craniosacral therapy and hydrotherapy."

## APPENDIX 5: MEETING MATERIALS

### Speaker Bios

**Natasha Spencer, Parent Advocate, Consumer Representative, and Caregiver**

Natasha has been a member of the Krabbe community since the symptomatic diagnosis of her son, Kenan, in 2011. She has worked with KrabbeConnect and Partner's for Krabbe Research in conjunction with the Program for the Study of Neurodevelopment in Rare Disorders at UPMC Children's Hospital of Pittsburgh to establish a biorepository specific for Krabbe leukodystrophy research. From 2015-2018, she was a Consumer Representative on the Illinois Department of Public Health's Lysosomal Storage Disorders Subcommittee. In 2017, her family was featured in an eight-story Chicago Tribune series that led to a legislative hearing ending Illinois's 10-year delay in implementing Krabbe disease testing as part of newborn screening. She recently co-authored an article, "Family Attitudes Regarding NBS for KD," published in the International Journal of Neonatal Screening's special edition, NBS and Follow-Up Diagnostic Testing for KD, June 2020. Kenan lost his battle with Krabbe at age 7 on May 31, 2018.



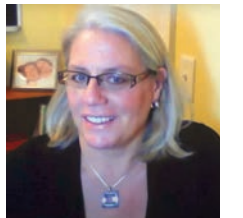
**Kevin Cushman, Caregiver**

Kevin is from Wisconsin Rapids, WI. On December 19, 2010, he and his wife, Judy welcomed their first child, Collin Jon to the world. Collin was diagnosed with Krabbe leukodystrophy in January 2012. Collin lost his battle with Krabbe on January 6, 2019. His strength and determination to keep fighting still amazes me. Kevin became involved with KrabbeConnect in 2019 when he joined their Board of Directors and became their Outreach Coordinator. He has also served as a youth pastor for more than 20 years at the Grace Lutheran Church in Wisconsin Rapids.



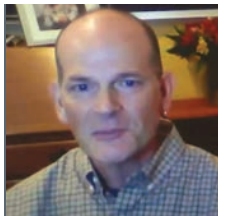
**Kirsten Isgro, PhD, Caregiver**

Kirsten Isgro has served on the Patient and Family Advisory Council for Vermont Children's Hospital at the University of Vermont Medical Center. Currently, she is on the National Executive Board of the Academy of Communication in Healthcare. She teaches health communication at the University of Vermont Health Sciences program and the State University of New York in Plattsburgh, NY. She and Tom are parents of 14-year-old twin girls, one living with Krabbe and one a carrier of Krabbe disease.



**Tom Schicker, MS, Caregiver**

Tom Schicker is a parent, home-baker, avid cyclist and part-time instructor of physics and mathematics. Currently, he is teaching physics remotely for Champlain College in Burlington, VT. He and Kirsten are parents of 14-year-old twin girls, one living with Krabbe and one a carrier of Krabbe disease.



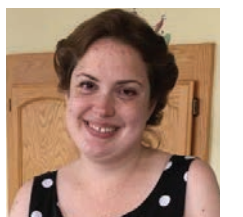
**Tammy Wilson, Caregiver**

Tammy is a wife and mother of five, two of whom were diagnosed with Krabbe disease. Marshall was diagnosed with late onset at 17 months of age, and Michael who was diagnosed at four and a half months. While Marshall was unable to receive a transplant due to his late onset diagnosis and ultimately lost his fight with Krabbe at the age of 7, Michael was transplanted and currently lives symptom-free as he approaches his 11th birthday. The Wilson family lives in Oregon.



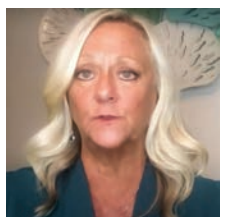
**Jhyrve Sears, Patient**

Jhyrve was diagnosed with Krabbe at 16 years old after a lifetime of undiagnosed symptoms. She is now in her early 30s, lives in California and works to spread awareness around those living with Krabbe disease through her affiliations with Hunters Hope and the Legacy of Angels Foundation.



**Anne Rugari, Caregiver**

Anne Rugari has over 34 years of experience with Krabbe disease. She has lost two of her three children who were affected by Krabbe, one as an infant and the other as a 15-year-old. As a parent and caregiver, Anne became inspired to create awareness and educational opportunities to support patients and families affected by Krabbe disease. She is the CEO and Founder of Partners for Krabbe Research (P4KR), a non-profit whose platform is to support and advance research by funding and collaborating with scientists, researchers and clinicians. Anne is also the Co-Founder and Vice-President of KrabbeConnect, a non-profit in the Krabbe disease space who's focus is to be the source of comprehensive information and access to resources for patients with Krabbe disease and to bridge the gap between science and patient knowledge.



Anne also is a consultant to the Neurodevelopment in Rare Disorders (NDRD) Brain and Tissue Bank. She works with families who wish to donate their loved one's brains and tissues for research after they have passed away from Krabbe disease and other leukodystrophies. Her role as a consultant also includes reviewing the inquiries from scientists who want to obtain tissues from the bank to advance research.

Anne is a published author of two children's books, "Just Like Me! A Book About a Girl with a Rare Disease" and "Just Like Me, Too!" As an advocate, Anne is dedicated to changing the outcomes of those affected by Krabbe disease—all in the hope that there will be an effective treatment and possible cure for patients who are diagnosed with this disease.

#### **Christin Webb, Caregiver**

Christin is a 5th grade math and science teacher and basketball coach from Powell, Tennessee. She is the mother of Mabry Kate and Owen Webb, both diagnosed with Krabbe leukodystrophy. Mabry Kate was born March 13, 2014 and passed away February 7, 2015. Though her life was cut very short, it was one of even greater purpose. Because of Mabry Kate, her little brother, Owen, was tested in utero and screened positive for Krabbe before he was born. Owen was born March 30, 2015 at Duke University Hospital and transplanted April 22, 2015. He is now 5 years old and doing remarkably well. Christin and her husband, along with the May and Measles families, advocated for Krabbe to be added to the Tennessee newborn screening panel. The Mabry Kate Webb Act was officially implemented in Tennessee on July 1, 2017. Christin also serves on the Steering Committee of the Leukodystrophy Care Network (LCN). She has also been a part of the LCN's treatment workgroup and their efforts to publish Clinical Practice Guidelines of transplant for both medical professionals and families, as well as participating in a workgroup aiming to publish a piece on the families' perspectives of the importance of Krabbe newborn screening. Christin is very passionate about helping in any way possible to add Krabbe disease to the newborn screening panel in every state.



#### **Karlita Blackwell, Caregiver**

Karlita is from St. Louis, MO, where she has worked in social services at a non-profit organization for over seven years. Recently, she worked with a small workgroup with the Hunter's Hope Foundation to publish a research article on the families' perspectives of the importance of Krabbe newborn screening. Her son, Ezra, was born in October 2016 and was the first infant in Missouri to receive a positive newborn screening for Krabbe disease. Ezra received a cord blood transplant at Duke University on November 17, 2016. He is now three years old and is doing wonderfully. She is passionate about educating others on the importance of newborn screening in each state and also has a heart for speaking with families who have just received their diagnosis.



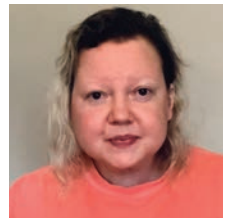
#### **Laura Nitahara, Caregiver**

Laura is a Nurse Practitioner in Glenview, Illinois. She holds a Bachelor's degree from Bradley University and a Masters from North Park University. She is married to her husband, Ryan, and they have one child, Quinton, who was born with asymptomatic Krabbe, which was diagnosed via newborn screening in August 2018.



#### **Scarlett Measels, Patient**

Scarlett was diagnosed with Krabbe at the age of 17 and transplanted at the age of 18. She is now in her early 40s, married, and lives in Pikeville, TN, with her husband. She volunteers with Hunters Hope Foundation and Advocates for all those living with or caring for someone living with Krabbe disease.



#### **Pamela K. Gavin, Chief Strategy Officer, NORD**

Pamela Gavin sets the strategic direction for NORD and implements programs and services that provide innovative solutions to address the needs of the rare disease community. She is responsible for bringing together all stakeholders within the rare disease space and works closely with NORD's board of directors, donors, corporate council and member organizations, other partners and staff. Prior to joining NORD in 2010, Pam spent 13 years executing complex, multi-stakeholder programs aimed at improving health care safety. As a consultant to the Federal government, she implemented a new web-based portal for reporting pre-market and post-market safety data to FDA and the National Institutes of Health (NIH), for which she received special citations from the FDA Commissioner and Director of the Center for Food Safety and Applied Nutrition (CFSAN) for outstanding leadership and teamwork. As Senior Director in the Office of the President at the University of Pittsburgh Medical Center, Pam worked in an equity partner business unit, bringing new concepts and emerging technologies to market to improve health care delivery. She oversaw several strategic business initiatives, including a clinical trial enrollment and adverse event reporting system; a multi-biomarker assay for the early detection of ovarian cancer; a medical simulation training system; and a clinical decision support system for infection control and antibiotic management. Pam is the co-founder of SafeCare™ Systems, LLC, which developed one of the country's first patient safety management systems and provides data driven solutions to health care providers, clinicians, administrators, and support staff. She served as director for RMF Strategies, a division of the Risk Management Foundation of the Harvard Medical Institutions, responsible for the commercialization of data driven risk management solutions. Pam earned an undergraduate degree in biology from Smith College and an MBA, with a concentration in health care management, from Northeastern University.



#### **Stacy Pike-Langefeld, Co-founder & President, KrabbeConnect**

Stacy holds a Bachelor of Arts degree in Sociology, an Associate of Science degree, and comes with more than 10 years of experience in the medical and pharmaceutical industry. Stacy's most recent role at Novo Nordisk involved increasing patient awareness, maximizing growth opportunities for hemophilia products, and educating the community on support services. In 2016, Stacy became the Director of Programs and Administration at the Legacy of Angels Foundation, applying her biotech knowledge and passion to an organization that was created, in part, as a legacy for her daughter and others diagnosed with Krabbe disease. Stacy brings a diverse set of work skills paired with being the parent of Makayla Pike, who lost her life to Krabbe disease in 2003. Stacy resides in Rosemount, MN, with her husband Josh and three children, Jack, Allyson and Ava. She currently serves as the President of KrabbeConnect.





## CLINICAL OVERVIEW

### Joanne Kurtzberg, MD, Pediatric Bone Marrow Transplant Specialist, Duke Children's Hospital & Health Center

Dr. Joanne Kurtzberg is an internationally renowned expert in pediatric hematology/oncology, pediatric blood and marrow transplantation, umbilical cord blood banking and transplantation, and novel applications of cord blood in the emerging fields of cellular therapies and regenerative medicine. Dr. Kurtzberg pioneered the use of umbilical cord blood as an alternative stem cell source for unrelated HSCT. Over the last two decades, Dr. Kurtzberg has established an internationally known pediatric transplant program at Duke which treats children with cancer, blood disorders, immune deficiencies, hemoglobinopathies and inherited metabolic diseases. In 2010, Kurtzberg established the Julian Robertson Cell and Translational Therapy Program (CT2) at Duke. CT2 focuses on translational studies from bench to bedside with a focus on bringing cellular therapies in regenerative medicine to the clinic. Recent areas of investigation in CT2 include the use of autologous cord blood in children with autism spectrum disorder, neonatal brain injury and cerebral palsy, as well as preclinical studies manufacturing oligodendrocyte-like cells from cord blood to treat patients with acquired and genetic brain diseases. Studies of autologous bone marrow ALDH bright cells in adults with stroke and radiation induced brain injury are also underway.



Dr. Kurtzberg established one of the largest unrelated donor cord blood bank in the world, the Carolinas Cord Blood Bank, at Duke in 1998. The bank has a current inventory of >40,000 units and has provided cord blood units to over 2,200 patients undergoing unrelated donor HSCT over the past 10 years. Dr. Kurtzberg's lab has developed novel assays to predict cord blood potency from segments attached to cryopreserved cord blood units, and is performing translational research testing cord blood expansion, cellular targeted therapies and tissue repair and regeneration. In 2012, under the direction of Dr. Kurtzberg, the Carolinas Cord Blood Bank received FDA approval for DuCord, a stem cell product derived from umbilical cord blood, for use in transplants between unrelated donors and recipients. Dr. Kurtzberg currently holds several Investigational New Drug (IND) applications for investigational clinical trials.

Dr. Kurtzberg has published over 300 peer-reviewed papers, multiple chapters and scientific reviews. She is a member of the American Society of Hematology, the American Association of Blood and Marrow Transplantation, the American Society of Pediatric Hematology/Oncology, the International Society of Cellular Therapies, the Pediatric Blood and Marrow Transplant Consortium (PBMTTC), and other organizations. She serves on the Board of the Foundation of Accreditation of Cellular Therapies, co-chairs the National Marrow Donor Program's Cord Blood Advisory Group and is a member of the Advisory Council of Blood Stem Cell Transplantation to Health and Human Services. Dr. Kurtzberg was awarded a Lifetime Achievement Award from the PBMTTC in 2012.

### Michelle Campbell, PhD, Senior Clinical Analyst for Stakeholder Engagement and Clinical Outcomes, Division of Neurology Products, Center for Drug Evaluation and Research, FDA



Dr. Michelle Campbell is a reviewer on the Clinical Outcome Assessments (COA) Staff and Scientific Coordinator of the COA qualification program in the Office of New Drugs (OND), Center for Drug Evaluation and Research (CDER), with the FDA. COA staff advises OND review divisions and other FDA centers by providing consultation and advice on clinical outcome assessment development, validation, and interpretation of clinical benefit endpoints in clinical trials to support drug development, labeling and promotion. Additionally, the COA staff leads and manages CDER's Clinical Outcome Assessment qualification program and engages with internal and external stakeholders to advance good scientific clinical outcome measurement standards and policy development. Her prior research experience includes the use of both qualitative and quantitative methods to develop instruments, program evaluation and the application of various study designs including clinical trials. Dr. Campbell earned her BA in Biology from the College of Notre Dame, her MS in Health Science (concentration in community health education) from Towson University and her PhD in Pharmaceutical Health Services Research from the University of Maryland School of Pharmacy.

### Melanie Blank, MD, Senior Clinical Analyst for Stakeholder Engagement & Clinical Outcomes, Division of Neurology Products, FDA



Dr. Melanie Blank is a nephrologist and clinical team leader in the Division of Clinical Evaluation and Pharmacology/ Toxicology (DCEPT) in the Office of Tissues and Advanced Therapies (OTAT) in CBER. Dr. Blank has served at FDA for 16 years in several divisions including the Division of Cardiology and Nephrology and CDER's Rare Disease Program. She has a keen interest in rare diseases and is currently engaged in many rare disease gene therapy development programs.

### Rebecca Aune (Moderator), Director of Education Programs, NORD



Rebecca is the Director of Education Programs for NORD. In this role, Rebecca works with the Educational Initiatives team and cross departmentally to implement strategies to grow NORD's educational content and programs for medical professionals, patients, caregivers and students. She liaises with NORD's Education Committee and directs the continuing medical education (CME) program. Rebecca also leads the project team and develops programming for NORD's annual Living Rare, Living Stronger Patient and Family Forum and the Rare Diseases and Orphan Products Breakthrough Summit. Rebecca also oversees NORD's student programs. Rebecca comes to the Educational Initiatives team with more than 12 years of nonprofit program management experience. Her most recent work was with the Pulmonary Hypertension Association (PHA), a NORD member organization. At PHA, Rebecca directed PHA's CME programs, resulting in 6,500 hours of CME delivered to more than 2,500 health care professionals annually. Additionally, Rebecca led the patient and caregiver education programs that educated more than 400 patients and caregivers in person each year and provided a video library that received 36,000 video views annually. She successfully led a team to reinvigorate online educational programming with professional videography and animatography, and migrate PHA's online learning platforms to new content and learning management systems for an improved learner experience and increased CME course completion. Rebecca's work in the field began at Starlight

Children’s Foundation, where she supported thousands of pediatric patients and families living with serious chronic, and often rare diseases with family outings, entertainment in the hospital, and health care facility renovations. Rebecca’s personal life has been affected by rare disease as an infant when her brother survived treatment for a rare pediatric cancer, as she survived treatment for rare cancer as a young adult, and now as her father-in-law lives with a rare cancer. Rebecca earned her Master’s in Public Administration from Saint Louis University and her bachelor’s degree in Political Science and Criminal Justice from the University of South Dakota.

**Debbie Drell (Moderator), Director of Membership, NORD**

Debbie serves as the Director of Membership at NORD. In this role, she oversees NORD’s membership programs, which support the collective and individual needs of rare disease patient organizations, patients and advocates through education, research, advocacy and mentorship. She brings to the organization over 22 years of leadership in nonprofit public health education, awareness and advocacy. Prior to joining NORD, Debbie spent 13 years with the Pulmonary Hypertension Association, a NORD member organization. During that time, she led the growth of the organization’s network of support groups from 80 to nearly 300, developed new services personalized to the diversity of patients and caregivers, and convened the largest gathering of pulmonary hypertension patients in history. Debbie has represented the patient perspective on several national platforms, including as a guest on National Public Radio’s Kojo Nnamdi Show. She has served as a member of the board of trustees of the American Thoracic Society, a 115-year-old medical society with a global membership of 16,000 pulmonologists, critical care and sleep disorder researchers, clinicians and other medical professionals. An accomplished public speaker, she has presented extensively at colleges and universities on women’s health issues, delivered speeches on caregiving across the country, including at Johns Hopkins University events, and moderated panels at the World Orphan Drug Congress European and American meetings. A graduate of the University of California, Irvine, and the University of Kent, Debbie’s dedication to the rare disease community is rooted in a deeply personal connection. She was inspired to enter the field after her older sister, Alex, was diagnosed with pulmonary hypertension.



**Agenda**

**Externally-led Patient Focused Drug Development Meeting for Krabbe disease**

October 29, 2020

<b>12:30pm</b>	<b>Opening Remarks</b> Pamela Gavin, Chief Strategy Officer, NORD Stacy Pike-Langefeld, President, KrabbeConnect
<b>12:35pm</b>	<b>Clinical Overview of Krabbe disease</b> Joanne Kurtzberg, MD, Pediatric Bone Marrow Transplant Specialist, Duke Children’s Hospital & Health Center
<b>12:50pm</b>	<b>FDA Introduction to PFDD</b> Michelle Campbell, Senior Clinical Analyst for Stakeholder Engagement and Clinical Outcomes, Division of Neurology Products, Center for Drug Evaluation and Research, FDA
<b>1:00pm</b>	<b>Regulatory Remarks</b> Melanie Blank, MD, Clinical Team Leader, DCEPT, Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, FDA
<b>1:10pm</b>	<b>Overview of Discussion Format &amp; Demographic Polling Questions</b> Debbie Drell, Director of Membership, NORD Rebecca Aune, Director of Education Programs, NORD
<b>1:15pm</b>	<b>Topic 1: Living with Krabbe Disease—Burdens and Symptoms</b> Natasha Spencer, Caregiver Kevin Cushman, Caregiver Kirsten Isgro, Caregiver Tammy Wilson, Caregiver Jhyrve Sears, Patient
<b>1:55pm</b>	<b>Polling Questions and Facilitated Audience Discussion on Topic 1</b>
<b>2:40pm</b>	<b>Break</b>
<b>2:50pm</b>	<b>Topic 2: Current &amp; Future Treatments</b> Christin Webb, Caregiver Anne Rugari, Caregiver Karlita Blackwell, Caregiver Laura Nitahara, Caregiver Scarlett Measles, Patient
<b>3:20pm</b>	<b>Polling Questions and Facilitated Audience Discussion on Topic 2</b>
<b>4:15pm</b>	<b>Closing Remarks &amp; Next Steps</b> Debbie Drell, Director of Membership, NORD



## APPENDIX 6: ACKNOWLEDGEMENTS

### Sponsors

Special thanks to our sponsors, including:

- Gain Therapeutics
- Magenta Therapeutics
- Neurogene, Inc.
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### About the National Organization for Rare Disorders (NORD®)

The National Organization for Rare Disorders (NORD) is the leading independent advocacy organization representing all those affected by rare diseases. NORD is committed to the identification, treatment and cure of the more than 7,000 rare diseases, of which approximately 90 percent are still without an FDA-approved treatment or therapy. Rare diseases affect more than 25 million Americans.

NORD began as a small group of patient advocates that formed a coalition to unify and mobilize support to pass the Orphan Drug Act of 1983. For almost 40 years, NORD has led the way in voicing the needs of the rare disease community, driving supportive policies and education, advancing medical research and providing patient and family services for those who need them most. NORD is made strong together with over 330 disease-specific member organizations and their communities and collaborates with many other organizations on specific causes of importance to the rare disease community.



The Legacy of Angels  
FOUNDATION

### About The Legacy of Angels Foundation

The Mission of The Legacy of Angels Foundation, a 501 (c)(3) private giving family foundation established in 2008, is to improve the lives of children by working to promote the expansion of newborn screening, and to further education, awareness and research of Krabbe disease and Cystic Fibrosis to provide a better treatment and a cure.

[www.tloaf.org](http://www.tloaf.org)



HUNTER'S HOPE

### About Hunter's Hope

Hunter's Hope Foundation was established to address the acute need for information and research with respect to Krabbe disease and related leukodystrophies. In addition, our mission is to strive to support and encourage those afflicted and their families as they struggle to endure, adjust and cope with the demands of these fatal illnesses.

[www.huntershope.org](http://www.huntershope.org)



### About KrabbeConnect

KrabbeConnect's mission is to be the source of comprehensive information and access to resources for patients with Krabbe disease. The foundation will drive state of the art research by bridging the gap between science and patient knowledge. The organization seeks to revolutionize the practice of medicine by identifying, optimizing, and implementing advances

in the care and cure of globoid cell leukodystrophy, utilizing a multicenter network. The organization's goal is to achieve complete disease eradication through cooperation between patients, patient advocacy groups, clinicians, researchers, industry and government. The organization is dedicated to the cooperative planning, implementation, analysis and reporting of controlled clinical trials, as well as observational studies and educational activities within the Krabbe community.

[krabbeconnect.org](http://krabbeconnect.org)



### About Partners for Krabbe Research

Partners for Krabbe Research (P4KR) is dedicated to engaging with researchers, clinicians, families, other foundations associated with Krabbe and other leukodystrophies, to support the need for an effective treatment for patients affected by Krabbe disease. By supporting research through fundraising opportunities, P4KR will donate funds to researchers, with the hope of wiping out the devastating symptoms of Krabbe disease.

Through all forms of social media, internet communications and other networking relationships, P4KR will create and develop opportunities to educate and create awareness about Krabbe disease. By establishing a network to service the Krabbe community, P4KR will utilize every resource available not only to find support for patients, but to also ease the pain and suffering that Krabbe disease brings to children and families affected with this disease.

[www.krabbes.org](http://www.krabbes.org)

### Mission Statement

The National Organization for Rare Disorders (NORD®), a 501(c)(3) organization, is a patient advocacy organization dedicated to individuals with rare diseases and the organizations that serve them. NORD, along with its more than 330 patient organization members, is committed to the identification, treatment and cure of rare disorders through programs of education, advocacy, research and patient services.



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