S. HRG. 118–177

UNLOCKING HOPE: ACCESS TO THERAPIES FOR PEOPLE WITH RARE, PROGRESSIVE, AND SERIOUS DISEASES

HEARING

BEFORE THE

SPECIAL COMMITTEE ON AGING

UNITED STATES SENATE

ONE HUNDRED EIGHTEENTH CONGRESS

FIRST SESSION

WASHINGTON, DC

OCTOBER 26, 2023

Serial No. 118–09

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Available via the World Wide Web: http://www.govinfo.gov

U.S. GOVERNMENT PUBLISHING OFFICE

54–248 PDF WASHINGTON : 2024

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UNLOCKING HOPE: ACCESS TO THERAPIES FOR PEOPLE WITH RARE, PROGRESSIVE, AND SERIOUS DISEASES

U.S. SENATE
SPECIAL COMMITTEE ON AGING
Washington, DC.

The Committee met, pursuant to notice, at 10:03 a.m., Room 106, Dirksen Senate Office Building, Hon. Robert P. Casey, Jr., Chairman of the Committee, presiding.

Present: Senator Casey, Gillibrand, Blumenthal, Warren, Warnock, Braun, Rick Scott, Vance, and Ricketts.

OPENING STATEMENT OF SENATOR ROBERT P. CASEY, JR., CHAIRMAN

The CHAIRMAN. Good morning. The Senate Special Committee on Aging will come to order. Welcome, everybody. Welcome to the Committee's eighth hearing of the 118th Congress about drug development for rare and serious diseases.

As is the tradition of the Committee, the Aging Committee Ranking Member, Ranking Member Braun on this case, will offer an opening statement.

OPENING STATEMENT OF SENATOR MIKE BRAUN, RANKING MEMBER

Senator BRAUN. Thank you, Senator. I thank the witnesses for coming and for all the folks from around the country here today.

There are over 7,000 rare, progressive, and serious diseases known to man. It is estimated that 95 percent lack treatment. Yet in my time as Senator, there has not been one Senate hearing to examine promising therapies for people with rare, progressive, and serious diseases.

The room is packed with people, patients, and caregivers that live this reality every single day. Right here, 350 patient stories from 44 states. This is long overdue. People that watch their bodies deteriorate in real time. Family members who have seen their loved one go from the picture of health to knocking on death's door.

Parents that buried their children before they even started school. I want to recognize and thank each one of you that are here in the audience and let you know I think this is the beginning of a new day for what we are all interested in.

Chairman Casey, in response to this hearing, our Committee has received these letters, 350 of them, 44 states, with personal experi-

ences. I ask by unanimous consent that we enter these into the record.

The CHAIRMAN. Without objection.

Senator BRAUN. Thank you. A wide variety of disease groups are represented in these submissions, including ALS, DIPG, an extremely aggressive pediatric cancer, and Barth syndrome, an ultra-rare genetic disorder that regularly results in death from heart failure before a child's fifth birthday.

Importantly, none of the diseases that our constituents have contacted us about have any form, have any form of FDA approval treatment. Not one of them. These diseases are relentless.

They are widespread and devastating. Most are considered a death sentence, but they are not invincible, and our constituents are not helpless. Patients deserve a promising pathway at the FDA.

Today, I am joined by Senators Gillibrand, Wicker, Cramer, Murkowski, Manchin, and Warnock in sponsoring the Promising Pathway Act to create a more flexible, accessible, and compassionate drug approval system at the FDA, and if there is any indication from the hour and a half I spent on the Senate floor yesterday, we are going to be getting a lot more Senators on this Bill. The Promising Pathway Act would create a rolling, real time drug approval pathway to speed access for individuals with these rare diseases.

This Bill does not undermine patient safety or FDA's gold standard for drug approvals in any way. Therapies developed through the pathway will be rigorously evaluated and continuously studied using real world data.

I ask unanimous consent to enter into the record a letter of support for this hearing signed by 15 individuals and organizations.

The CHAIRMAN. Without objection.

Senator BRAUN. The Promising Pathway Act is a commonsense step to give the FDA the flexibility it needs to serve Americans with these most trying diseases.

Our constituents continue to fight for new treatments, greater access, and full lives. I ask my colleagues to join me in unlocking hope for these constituents. I yield back to you, Senator Casey.

The CHAIRMAN. I want to thank Ranking Member Braun. Of course, he worked to put this hearing together, and his staff and our staff, and I am grateful for your work on this. This is a topic that is obviously meaningful to everyone in this room and every member of the Committee, and we look forward to a robust discussion about this topic today.

As Ranking Member Braun outlined, rare diseases are those that affect some 200,000 Americans, and over 7,000 rare diseases have been identified, 7,000. While each individual rare disease may affect only a small number of people.

Collectively, it is estimated that some 25 to 30 million Americans are living with a rare disease. We have done a lot of research into and drug development for these rare diseases. In 1983, prior to the passage of the Orphan Drug Act, there were just 38 drugs approved to treat rare diseases.

In the 40 years since, we have over 1,100, 1,100 new drugs or new indications for drugs approved for rare diseases. I am proud to have worked on legislation entitled the Creating Hope Act to

incentivize the development of drugs for rare pediatric diseases, in particular, and other legislation to address some of the challenges faced by those living with what you might call ultra-rare diseases, which affect even a smaller number of people.

My legislation, the Creating Hope Act, captures what we as legislators are trying to do, to give Americans living with rare diseases hope for the future, and while we have made some progress, many challenges remain as we will hear from our witnesses today. To many people living with and dying from rare diseases still do not have FDA approved therapies to treat or mitigate their conditions.

I believe that every one of these individuals deserves access to an FDA approved safe and effective therapy, so we must make sure that research continues and that clinical trials are designed to allow effective therapies to reach patients as quickly as possible.

Rare diseases and the research and clinical trials for drugs to treat them are fundamentally different from more common conditions. We will explore some of those differences today and the ways in which they present challenges for drug development through our witnesses and their testimony today.

It is important to note that my observations on the challenges facing the rare disease community and the steps we might consider to address these challenges don't necessarily apply to other non-rare conditions, but as we will hear today, the challenges for drug development start from the earliest stages of development.

When patient populations are small, it is hard for clinicians and researchers to develop what is known as a "natural history" for the disease and what the trajectory of the disease is when it is not treated.

Natural histories are important for developing therapies because if you don't understand how a disease progresses, it is hard to measure whether a new therapy is working. Rare diseases often are heterogenous, meaning that not every patient disease will progress in the same way, compounding the problem of poorly understood natural histories.

Once a promising drug candidate makes it to clinical trials, there are further challenges. Drugs intended to treat common conditions are tested in hundreds of thousands of people. When your entire patient population is only a few thousand or a few hundred, or a few dozen, it is simply not possible to do the same type of clinical trials.

When you have smaller trials, it is more difficult to demonstrate efficacy. In recent years, the FDA has taken action to improve how it works with companies developing drugs for rare and serious conditions, and the agency has done a lot more work to hear directly from patients affected.

More recently, the FDA has announced new initiatives specifically aimed at supporting drug development for rare diseases, such as the Support for Clinical Trials, Advancing Rare Diseases Therapeutics, or START, the acronym START, S-T-A-R-T. This is a pilot program to enable real time communication between a drug sponsor and the FDA staff on these development issues.

Another important initiative of the FDA is the Rare Disease Endpoint Advancement Pilot Program to support drug sponsors' ability

to engage with the FDA around the development of so-called end points, the metrics of efficacy for drugs for rare diseases.

In the last decade, the FDA has also done more to hear directly from patients with patient focused drug development. These are meetings that give the FDA staff the opportunity to hear directly from patients about how their disease affects them and what drug effects are meaningful to them in their daily lives.

I support the agency's recent steps, but we should continue supporting and strengthening their authorities and to do more to facilitate more approvals of safe and effective drugs. I look forward to hearing today's recommendations from our witnesses about the steps we can take to lead to more FDA approved treatments for rare diseases.

Next, we will move to our witness introductions. I am pleased to turn to our first witness. Our first two witnesses, I should say, will be sharing their experiences as patients and advocates, but in this case, they will not be answering questions. They will be providing opening remarks virtually, and for our first virtual witness, I am glad to turn to Ranking Member Braun.

Senator BRAUN. Thank you, Mr. Chairman. My pleasure to introduce Brian Wallach. From the time that Chris Coons and I formed the ALS Caucus here in the Senate, which has been an active one, we have gotten to know Brian well over that time. Really needs no introduction.

He is a true changemaker and champion. Brian has a storied career as a regional campaign director and White House counsel for President Obama. He later became a Federal prosecutor in Chicago. His life took a turn in November 2017 when he was diagnosed with ALS and given six months to live at the age of 37.

Rather than accepting the status quo, he decided to fight. Along with his wife, Sandra, Brian co-founded I AM ALS, a nonprofit dedicated to cure ALS. Brian is a father of two young girls. Thank you for being with us here today, Brian.

The CHAIRMAN. Thank you, Ranking Member Braun. Now I will read an introduction from my colleague, Senator Durbin, the Senior Senator from Illinois.

"I am so pleased that the Senate Aging Committee will be hearing from my constituent, Brian Wallach, this morning and I want to thank the chairman for affording me the opportunity to share a few words about Brian.

One of the truly wonderful things about being a United States Senator is that people—is the people you get to meet along the way. People like Brian and his wonderful wife Sandra. Six years ago on the day they should have been focused solely on bringing their newborn second daughter home for the first time, this young family was confronted with an unimaginable diagnosis.

Brian had ALS, a disease for which there is no cure and which as of now is fatal 100 percent of the time. Brian and Sandra quickly turned their grief into action starting I AM ALS and galvanizing the ALS community around advocating for increased attention, research, and results for all ALS patients and their families, and boy, have they had success. Brian and Sandra have been the driving forces behind getting Act For ALS signed into law, ensuring Congress twice doubled the Department of Defense's ALS research

budget, eliminating the five-month waiting period for ALS patients to get Social Security disability benefits, and working with the Food and Drug Administration to finally get several new ALS treatments on the market for the first time in years, and they are not done yet. I hope the Aging Committee is as inspired by Brian as I am, as I always am, and I look forward to hearing his recommendations for how we can continue to utilize the patient voice to make progress for ALS families."

That is a statement from Senator Dick Durbin. Our second witness, Maureen Bell is from Chalfont, Pennsylvania. Maureen was diagnosed with a classic gulacta—I am going to make sure I pronounce this right, galactosemia, seven days after her birth in 1972.

Ms. Bell has experienced many of the challenges of those living with the disease have. She is an advocate for those living with this disease and a helpful resource for new patients with their newly diagnosed children.

Thank you, Maureen, for sharing your experiences and your story with us. Now, I will turn to Ranking Member Braun for two witness introductions.

Senator BRAUN. Thank you, Mr. Chairman. My pleasure to introduce Dr. Peggy Plews-Ogan. She is the Brodie Professor of Medicine at the University of Virginia Hospital. Peggy attended Harvard Medical School and completed residency at Brigham and Women's Hospital in Boston.

In December of 2021, Peggy's husband, James, was diagnosed with ALS. She has since become a caregiver and an advocate with I AM ALS. Peggy and her husband have two children. Peggy, thank you for agreeing to testify, and James, thank you for being here today.

Next witness, Dr. Anish Bhatnagar is the Chief Executive Officer of Soleno Therapeutics, which is a small biotech firm dedicated to treating rare genetic disorders. He has been with Soleno since 2006.

He is a physician with over 20 years of experience in developing biologics, drug device combinations, and diagnostics, as well as therapeutic medical devices. Thank you for being here today, and I will turn to Senator Vance to introduce the next witness.

Senator VANCE. Thank you, Ranking Member Braun, and thanks to the Chairman for hosting this important discussion.

As Senator for Ohio, I am proud to introduce a great Ohioan and a great Cincinnatian, Mr. Keith Desserich. Keith is the Chairman and Co-Founder of The Cure Starts Now Foundation, which is the leading international charity dedicated to finding cures for the rare pediatric brain cancers that may help cure other types of cancers.

He is also the President of the Pediatric Brain Tumor Consortium Foundation. He and his wife, Brooke, established their foundation in 2007 after losing their daughter to a cancer called DIPG at the age of seven.

Her public battle was memorialized in the best-selling book ″Notes Left Behind,″ which was eventually translated into 22 languages. Since then, the Cure Starts Now Foundation has invested more than $30 million in over 130 trials across 17 countries.

Keith helped create an innovative, organic, and linked registry that has become a model for other disease registries, and he is ad-

vocating today on behalf of public policy facilitating his important work rather than making it harder.

Keith is also a steering committee member of the Pediatric Brain Tumor Consortium, the premier NIH funded brain cancer research initiative. Thanks, Keith, for being with us today.

The CHAIRMAN. Thank you, Senator Vance. Now, I will introduce our sixth and final witness, Holly Fernandez Lynch. She is from Philadelphia, Pennsylvania. I should say, works in Philadelphia, but lives in Swarthmore, Delaware County, correct?

Professor Fernandez Lynch is Assistant Professor of Medical Ethics in the Department of Medical Ethics and Health Policy at the Perelman School of Medicine at the University of Pennsylvania.

A lawyer and bioethicist by training, Professor Fernandez Lynch's scholarly work focuses on the Food and Drug Administration pharmaceutical policy, access to investigational medicines outside of clinical trials, and clinical research ethics.

Thank you, Professor, for sharing your expertise with us today, and so, we will start with our first witness, Brian Wallach, and Maureen Bell will follow him. Mr. Wallach, you may begin.

STATEMENT OF BRIAN WALLACH, JD, CO-FOUNDER, I AM ALS, KENILWORTH, ILLINOIS

Mrs. ABREVAYA. and MR. WALLACH. Chairman Casey and Ranking Member Braun, thank you for the opportunity to testify today. My name is Brian Wallach. I have been living with ALS for six years. ALS has changed every part of me.

My legs no longer work, my arms no longer work. ALS has almost taken away my voice as well, which is why my amazing wife, Sandra Abrevaya, is reading this testimony. ALS is a disease that is 160 years old. Let me repeat that, for 160 years, ALS has killed literally everyone diagnosed with it, everyone. That is simply unacceptable. Today, we hope to reform the FDA's approach to diseases like ALS.

Under current FDA standards, it can take 15 years or more for effective drugs to move from pre-clinical work to approval. In the meantime, many people have rapidly progressive terminal conditions, including ALS, die and have no viable treatments or options or hope available to them.

One of the lessons from the Neuron ADCOM is that there is in fact no such thing as a so-called gold standard across the FDA for how to approve new treatments for rare or fatal diseases. Instead, today's reality is that whether a treatment will be approved or not depends on what FDA center is in and on these specific individuals in the FDA review team assigned to a treatment.

A second lesson is that the existence of the 2019 FDA guidance is simply not enough to ensure uniform approval standards of new treatments for ALS. We very, very unfortunately learned this lesson the hard way just a few weeks ago during the ADCOM for Neuron, when the question presented to the ADCOM did not incorporate the FDA's own 2019 guidance about regulatory flexibility.

The primary question put before the ADCOM was, do the data presented demonstrate substantial evidence of effectiveness for treatment of mild to moderate ALS? This question did not at all make reference to the 2019 FDA guidance that stated, "when mak-

ing regulatory decisions about drugs to treat ALS, FDA will consider, one, patient tolerance for risk. Two, the serious and life-threatening nature of the condition, and three, also within the context of statutory requirements for safety and efficacy." This is exactly why legislation, such as the Promising Pathways Act, is absolutely critical for people living with ALS. There is no FDA approved biomarker for 95 percent of us living with ALS.

What is the result of that? The result is that treatments for 95 percent of people living with ALS, including Brian, do not qualify for accelerated approval. The Promising Pathways Act addresses this issue by creating provisional approval.

The Promising Pathways Act is also building the infrastructure to require drug sponsors to move faster in conducting their phase three trial and giving the FDA the authority to remove provisional approval if additional data makes clear that that is merited.

We support efforts to bring safe, promising therapies to more people living with terminal diagnosis, pending full FDA approval. We also support efforts to increase spending on research into the causes of ALS and potential treatments, but we do not support saying to this generation, thank you for your contribution to research, now go home and prepare to die.

While academics and bioethicists may have the luxury of debating theoretically what might look like some perfect system, us, people living with ALS today whose lives are literally on the line, we, we do not have that luxury and we are looking to you to provide them with the hope that they can live a little bit longer and maybe even be here to see a cure for ALS.

The key here is that PPA approval is merely provisional. It affords early access to promising drugs to people with extremely serious conditions who are willing to take risks. It allows additional evidence about a drug's efficacy to be collected during the short two-year provisional approval windows.

Provisional approval can occur only if a drug has been shown to be safe, and required patient registries enable much broader data collection about a drug's efficacy and safety than can even occur in traditional clinical trials. This data will help the FDA make even better decisions when it comes to the approval and labeling of new treatments.

Moreover, drug sponsors presumably want to obtain full approval of any provisionally approved drug. Other than allowing the use of real world evidence to supplement an application, the PPA does not alter the current FDA standards for full drug approval in any way.

The ALS story is slowly changing with—and with measures such as the PPA, we can make faster changes needed to finally get treatments to the community that will allow people such as myself to live longer and to potentially be around to see ALS transform from fatal to chronic.

I want to take a moment to recognize the caregivers and the people living with ALS in this hearing room today. We represent the 30,000 Americans living with ALS right now. I hope you or your staff will take the time to hear their stories and why they believe in the need for the Promising Pathways Act.

I also want to recognize Dr. Peggy Plews-Ogan who is before you as a witness and who has been living and breathing ALS and the

PPA for the last year and a half. Thank you. Thank you for your time.

Thank you for allowing me to be a part of this discussion and thank you for understanding how important the Promising Pathways Act is.

The CHAIRMAN. I want to thank Brian and Sandra for their testimony and for being with us today. Now we will hear from Maureen Bell.

STATEMENT OF MAUREEN BELL, GALACTOSEMIA PATIENT AND ADVOCATE, CHALFONT, PENNSYLVANIA

Ms. BELL. My name is Maureen Bell. I am 51 years of age and I live in Chalfont, Pennsylvania. I have lived with galactosemia for my entire life. Shortly after my birth in 1972, I began to show the classic hallmark signs of failure to thrive, jaundice, repeated vomiting, and weight loss.

Seven days later, I was diagnosed by an intern as having classic galactosemia. I remained in the hospital for three weeks. My mom and dad were given a 32-page booklet entitled, A Parent's Guide to a Galactose Restricted Diet." They were instructed to follow this booklet as I would need to be on a lactose-free, dairy free diet for the rest of my life. That was the only treatment for galactosemia in 1972.

I doubt my parents knew that many more challenges would lie ahead following the years to come than just having me follow a dairy free diet. It seemed that everything was working fine for me at the time, but I was getting older, and it made me feel very left out when I could not eat the same foods as my peers.

Without modern day advances we have today in nutrition, I cannot tell you how isolating it was for me. There were many social events that I could not attend. My mom tried so hard, always sending me to parties with a special treat, not just for me, but enough for everyone so I was able to share.

Not being able to eat the same cake that everyone else was eating at the birthday party as it just—was very difficult as a child. I also could not process information the same way. I always was a low average student and math was my most difficult subject, and still is today.

I struggle with making change, leaving tips at a restaurant, and figure out—figuring out percentage. I cannot process it. Basic life circumstances became a struggle, and only when I met other people living with galactosemia did I realize that comprehension issues were similar for all of us. Just as I was slow academically, I was also slow in developing physically.

While my friends were going through puberty, I was not having any issues of this. No normal signs of puberty or nothing like late development, and still—I still looked like I was in grade school physically, as opposed to being in high school.

This continued and the sense of isolation also continued. I began to have unusual symptoms such as hot flushes, night sweats, and mood swings. After about a year of experiencing these symptoms and having bloodwork, I was diagnosed at the age of 18 as having premature ovarian insufficiency, which is a direct result of having galactosemia in female patients.

This was something that I—this is something that I continue to struggle with today. As a result of this diagnosis, I became very reclusive. I wanted no part in dating or socializing like any other 18-year-old would.

That was the impact of POI, premature ovarian insufficiency. Secondary to having galactosemia, this was very difficult in my 20's. I just wanted to be like any other woman at my age, socializing and having fun.

However, I was depressed and had a very difficult time making friends and meeting new people. There were nights that I cried myself to sleep. At a church event in 1999, I met a man named Bill who showed interest in me and started spending time with him.

I was very apprehensive about getting involved in the relationship, even though I was 26 years old. The fear of falling for someone only to have to tell him that I was infertile and taking a chance on losing this relationship weighed on me very heavy. However, I finally got the nerve up to tell him.

Bill is a pharmacist, and his response was priceless, not caring about my diagnosis and instead advising me to take my calcium because I was such a slacker at taking my calcium. What a huge weight that was lifted off my shoulders, and we recently celebrated our 23rd wedding anniversary.

I was told that having galactosemia is like looking through a window at everyone at a party and eating—they are eating all kinds of foods that I cannot have. I could see them through the window and through the glass but could not break it or join them. The same is true for infertility. I can see moms, I can see children and families, but I cannot break the glass.

This experience—I cannot break the glass but cannot experience what it is truly like to be a mom. All my life, I have longed to be on the other side of that window. There could finally be a treatment for people like me, and even though it is too late for me, for younger ones living the way I grew up.

I spoke at the patient focused drug development meeting, but our community never heard from FDA after that. They had no questions, no clarification, and that made us worry they had not taken the time to learn from our work before reviewing the drug. Will they understand that speech issues don't matter to us the same way as cognition and developmental delays do?

Some of us even have more scary symptoms than the ones that I have mentioned like seizures, kidney issues, tremors, cataracts, neurological impairments, and intellectual impairments.

Will they understand that if they ask for another trial, rare diseases often don't have enough patients for another trial? Will they understand that if the drug is approved for something else rare, our doctors have seen the improvements in our community and will want to prescribe it for us to?

The drug is already being studied in other rare diseases. Whether it is Government insurance or through my job, insurance companies don't treat rare diseases like cancer, so that is a whole other hurdle. These days we must fight for approval, but also fight insurance too.

The Galactosemia Foundation is working hard on both things, and I hope you can help us all. I am learning about what places

like FDA and CMS and Congress can mean to me and the others whose lives are impacted by diseases like galactosemia.

I don't pretend to understand, but I know even one person can make a difference, and I want you to help the little girls with galactosemia going through isolation, the puberty, depression, and fear, the ability—the inability to understand and process. If all of you can make—can take my story and help them, it will mean so much. Thank you.

The CHAIRMAN. Well, Ms. Bell, thank you for your testimony and for sharing your personal experiences with galactosemia, and we are grateful you are able to spend this time and hoping and listen to the whole hearing. We will now turn to our next witness, Dr. Plews-Ogan.

STATEMENT OF MARGARET PLEWS-OGAN, MD, BRODIE PROFESSOR OF MEDICINE, UNIVERSITY OF VIRGINIA, CHARLOTTESVILLE, VIRGINIA

Dr. PLEWS-OGAN. Chairman Casey, Ranking Member Braun, and the members of the Committee, thank you so much for the opportunity to present to you today.

The testimony I give here is reflective of my own views and is not intended to reflect the positions of the University of Virginia. My name is Peggy Plews-Ogan, and I am first and foremost the wife and caregiver to my husband, Jim. We are both physicians. On December 2nd, 2021, our lives cracked open. Jim was diagnosed with ALS.

At the time, we were both busy clinician scholars. Our lives were full with meaningful work, close family, a community of friends. With this diagnosis, our lives were completely upended. What I remember from medical school about ALS is that is a diagnosis that a physician dreads more than ever, more than any other.

Why? ALS is a disease that robs a person of almost everything essential to living our lives, the ability to move, to communicate, to eat and drink, and eventually to breathe, but the double-edged cruelty is that awareness and cognition are left intact. People living with ALS can feel each loss and fear the next one every moment.

ALS is 100 percent fatal. No one has ever survived. Average life expectancy after diagnosis is two to five years. When given this diagnosis, patients commonly hear, go home, hug your loved ones, and get your affairs in order.

People worry about giving patients false hope, but I think they don't understand the devastation of having no hope, of simply waiting for the inevitable decline. Both being physicians, we were not naive about ALS, but having no hope was not an option for our family, so like many ALS families, we got moving.

We read, we investigated clinical trials, we got involved in advocacy. One unacceptable reality we faced was that the disease moves faster than the FDA. AMX0035 was a drug in the pipeline that had excellent safety and better evidence for efficacy in a phase 2/3 trial than anything that was currently available, but it was initially denied approval by the FDA, who wanted an additional confirmatory phase three trial. This drug is a combination of two drugs that have been on the market for many years. One that was the counter. The only way to obtain the medication was to get the one component, Tudca is called, online, and the other component from

a specialty pharmacy in New Jersey off label at a cost of around $1,500 to $3,000 a month.

Most of our friends in the ALS community could not afford this. Only after fierce advocacy did the FDA take another look at the data and approve it, thankfully, over two years after the results of the clinical trial were clear. What does that two years mean for an ALS patient? Two years ago, Jim was running races.

He was the chief medical officer for a new integrated care network for children across the State of Virginia. He started a new program at UVA to care for medically complex children. He had a thriving pediatric practice full of kids and parents who adored him. Today he is confined to a wheelchair. He needs help to eat.

He cannot roll over in bed or even scratch an itch. He is losing his ability to speak. Inside the body that is failing him, Jim is the same brilliant, compassionate, creative, loving human being. The courage he displays every day is stunning. I am Jim's primary caregiver. The nights are the toughest.

Every time Jim needs to turn over or adjust his vent mask to pull up the covers, I need to do that for him, and he needs to somehow communicate that need. Were it not for the support of our amazing grown children, extended family, neighbors, and dear friends, I am not sure what we would do. ALS is relentless. What do you think our life will be like in six months? One thing I know, Jim needs to be here.

He has got a new grandbaby and a wedding to attend. As a physician, one of my areas of expertise is reducing errors in medicine. Doctors are naturally focused on getting all the data to make a certain diagnosis before we start treating someone, but we have learned over time that in rapidly progressive, life-threatening illnesses, delaying treatment while awaiting that certainty can cost someone their life.

We start treatment while confirmatory data are coming in. I have watched helplessly as my husband lost the ability to use his hands, then his legs, then his voice. In the face of this 100 percent fatal disease, delaying access to a safe, promising therapy until a confirmatory trial can be achieved is cruel. Jim and I are both old enough to have lived through the AIDS crisis.

When I started residency, there were no treatments and the medical wards were filled with AIDS patients and their loved ones, the patients dying no matter what we did. Then patients and their loved ones got activated. They fought for more research funding.

They fought for early access to therapies. I watched as each new therapy, one by one, turned the disease around. The earliest therapies were less effective and had more side effects, but they saved people's lives while new drugs were added and combined together into cocktails.

Like those early HIV activists, we in the ALS community are fighting for more research funding. We are fighting for early access to safe and promising therapies. You have the power to change the landscape of ALS in this Congress, transforming it to a manageable and eventually a curable disease.

This is not false hope. It is real hope. We need urgent action, and we are counting on you. Thank you very much.

The CHAIRMAN. Doctor, thanks very much for your testimony, and thanks for sharing your story and Jim's as well. Dr. Bhatnagar, you may begin your testimony.

STATEMENT OF ANISH BHATNAGAR, MD, CHIEF EXECUTIVE OFFICER, SOLENO THERAPEUTICS, REDWOOD CITY, CALIFORNIA

Dr. BHATNAGAR. Chairman Casey, Ranking Member Braun, and honorable members of the Committee, I am honored to testify at today's hearing. Thank you for inviting me. My testimony today is my personal opinion based on my experience over the years. I am a physician by training.

My 25-year career almost entirely at small companies has involved developing treatments for cancer, for neurological psychiatry, cardiovascular, and other diseases, and for the last several years for rare diseases.

None of my work, including that on life saving cancer drugs, has been as meaningful as working with this amazing community of families who have children and adults with Prader Willi syndrome.

Many of them are in the audience today. While the regulatory challenges across therapeutic areas are similar, there is a much more disproportionate impact on patients with rare diseases. A similar disproportionate impact is seen on small companies like ours, which do a large proportion of the high-risk work.

Our ability to raise money and continue work depends predominantly on regulatory clarity. If the minutes of an FDA meeting do not clearly State a path forward, or if a company receives inconsistent feedback, it could be the difference between having money to carry out a pivotal trial or giving up on a drug to treat a disease that has no options.

Speaking of diseases with no options, Prader Willi syndrome, PWS, is a rare and life threatening genetic condition which occurs randomly and affects about 10,000 to 20,000 patients in the U.S.

Children with PWS are often recognized within weeks of birth. By the age of three or four years, they would start to show more of an interest in food, which increases over time until they ultimately developed a hallmark symptom of hyperphagia, an insatiable desire to eat, the brain telling you that you are starving even as you eat.

Individuals affected by PWS never feel full and are constantly focused on one thing, food and how to get it. Left unsupervised, they have the potential to literally eat themselves to death. Much like a teenager with PWS who recently ran away from home, ate enough that his stomach ruptured, and he passed away.

The only remedy for hyperphagia is to restrict access to food, close kitchens, lock refrigerators and pantries, motion activated cameras and alarms. Families live in the constant fear of extreme outcomes like visits to ERs, police intervention, and in many situations, the need to be cared for in an institutionalized setting. Invariably, there is a need for constant supervision for life.

Numerous drugs have been tried, tested to treat hyperphagia and PWS in late-stage trials. Each one of them has failed and many companies have been dissolved. Our drug, DCCR, is a once-a-day pill based on a known parent molecule, which was evaluated

in an approval directed study from 2018 to 2020, ending a few months after the start of the COVID–19 pandemic.

The study missed its primary endpoint, but the analysis of the pre-COVID data showed statistical significance in favor of the drug. Long term data, now up to four years in some patients, and comparisons to natural history of the disease show statistically significant and clinically meaningful improvements with the drug.

We have been asked to generate additional controlled data before submitting a marketing application to the FDA. We have just completed the study, which shows highly statistically significant and clinically meaningful benefits of DCCR, and we hope to submit an NDA to the FDA next year.

We need a regulatory framework that recognizes the novel, complex, and heartbreaking nature of diseases like PWS. We cannot continue to apply the same regulatory paradigm to all diseases and all drugs. Context must play a role. It is amazing to see new options available for people with ALS and the first approval of a drug for Friedrich's Ataxia, but there is also diseases like Barth syndrome, where a drug with promising data may not have a path forward. Regulatory delays such as the three plus a year back and forth with the FDA have real life impacts. For companies like ours, programs will be cut. Some will even shut their doors.

Every day, every week, every month, every year symptoms will worsen, sometimes in irreversible manners, and patients may even die as they wait for treatments. The FDA is and needs to remain the premier regulatory body of its kind in the world. What is desirable is a rigorous regulatory process, but one that balances the risk of approving a drug with the risk of having no treatments available for a desperate population.

The Promising Pathway Act is a significant step in the right direction. Time limited provisional approval would allow patients the ability to access potentially life changing treatments, as additional meaningful data is generated to justify their use.

Availability of such treatments would be driven by clinically relevant data, and final approval would come only upon rigorous analysis of data generated from patient registries. In closing, I truly appreciate the opportunity to share Soleno's story, highlight the significant unmet needs of the rare disease communities, in particular the PWS community.

Thank you for your time. I look forward to your questions.

The CHAIRMAN. Doctor, thanks very much for your testimony. Next, we will move to Professor Fernandez Lynch for your testimony. You may begin.

STATEMENT OF HOLLY FERNANDEZ LYNCH, JD, MBE, ASSISTANT PROFESSOR OF MEDICAL ETHICS AND LAW, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, PENNSYLVANIA

Mrs. FERNANDEZ LYNCH. Thank you. Thank you for the opportunity to inform today's discussion about how best to achieve a goal we all share, helping patients with rare serious diseases live better and survive longer.

My name is Holly Fernandez Lynch. I am an Assistant Professor of Medical Ethics and Law at the University of Pennsylvania, speaking only on my own behalf. As you heard, my scholarship fo-

cuses on FDA drug approval policy, access to medicines prior to FDA approval, and clinical research ethics and oversight.

I sit before you as an academic on a panel filled with lived experience, in a room filled with lived experience. I am not personally living with a rare, serious disease, but the sad reality is that rare diseases are not rare in the aggregate.

Any one of us could find ourselves or our loved ones affected at any time, and like many, my family has not been spared from serious and life-threatening diseases, including Parkinson's and childhood cancer. We all have an interest in these important issues, whether we are suffering today or may be suffering tomorrow.

My key message to the Committee is that weakening FDA's approval standards risks conflating the essential goal of getting patients access to more drugs that work with the deflated goal of simply getting them more drugs. Of course, we should tolerate more uncertainty when considering drugs for serious diseases.

Thankfully, FDA already has expansive regulatory flexibility, allowing it to do just that. The agency is granting accelerated approvals more frequently and more broadly than it has in the past. It has also demonstrated willingness to approve drugs when trials fail to show benefit on pre-specified endpoints, when benefit is supported by just one pivotal study, when trials are very small, and when they lack concurrent control groups.

Unfortunately, this flexibility is not always met with rigorous confirmation of benefit after drug approval, which is a concern also raised by the Promising Pathway Act. The proposed bill has some important strengths.

For example, it seeks to limit how long drugs with uncertain benefit can stay on the market, and it emphasizes that uncertain drug approvals should always be followed by efforts to collect additional evidence. However, I fear that the Promising Pathway Act would set the bar too low for both provisional approval and later confirmation of benefit.

Now, I certainly understand why any individual patient might be willing to pursue access to a new drug based on relevant early evidence of a positive therapeutic outcome, the bill's proposed standard. The problem is that weak approval standards affect all patients, not only those who choose to take a provisionally approved drug.

Companies produce evidence about safety and effectiveness because it is a legal requirement for marketing and to profit from their drugs. If FDA demands less evidence, patients and clinicians will have less evidence.

We see this today in the dietary supplement industry, but imagine if what you had available to treat your life threatening illness was rows and rows of products, none of which were known to work.

Weak approval standards can also entrench poor treatments by making it difficult to study potentially better treatment options, both because of reduced willingness to enroll, and challenges interpreting results when new drugs are compared to unproven ones.

The Promising Pathway Act proposes to address these challenges by relying on patient registries, but because registries lack randomization and blinding, observed differences in outcomes might be at-

tributable to underlying differences between patients rather than a result of the drug of interest.

Instead of weakening FDA's already flexible approval standard, the stronger path forward is to address scientific bottlenecks. FDA and others have already taken important steps in this direction.

The agency recently launched a program informally dubbed Operation Warp Speed for Rare Disease, which will provide real time advice to companies starting at the earliest stages of drug development to speed successful trials, address manufacturing issues, and other challenges.

The agency also has a pilot program to advance development of new end points for rare diseases. Its action plan for rare neurodegenerative diseases and its ALS science strategy emphasize improved scientific understanding of rare disease, enhance clinical trial infrastructure, and innovative trial designs to support the development of better drugs.

While the science continues to develop, the best way for this Committee to improve access to effective rare disease treatments is by ensuring adequate funding for rare disease research, promoting clinical trial accessibility, encouraging use of FDA's expanded access pathway, and clarifying that FDA has the authority to require and enforce rigorous post market efficacy studies whenever it approves a drug with uncertain benefit.

Thank you for your commitment to these important issues and I look forward to your questions.

The CHAIRMAN. Professor, thanks very much, and our sixth and final witness, Mr. Desserich.

STATEMENT OF KEITH DESSERICH, CHAIRMAN/CO-FOUNDER, THE CURE STARTS NOW FOUNDATION, PRESIDENT, PEDIATRIC BRAIN TUMOR CONSORTIUM FOUNDATION, CINCINNATI, OHIO

Mr. DESSERICH. Thank you, Chairman Casey, Ranking Member Braun, and distinguished members of the Committee for the opportunity to discuss the Promising Pathway Act. It is something that I consider vital to our efforts to find the homerun cure for cancer. I am Keith Desserich.

I am Chairman, Co-Founder of The Cure Starts Now Foundation, Board Member of the DIPG-DMG Collaborative, I am President of the Pediatric Brain Tumor Consortium, but most importantly, I am a father.

My daughter, Elena, fought a cancer called DIPG when she was just six years old. We had no hope. There were no trials available, and they told us to go home and make memories. Sadly, she understood this as well, fully aware until her very last day that there was nothing that we could do.

You see, with DIPG, each day you see your child lose something. One day, it was her ability to be able to see out of her left eye. The next day it was her ability to speak. Then her ability to walk. Until one day it became her ability to swallow, to breathe, and her heartbeat. What is particularly cruel about this type of disease is that it affects children, and it is very, very rare in adults, but at the same time, many experts believe that this is a cancer that can show the most promise, at the same time is believing that this is

a cancer that they fear most. Universally, for this reason, it is known as a home run cure cancer.

We have made it our mission to focus on these rare cancers, building tools from scratch, such as a registry that spans 129 hospitals, intelligent patient tools, strategic research, and even virtual hospitals to try to leverage all of the great guidance and intelligence that we can find worldwide to come to bear on one specific patient, and in the 17 years since Elena lost her fight, we have invested in over $30 million in research and support through 135 projects. I understand the perspectives of the researcher. I understand the perspectives of the parents. I understand the perspectives of the registry.

I come to you having seen each of these various elements of it, in addition to talking with parents each and every day when they are in their last weeks. I also come to here with hope. I hope for a new way to fight cancer. I believe that the FDA is well-intentioned, but in the end, no one plans for this type of devastating cancer.

Sadly, I believe that there is much confusion inherited from bureaucracy, and whether by regulation or guidance clarity, I argue that the system is broken, and the status quo will not do. For our purposes, there are effectively only two measures that we can consider when we start to talk about DIPG.

One is expanded access, and the other one is Right to Try. It is important to note that with expanded access or compassionate use, it is not an alternative for the Promising Pathway Act. I know this not only from dealing with the loss of my daughter, but also in calls with over 200 families per year asking for help, any help in their last and final days.

With DIPG, a patient is frequently only given two weeks after progression to act. Expanded access requires four levels of approval, 24 hours for a family to reconcile with the news, three days for a doctor to determine the strategy, two weeks for an internal review board to approve a methodology, three days for a pharmaceutical company to respond, and up to 30 days for the FDA to effectively approve the entire process.

That is one week longer than our child survives. It doesn't work. Then there is Right to Try. It is slightly better with the two-level approval process, but it lacks data transparency to patients and families with an annual report model that submits to the FDA. We think clarity, we think transparency are cornerstones of being able to find the cure.

All of these, though, and the current guidelines assume that terminal means months or years to live. They assume that patients are not intelligent to make decisions for themselves. They assume that data in less than ideal situations are worthless, and they assume that every patient is an adult, and the assumptions are wrong.

The reality is we don't get doctors that understand the systems. We don't get a call back on the weekend, and none of these acts were designed for pediatric terminal diseases. The Promising Pathway Act is different.

It offers an alternative to FDA mandated unethical practice of trials, giving the wrong drug to the wrong patients for pediatric

terminal diseases. Right now, nearly every therapy designed for pediatric cancer is guided through a three-phase adult trial before we can even get to try it on a terminally diagnosed child.

Sadly enough, some of these cancers don't even affect adults like DIPG, meaning that we either misapply a trial on the wrong patients, or worse yet, the drug company simply gives up. Now remember that some of our biggest advances in cancer started with pediatric cancer. You want to know why we can't advance a cure? This is why.

The PPA also preserves critical data on outlier participants in a trial and retains it for the use by the FDA, the drug companies, the researchers, and the patients in any third-party registry of substance thus improving transparency. PPA also addresses insurance coverage and financial burdens in ways that neither previous alternative has.

Finally, the PPA, or promising Pathway Act, advances innovative therapies that may be impossible to subject to current trial design. Keep in mind that trials for rare cancers rarely ever get full accruals, leading us to either give up on good ideas or enrolling children in older trials that we already know don't work. It is not lost to me the value of a clinical trial, but what is lost to many others is the value of a quick and efficient clinical trial.

Unfortunately, with rare pediatric cancers, we have to consider both this, and sadly in their final days, we also have to consider compassion. I have this pile in front of me of grants. These are grants that we have worked to build, to fund at many different institutions. There is 46 of them.

This is a pile which has hope. This is a pile which is the dreams of the researchers, and frankly, it could be the lives of these kids. This is 46 chances to be able to cure cancer, and sadly, the whole reason why I am here today is because I believe that these 46 opportunities to be able to cure cancer may never reach bedside unless we get PPA passed.

I am a big believer in personal initiative, but in this case, we may be able to go no further unless Government gets out of the way. The Promising Pathway is how we do this. Families are desperate for another chance, a chance to see their children go to kindergarten, a chance to see their child get a driver's license, a chance to see them graduate from high school, a chance to see them go to college and get married.

We want a chance to see them grow up. Rarely do you have a chance or a bill that asks for no money, and the money is not really part of what we are asking for. This is that rare case when you can act to give patients fighting for the lives the power to save their own lives. I lost my daughter, but I refuse to believe that we cannot save others.

You have heard today from some very compelling and well-educated witnesses. I am the only one, however, that has lost everything in this and was given no options because there wasn't any. There was existing barriers that were either too cumbersome or our policies were built around the majority, and while some of these numbers may appear small from the aggregate, in the end, it is not—it is with this type of cancer that experts also believe

that we all have the greatest impact to be able to cure it, and so what we may ignore may be precisely what must save us.

The Promising Pathway Act may be the single biggest piece of legislation that costs nearly nothing but may change everything about how we win this war against cancer. Thank you.

The CHAIRMAN. Mr. Desserich, thanks so much for your testimony and for sharing the story of your family and your daughter.

Mr. DESSERICH. Thank you.

The CHAIRMAN. I will now turn to Ranking Member Braun to begin a round of questions.

Senator BRAUN. Thank you, Mr. Chairman. First question is for Brian Wallach. Brian, if you are still with us here on Zoom, we appreciate your testimony earlier, and because of your work, you have got so many people engaged in the cause and kudos to you for that.

Question, what would your risk tolerance be for a new therapy that has documented, real world evidence showing efficacy and has received provisional approval from the FDA?

[No response.] We will come back to Brian if he is still with us on Zoom.

The CHAIRMAN. I think——

Senator BRAUN. Go ahead, Brian.

The CHAIRMAN [continuing]. delay——

[Technical problems.]

Mrs. ABREVAYA and Mr. WALLACH. Thank you, Senator, for your question. As a patient who has lived six and a half years with ALS, I have no other options for new treatments other than—other than the expanded access program or provisional approval, and as my disease is 100 percent fatal right now, I am willing to take risks that other patients may not be. I know that if I do not try—I know that if I do not try safe, promising treatments, I will die.

As Peggy said, we know that each treatment does not make a cure, but together they can create a cocktail similar to what we had in HIV that will keep me alive and turn ALS from fatal to chronic.

My simple answer is that ALS patients are willing to accept greater risk because we know what is behind door number two.

Senator BRAUN. Thank you, Brian. Next question will be for Mr. Desserich. Thank you for sharing your story. Sorry for the loss of your daughter. Your advocacy, you know, of course, means a lot to her and her legacy. Do you feel that any kind of drug approval or access programs at the FDA address rare, terminal pediatric cases like DIPG?

Mr. DESSERICH. I don't. That is the reason I am here. I am here because there isn't anything that applies to this.

I mean, the amount of patients that we talk to that are reaching out to us, and they are reaching out to us partially because they are not getting any answers from medicine or drug companies or anything of that sort, or it is impossible at that point, and it is because of really two things.

One reason is because of time. We don't have that time. We have two weeks. Nothing gets done in those two weeks. I have had so many times where I have seen a compassionate use has been approved for a patient, but it usually comes in several days after the patient has already passed.

You want to talk about a difficult call, that is a horrible call to make. I have also seen where it doesn't address anything having to do with pediatric. We write laws with the idea of adults, and if you look at any of these guidelines that we have put forth through the FDA, we grant waivers for them not to do it in pediatrics, but we never go the opposite way, and so, because of that, we have to wait, and we have to hope that it can go through all of the adult trials first before it can ever get to a child trial, and so, it never gets started, and so, at the end of the day, we can't get access to those drugs.

The time is not the right amount of time, and the children are being ignored in this and it shouldn't be that way.

Senator BRAUN. Thank you. I yield back. I do have more questions. Back to Chairman Casey.

The CHAIRMAN. Senator Ranking Member Braun, if you want to——

Senator BRAUN. Go ahead?

The CHAIRMAN. You want to, ask another one. You still had about a minute, so.

Senator BRAUN. This question will be for Dr. Plews-Ogan. FDA has a variety of drug approval pathways and designations. In recent years, the agency has begun to take steps toward creating a more accessible and flexible system.

However, millions of Americans with these diseases still lack any FDA approved treatments. Could you highlight the holes in the FDA's drug approval and clinical trials system that your husband James has fallen through?

Dr. PLEWS-OGAN. Thank you for that question, so I will just mention two. One, I think we have heard a lot about today, and I want to be really clear that that problem is really important to me, and that problem that I would like to see solved is that patients who are dying don't have timely access to promising, safe therapies. Just to be clear, I don't think anyone you have heard speak is suggesting a change to the safety standard.

This is about time. It is about access. The FDA process involves, first of all, early trials to establish safety, phase two trials to confirm safety and establish potential efficacy, and then phase three trials.

The phase three confirmatory trials to confirm efficacy can take an additional four to eight years. These are years obviously, that no one on this—sitting at this table has had for themselves or their loved ones. The time it takes for these confirmatory trials is simply too much for these particular patients with these particular diseases, so we want access to promising therapies when early evidence has been established and is being confirmed.

All we want as an alternative to certain death is a pathway that allows us access to these therapies at the point where safety and promising evidence and effectiveness have been established. The second point I want to make is that there's been a lot of talk about the accelerated pathway.

Accelerated pathway is really not available to patients with ALS at this point, at least 95 percent of patients with ALS, because there is no reliable biomarker, and the accelerated pathway requires or relies on biomarkers or surrogate endpoints, so that is an-

other huge hole for someone like Jim. That pathway really doesn't apply.

Senator BRAUN. Thank you. This question is for Dr. Bhatnagar on biotech risk. On these diseases, mostly smaller companies address them. Could be billions of dollars, years to submit a new drug application to the FDA. Larger companies generally don't do it. Tell me a little bit about is the market cooling for this due to the fact that we have got a process that is stubborn and bureaucratic?

Dr. BHATNAGAR. Thank you, Senator, and the answer is yes. There are parts of the biotech ecosystem that are doing well. I mean, science is robust. Patient advocacy is stronger than it has ever been before, but what is cooling is the funding environment, and you can see that if you look at the XPI, which is, you know, a gauge of public companies. It is down more than—about 30 percent this year.

This may be the third year in a row it is down, at a stretch which would be the first time that is the case since it was first conceived. Number of companies going under has been phenomenal. Number of layoffs has been extraordinary, so yes, the ecosystem——

Senator BRAUN. Would the Promising Pathways Act address that in a way that would be meaningful, so we at least keep businesses in business to try to work on these ailments?

Dr. BHATNAGAR. I think so. When you think of why that is the case, I think the uncertainty in the regulatory environment is a big factor for rare disease companies. Companies like mine, we work on one or two programs, and if you don't have the clarity, then it is hard to get the funding to do the work, so yes, if there is a pathway that is more certain, it would definitely help.

Senator BRAUN. Thank you. I yield back.

The CHAIRMAN. Thank you, Ranking Member Braun. I will next move to my questions. I also wanted to note. We obviously have a number of Senators who have been here. Some have been here and won't be back.

Some will be back, but after my questions, in order of appearance, we will go to Senator Scott. We have also had Senator Gillibrand, Senator Blumenthal here, and let me just go to my first maybe two questions.

Dr. Bhatnagar, I wanted to ask you a question, but as a predicate for that, I understand that one of the challenges in rare disease drug development is that there are often very few true experts in the disease and that this presents difficulties at different stages of the drug review process.

FDA has acknowledged these challenges and indicated they are open to revising some of the policies to ensure clinical expertise for rare disease therapies, so doctor, here is my question.

As you have worked through this drug development process, are there areas where greater expertise in rare diseases like, as you mentioned, PWS, Prader-Willi syndrome, among FDA expertise for that syndrome among others, among those FDA reviewers, are instances where that would be helpful, that greater expertise?

Dr. BHATNAGAR. Thank you, Senator, and yes, it would be helpful. When you are dealing with a disease like Prader-Willi syn-

drome, we don't expect that there would be expertise at the FDA because it is a rare disease.

We would hope that there is that understanding, and the idea that from the very beginning of the process, there would be experts at the other end. That has not been the case. We generally take physician experts with us, but unfortunately, they are considered to be conflicted.

The problem in rare diseases, which is very different from other large, mass market type of diseases, is that you generally involve all experts in the clinical trials, otherwise you would not be able to enroll those trials, so if you believe them to be conflicted, then who would be the expert?

I think this is one not very difficult thing that can be implemented, and you can take that opinion with a grain of salt, but at least consider them to be not conflicted and speaking for the disease.

The CHAIRMAN. Doctor, thanks very much. I just have one more question before I turn it to Senator Scott. Professor Fernandez Lynch, how can the FDA ensure it is consulting with these appropriate disease experts, while also ensuring transparency around say potential conflicts of interest during the review of products for rare diseases?

Mrs. FERNANDEZ LYNCH. Thank you, Senator, for the question, so this comes up very often when FDA is trying to populate the advisory committees of external experts that it often calls upon to help them understand various issues related to whether or not they should be approving products, as well as broader questions about drug development in particular areas.

FDA can waive, you know, the conflicts in certain circumstances, for example, where there is a dearth of experts in a given area, and they often do waive the typical conflict of interest rules. There are other ways also of managing conflict.

For example, if you include somebody who has ties with industry or has participated in trials, you can also invite additional people to provide their broader perspectives, so I think this is already something that is happening at FDA.

They are well aware of the challenge, and in fact, it is more often academics like myself who are pushing FDA to be more careful about conflicts than they already are.

The CHAIRMAN. Thank you, professor, and I will move to Senator Scott.

Senator Rick SCOTT. First, I want to thank the chair and ranking member for putting together this hearing.

I thank everybody for being here. I want to thank all of our witnesses. I think everybody in this country has probably been impacted—has somebody who has been impacted by a rare disease, and in health care, they have either impacted by something that they did not had access to, or if they did, the difficulty of affording the health care in this country.

It is really tough. I built a hospital company and your just heart goes out to people. How expensive things have also gotten on top of the regulatory hurdles you go through, so my first employee in my hospital company actually had and passed away with ALS, and it is a devastating—it is a devastating disease, so your heart goes

out to anybody that has it. One thing I did as Governor of Florida is I—when I was Governor, we got all of our, all the money—we dramatically increased our research dollars on cancer and we got to all of our cancer centers, and everybody was doing research and say they got money, they had to share all their data which—to accelerate it, and that seemed to have some impact.

We have put a lot of money into NIH. In the 2000's I think we doubled the budget of the NIH, but clearly cures haven't come out, so I think we have to just do what all of you are saying, rethink what we are doing to see if there is something better we can do, and this is—I am glad you are here because this is how we get things done by getting—by people telling their stories, and so, because of your story, you can come up with how you can try to solve it, so Dr. Bhatnagar, what can Congress do to expedite the delays that you are seeing?

Dr. BHATNAGAR. Thank you, Senator. First, I want to just acknowledge that Florida is the epicenter of PWS care in the world. The University of Florida has a physician by the name of Jennifer Miller, who sees the largest population of PWS patients in the country.

To answer your question, it is probably true that the FDA already has the authority needed to provide regulatory flexibility in the circumstances that we are talking about. Unfortunately, there is no consistent application of that flexibility.

I don't know what tool it takes, but I think to mandate the consideration of regulatory flexibility in all rare disease applications is valuable. I think to work with experts to define for a given disease setting what that flexibility should look like is important, and then to come up with an enforcement mechanism to ensure that it is happening is important. I am not sure what tool it takes, but I think conceptually that is how I would go about it.

Senator Rick SCOTT. Yes. Well, in May of this year I joined with 24 my colleagues in both the Senate and the House asking for change at the FDA. We requested a task force be developed to include leaders from all divisions, offices, and centers which process rare disease therapy applications to fully examine areas of policy and procedural inconsistency and shortcomings to see what we can do better.

We also asked that the task force provide Congress recommendations. The FDA disagreed with our request to form a task force. They said they were going to share relevant reports. I think a lot of times up here people do have the authority to do the right things. It is just the way the process is set up, and then there is no accountability, that it doesn't work the way it is supposed to work.

The more specific you guys are to any of us, the greater chance we are going to be able to get something done. Do any of you know what type of patient experience the FDA collects in its clinical trials, and how does the FDA use that? Does anybody have any ideas?

Dr. BHATNAGAR. I think patient experience is going to be collected in a variety of ways. One of the newer mechanism which the FDA has been using is a patient focused drug development meeting

where the FDA attends and listens to the patient populations about the unmet needs, etcetera.

During trials, in trials like ours, we collect patient information based on questionnaires, looking at symptoms and signs that are relevant, so the agency definitely has a lot of that evidence in their hands.

Real world evidence is something that they have been discussing, but it has been part of very small number of applications for approval, and it is certainly not been the primary way any drug has been approved so far. Dr. Lynch, if you have something to add.

Mrs. FERNANDEZ LYNCH. Just to add onto that, importantly, of course, it is not FDA that is gathering the evidence, right. It is companies that are responsible for conducting the research, but through the patient focused drug development program at FDA, they have put out several guidance documents to promote systematic methodologies in gathering patient experience data to inform the development of clinical trials, to make sure that they are asking the questions that are important to patients, and systematically gathering information so that it can inform regulatory decisions.

FDA also has made great strides in incorporating patient perspectives. For example, having patient representatives on advisory committees.

Senator Rick SCOTT. Yes. Thank you. Thank you, Chair.

The CHAIRMAN. Thank you, Senator Scott. Ranking Member Braun.

Senator BRAUN. I think from the discussion you have heard today that it is clear that there is a difference between the broad array of diseases out there, the places where most pharmaceutical companies go, and that with everything we are talking about here, it is just not being addressed.

Keith, I would like you to comment on, is the paradigm that we have currently, working, especially in the case of one with a narrow window of survival? Within the paradigm that is to me bureaucratic, it has not responded in a way to these over a long period of time, what—is there any hope that we can get it done within that current structure?

Mr. DESSERICH. I think that the comments that we were talking about of, you know, what is being collected and also comes down to, you know, the guidance as opposed to regulations, and, you know, as was pointed out, you know, the idea that it probably could be done in the right way, but unfortunately it isn't. I think that there is a lot——

Senator BRAUN. Is that called compassionate use in the current framework?

Mr. DESSERICH. Yes. I mean, I guess it could be. I mean, but I mean you could—they could take any of these measures and they could probably try to—with it, but it doesn't happen.

I think that is the reason why PPA really needs to be there is because otherwise without it, there is nothing that is going to make sure that there is any accountability to deliver the right decision on it. You know, we witnessed it time and time again. I have talked to drug companies, and they tell me they can't figure it out.

They feel that, you know, what is in the guidelines versus what is in the guidance or the suggestions that they receive back is not matching up. You know, I talked to a drug company just last week and they said they are probably not going to be focusing on our realm and on pediatric drugs because——

Senator BRAUN. That is why we need the formality of PPA.

Mr. DESSERICH. Exactly. They see no way that it is going to work, and, you know, they are giving up, and we can't have that. You know, these are small drug companies, but that is where sometimes the best ideas come from, and if we take away the opportunity to consider those good ideas, that is a problem.

I think the other thing that we miss is really the patient right type of thing. We talk about data collection. We talk about the idea of being able to have it at the pharmaceutical level or in the FDA. Data isn't the property of one entity over another.

You know, there has to be also a patient element to this. That is the beauty of what is in the Promising Pathway Act. Is also the international register or these registries that are in there, these independent registries, which allow for everybody to be able to communicate that, but still protect the patient privacy at the same time, and you know, otherwise we are just going to get half of the information.

We are going to be following what we think is necessarily the guidance on it, and effectively, what we are left with is a Wild West type of mentality as to how we deal with drug trials, and we can't keep doing it that way because if that is the case, we are never going to be able to get anywhere on this.

Senator BRAUN. Thank you. I yield back.

The CHAIRMAN. Thank you, Ranking Member Braun. Senator Warren.

Senator WARREN. Thank you very much, Mr. Chairman, and I want to say I very much appreciate Senator Braun holding this hearing and advancing this important idea. For individuals who are experiencing a devastating diagnosis, the promise of a new therapy or a cure provides hope in a profoundly dark time, and that is why I have long described Federal support for medical research as one of the best investments that our Nation can make and why I have introduced legislation to ensure that we fully invest in medical breakthroughs.

I want to, if I can today, talk about just a slightly different part of what happens in the drug approval process that I am concerned about. I want to talk about how we get research from the lab to the pharmacy, and one of the key parts of that, as many of the people in this room know, is clinical trials.

Once a promising therapy is identified, pharmaceutical manufacturers have to test the drug for safety and effectiveness, which involves enrolling patients in clinical trials. Patients place enormous trust in the people running clinical trials, which is why all research involving human subjects in the United States must be approved by institutional review boards or IRBs.

Professor Fernandez Lynch, you lead work on the quality and effectiveness of IRBs. Can you just say a little bit more about what the job of IRBs actually is?

Mrs. FERNANDEZ LYNCH. Of course. Thank you, Senator, for the question. IRBs have been required to review nearly all federally funded research and federally regulated research for several decades now, and their responsibility is to protect the rights and welfare of people who participate in studies by making sure that the risks and benefits of research are appropriately balanced and that there is adequate informed consent, they prevent ethically problematic research from proceeding, and they also help make sure that the science is strong.

When people are giving their time and energy to participating, that is an important element of trust, and they shouldn't be exposed to unnecessary burden and risk, but then IRBs also have a very important responsibility to facilitate high quality research and to promote ethical research to answer questions that will benefit patients and society.

Senator WARREN. All right, so as I understand this, if a clinical trial can't answer the questions it sets out to study or doesn't properly communicate the risks of the study to the people who participate in it, then it is the job of an IRB to step in and keep patients safe, but rapid consolidation and private equity ownership of IRBs has raised some serious questions about whether these boards are leaving vulnerable patients exposed to unnecessary risks. Now, while most IRBs are affiliated with universities, IRBs that are not associated with any institution, they are known as commercial IRBs, are reviewing a larger share of drug clinical trials.

According to a recent GAO report, despite representing just two percent of the review boards, these commercial IRBs now review over half of studies involving investigational new drugs, and 92 percent of them are reviewed by just two private equity backed companies.

The GAO reported that private equity backed IRBs, I am going to quote here, "are beholden to their clients or equity holders." In other words, the people who put the money up. Professor Fernandez Lynch, what are the risks that this creates for clinical trial participants?

Mrs. FERNANDEZ LYNCH. Thank you, Senator Warren, and I very much appreciate that you pushed the GAO to examine this issue. I wasn't surprised by their finding that we still lack meaningful measures of IRB quality. This is something that has come up time and time again, and the lack of our ability to assess quality meaningfully makes it hard to comparatively assess these different types of IRBs, which is a problem that I am working on in my own research.

One challenge and concern about private equity ownership and profit oriented goals in the IRB space is that it creates a primary emphasis on speedy approvals of proposed research and keeping the sponsor happy, and that emphasis on speed also kind of trickles down from the private equity IRBs to the university IRBs, who have to compete with them. Now, of course, speed can be a very good and important thing when we are talking about research. We want high quality research to move quickly.

Focusing on speed can also inhibit deep attention to ethical concerns, and it can also limit the focus on maximizing scientific quality and really just approving science that is good enough, kind of

meets the floor of regulatory requirements, rather than making sure it is maximally valuable, and so, I think that is a primary concern here.

Senator WARREN. I appreciate you raising this because I just want to make sure we get this right. You know, the GAO found that an emphasis on profits can lead private equity backed IRBs to rubber stamp reviews of drug clinical trials and focus less on potential harm to research subjects.

While HHS and FDA are responsible for inspecting IRBs to ensure that participants are protected, the number and frequency of these inspections has been steadily decreasing, so HHS and FDA need to step up their oversight efforts in this area, and that includes clarifying what it means for an IRB to be working effectively, something that these agencies have never done despite years of decades of requests, so that clinical trial participants have complete confidence in the scientific integrity of the trials that they join and feeling certain that these have been fully vetted.

That is my concern in this space and why I wanted to raise it. I want to say again thank you to Senator Braun for holding this hearing. I look forward to continuing to fight alongside you for patients with rare and progressive diseases. We need to do better in this space. Thank you.

The CHAIRMAN. Thank you, Senator Warren. Senator Vance.

Senator VANCE. Thank you, Mr. Chairman, and I am going to direct my questions to Mr. Desserich, so first, let me just say, you know, I have got a six-year old, a three-year old, and a one-year old, and my heart goes out to you because I know that you have engaged in this fight because you lost a seven-year old daughter.

I know a lot of other folks here who have lost kids, and my heart goes out to you as well. The goal here, of course, is to try to get to a society where no parent has to bury their own kid because of an illness that is currently incurable. I know we are all working toward that goal, and the worry that I have is that given the limited patient populations, because some of these diseases are incredibly rare, and because of how differently we treat pediatric illnesses and the medicines to treat pediatric illnesses, that we are making some mistakes here.

I know, Mr. Desserich, there is an argument that the Right to Try legislation, the expanded access that happened during the last Administration, which I think was a good thing, that that satisfies some of the concerns that you have with the current way in which we give patients access to these drugs.

I would like you maybe just to explain why that is not right. What are we still not doing correctly in this space?

Mr. DESSERICH. Well, I think any time that we have tried any of the Right to Try elements within our specific disease classification, there has been a unwillingness to make it apply to pediatrics.

You know, Right to Try seems to be something that may have some adult applications to it, and I can't really speak to it because I don't touch those populations, but within the pediatric realm with it, everybody has kind of looked at it and said, well, yes, it is not going to go for children's cancers.

I think that is—you know, that is really the cornerstone of everything that we are talking about here is because I think what we

tend to do is we tend to think it along the lines of the ideal circumstance.

We think of it as a clinical trial, and how these can be perfected, and how we can do better with it, but at the end of the day, you know, all these acts and all these regulations are dealing with imperfect scenarios. You know, a clinical trial requires things such as investment accrual, time, biomarkers, and certainly a completion, and the issue is, while we all, I think, see the need for clinical trials, we are dealing with scenarios to which these things don't exist.

We can't get it. You know, we can't get accruals. I mean, I am witnessing right now a trial that we are putting out there with kids in our disease classification, and they have an accrual number of 400 patients.

We only have 400 kids that are diagnosed per year. That means this trial is never going to get finished. It is going to have eight years to be able to get there, and by then we are already going to know whether it works or doesn't work with it, and so, you can't think of it in those ways.

We have to go into this with the idea that we don't have the things to do the clinical trials sometimes, and so, Promising Pathway effectively fills that need.

Senator VANCE. Mr. Desserich, can you explain to me just this particular point, so very often, and I have worked with companies in my private life, my prior life, I should say. When I was in the private sector, we actually worked with some biopharmaceutical companies doing clinical trials.

You know, one of the things, of course, you are trying to do in some of these cancer therapeutics is identify whether the addition of the therapeutic increases the life of the patient, right. It is sort of one of the primary endpoints oftentimes.

In some of the diseases we are dealing with, especially in pediatric cases, extending the time from, you know, three months of life to nine months of life is not really practical because the time given for the individual patient, for a child is so small, so the idea that you are going to somehow reach a classic adult endpoint in a pediatric case sometimes just doesn't make any sense, does it?

Mr. DESSERICH. Absolutely not. I mean, we can't reach those endpoints. I mean, frankly, I think our community is happy with anything that we can add. I mean, just another day is what we are looking for.

Senator VANCE. Sure.

Mr. DESSERICH. We have seen some things that have worked, that we have applied, and we tried to do this with, and, you know, they have added months. You know, right now I would guess from looking at some of the registry data, we see that we have probably expanded that by threefold, and that is good.

We were only talking about, you know, maybe six months, so threefold is a year and a half. That is not a life by any stretch of the imagination. Will it ever be at that case? It is just we have to take it and we have to try to grow it as much as we can.

Senator VANCE. I appreciate that. I appreciate all of you for being here, and the last comment I would make here is that we all understand that we have to do better.

What occurs to me, just in looking at the, you know, Senator Braun's PPA and just talking with Mr. Desserich both in this context and in others, is that we have a clinical trial situation, we have a clinical trial infrastructure in this country that is in some ways designed for adult diseases and very common diseases.

If we don't fix the underlying infrastructure, we may have a lot of kids out there who are languishing, who are dying, not because there aren't therapeutics and not because there isn't capital to invest in these new therapeutics, but because the regulatory regime doesn't allow us to actually try these things and figure out whether they work.

I think we need to fix that problem. I applaud Senator Braun for trying to take a swing at it.

Mr. DESSERICH. If I may add something to that as well. The other thing I think that we also miss is that for the most part, we view our kids as not the same level as an adult case, and so, what we do is we tend to say, let's take a drug that we know works in some other cancer and let's give it a try in kids, and for that we can do clinical trials. For those, we can put them out there, but what happens most often, especially right now, with all the knowledge and all the investment that we put into this, and the registries, and the tracking, and the patterns, and everything we have been able to find, for the first time we have an ability to craft a drug that focuses on DIPG.

I can't get it out. I can't get it to a bedside because I can't put it in adults. Adults don't normally get this, so we are at a stop point. You know, my reference to you and the reason for bringing these 46 grants is to impress upon you how important it is, because I can't—I don't think I can get a lot of these into a clinical trial.

The CHAIRMAN. Thank you, Senator Vance. Before turning to Senator Warnock, I just want to give a sense of the time constraints we are under. Now we have a vote that is opened and well underway.

After Senator Warnock, I will turn to Senator Braun, and then I might have one quick question and then we will have to conclude the hearing, but, Senator Warnock.

Senator WARNOCK. Thank you very much, Chair Casey and Ranking Member Braun, for holding this important hearing today, and I am really grateful for your leadership on this issue, particularly Ranking Member Braun.

It is great to work with you on legislation to advance this important work. I have heard from Georgians across the State who have been personally affected by rare and serious diseases, from ALS to Barth syndrome, to many others, and despite the differences in these diseases, there is one thing they have in common, patients desperately, desperately need improved access to treatment, and that is why I was proud to co-sponsor Ranking Member Braun's Promising Pathway Act. That is good public policy, and it would help patients with life threatening diseases receive early access to promising treatments.

Mr. Desserich, how would the Promising Pathway Act improve access to lifesaving treatments for patients who have serious diagnoses? I ask this, you know, recognizing that you have been personally impacted by this, even as you remember your own daughter.

Let me thank you for translating your pain and the power and being such an important voice on this, and so, from your experience, how would the Promising Pathway Act help?

Mr. DESSERICH. I think in our case with it, it is a question of time and direction toward pediatrics. I think, you know, everybody looks at this, at the Promising Pathway Act, as an ability to be able to, you know, find something that, you know, generally satisfies the safety requirements and we can try to move it toward, you know, giving it a conditional approval.

We are certainly moving that up and I think that helps any patient in a terminal diagnosis. With regards to the pediatrics side of things, what Promising Pathways does that I think better than others is it allows it to move faster into the pediatric realm by—especially in those rare and terminal cases.

Now, that is not all cases. You know, there is also some specific definitions of what is a terminal case in this that I think really help to, you know, provide some clarity to it, but you know, short of that, we can't get it there. You know, we can't get these trials into the pediatric realm with it.

We need a perfect, ideal scenario and the cancers that we are dealing with are absolutely nothing close to ideal. You know, they—it changes everything.

Senator WARNOCK. It is also important that we include patient perspective and priorities into our therapy development. Professor Fernandez Lynch, can you discuss some of the advances that the patient focused drug development program have provided?

Mrs. FERNANDEZ LYNCH. Of course. Thank you for the question, Senator Warnock. FDA has a formal program called Patient Focused Drug Development, and it is worth acknowledging the major strides the agency has made over the past several decades, starting with the HIV/AIDS advocacy, pushed to help FDA recognize that patients deserve a seat at the table.

Patient focused drug development really refers to a systematic approach to ensuring that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into both drug development and FDA's evaluation of drugs, because it recognizes that patients have expertise in the diseases that they are facing.

It is important to hear from patients and FDA has stated that it needs to hear from patients about clinical trial design and what are the end points that are meaningful to them. What are the things that should be measured in trials? What makes clinical trials feasible to participate in?

Senator WARNOCK. Do you—and I hate to interrupt, but I am going to be out of time in a little bit. Do you have example of advances made by the program that you could share?

Mrs. FERNANDEZ LYNCH. I can—what I can share with you are the types of activities that FDA has engaged in, which are a variety of guidance documents to help companies understand how to systematically collect information from patients that will be meaningful, and they also have a program to develop clinical outcome assessments, which are also intended to be specific endpoints that are meaningful to patients, and then in addition to the patient focused drug development program, there has been further incorpora-

tion of patient voices as representatives on advisory committees to FDA.

Senator WARNOCK. Thank you. Patients voices are critical to this process and thank you for your leadership. Thank you, Mr. Chair.

The CHAIRMAN. Thank you, Senator Warnock. I will turn to Ranking Member Braun.

Senator BRAUN. Thank you, Mr. Chairman. Before my last question, Senator Murkowski from Alaska wants to enter into the—Senator Murkowski from Alaska wants to enter into the record by unanimous consent support for the Promising Pathways Act.

The CHAIRMAN. Without objection.

Senator BRAUN. Last question. Dr. Bhatnagar, so often you hear folks have to leave the country to get leading edge treatment. That is a shame. We should be that leading edge and we should have a system that accommodates it.

Could you talk about the difference between our system and one that seems to be working better, which would be in Europe in terms of how they have done provisional approval, and please comment on that because if that is better, we should at least be emulating that.

Dr. BHATNAGAR. Thank you, Senator. It is a good question, and I think it is debatable which one is better. I think it is true that there are certain therapies where access is more elsewhere.

I think our regulators are clearly top notch. The world looks up to the FDA for what they are going to do, but I think there are times when there are delays which are unnecessary. There are situations such as approving drugs early in the process where we don't have the same considerations.

Just very quickly, because I know we are almost out of time, the accelerated approval pathway as it exists in the U.S. really is focused on two constructs. One is you have a known biomarker or a surrogate that predicts benefit, and the second is an intermediate clinical benefit that predicts ultimate use.

The challenge with both of these is that neither of them is really present in most rare disease situations. Last year, CEDR approved 37 drugs. Six were accelerated. Five of them were oncology drugs. One was a nonmalignant hematology drug. The point is that oncology is an area where these diseases are really well understood.

Other rare diseases, we cannot use the pathways. Europe has prospectively defined certain things that they can do on a regulatory side. You can negotiate a study design with the regulators prior to approval and get an approval in that manner. We don't have the same provisions.

Senator BRAUN. Thank you.

The CHAIRMAN. Thank you, Ranking Member Braun. I just have one more question. I know we have to wrap up. Professor Fernandez Lynch, in your testimony, you stated the following, "it is certainly understandable for individual patients to be willing to risk substantial uncertainty for themselves before better evidence becomes available, especially when they have no time to lose, and I support their right to do so via expanded access. However, weakened approval standards affect all patients."

Could you talk about this balance that I know we all want to strike from an ethical perspective, the balance between the needs

of the patients when not all patients have the same needs or the same level of risk tolerance.

Mrs. FERNANDEZ LYNCH. Yes, of course. Thank you for the question. One of the things that I have often heard in the context of discussing Promising Pathways is if patients don't want to take a provisionally approved drug, then of course they don't have to.

That is absolutely true, but it becomes more complicated because when you lower FDA approval standards, that tells industry, this is the bar that you have to meet. When that bar is lowered, then industry responds accordingly.

What that does is push back to patients and clinicians the need to make decisions without evidence. Now, some people may have that high risk tolerance, but not everybody will, and that is why I think the dietary supplement example is so salient.

Dietary supplements do not have to show safety and effectiveness, and so industry does not demonstrate that. That is not what people who are facing these terrible diseases need. The other challenge is when the standards are low and you allow products on the market that have not demonstrated that they are beneficial, it complicates the development of potentially better drugs because it makes it difficult to accrue those studies and then you might also find yourself having to test new interventions against interventions that have not yet been proven to work.

You can't quite tell, are patients benefiting from this new drug, or is it that neither of these drugs are beneficial? So, you can entrench drugs that don't actually benefit patients.

FDA has to account in its public health responsibilities not only for the interests of patients today, but also the broader population of patients, which is why I am encouraging the Committee to draw on what we have heard about challenges to the expanded access pathway.

I think that is the avenue that really does need to be improved and provides this balance, allowing patients today who have high risk tolerance to take unproven medicines while we continue to gather rigorous evidence.

Unfortunately, patient registries are not going to get us there because they are not randomized, not controlled. They are not going to be able to answer these questions in the way that patients need to make autonomous, informed decisions about their treatment.

The CHAIRMAN. Thank you, everyone. We are going to turn to our closing statements, and I will turn to Ranking Member Braun, and if he has to leave before mine is completed, I won't be offended.

Senator BRAUN. Thank you, Mr. Chairman. I have been working on this for most of the five-years I have been here in the Senate, and I come from a world where I was in the logistics and distribution business, and it is frustrating sometimes when you want to get from here to there.

I think we have had a really good discussion with it today, and we have heard most importantly from folks that are suffering through it, and I think if there is one lesson to learn, we need to have more of that even on other diseases. Here the urgency is even more compelling.

This is a bipartisan effort. After much work, I think it is going to cascade into something quicker than what most bills take since

it took so long to get here. In the face of such cruel diseases, a more compassionate and flexible path has got to be there for patients. Why does Europe have such a pathway and we do not?

I look forward to working with my colleagues to speed up access for individuals with these diseases while maintaining the gold standard of the FDA. We can do both at once. This is not a Republican or Democrat discussion. This is a human discussion.

We all have stories that are deeply personal, seeing firsthand the impact of how these diseases ravage not only the victims, the families as well. It is time for us to turn the passion into action, and we are going to do so. Thank you, Mr. Chair.

The CHAIRMAN. Ranking Member Braun, thank you very much. As we have all heard today from patients and from family members who are desperately awaiting hope, awaiting a treatment, we have also heard today from patients who have lived their whole lives without any therapies for their condition.

We have heard about—from the caregiver perspective, spouses, family members, a father who lost a daughter, hearing how hard it is to watch a family member suffer with no treatment options. We have also heard about the challenges that the drug companies face when working to bring a drug for a rare disease to market.

We have heard about how to balance the unique challenges posed by rare diseases with regulatory processes that uphold, as Senator Braun said, the FDA's gold standard. We must continue the discussion with each other in the Senate, with the FDA, and all that have a stake in this, all the families who are represented here today.

We have got to substantially, substantially improve the process for getting new drugs to patients while maintaining standards of efficacy and safety, so I want to thank all the witnesses today for their contributions, for the time they spent here, and for sharing very personal details about your lives. That is not easy to do in a public setting.

For the record, if any Senators have additional questions for the witnesses or statements to be added, the hearing record will be kept open for seven days until next Thursday, November the 2nd. Thank you all for participating in this hearing. This concludes our hearing.

[Whereupon, at 11:57 a.m., the hearing was adjourned.]

APPENDIX

Prepared Witness Statements

Brian Wallach
Co-Founder, I AM ALS
Public Witness Written Testimony
Special Select Committee on Aging
United States Senate
October 26, 2023

Chairman Casey and Ranking Member Braun, thank you for the opportunity to testify today. My name is Brian Wallach, I have been living with ALS for almost six years and I am a Co-Founder of I AM ALS, along with my wife, Sandra Abrevaya. I AM ALS (IAA) is a patient-led community organization that provides critical support and resources to those living with ALS, their caregivers, and loved ones. Since we founded I AM ALS in 2019 , the organization driven by the community has been revolutionizing the ALS movement by empowering and mobilizing patients, engaging with policy-makers, and offering vital resources for people impacted by ALS.

It is my honor to be a part of today's hearing and, on behalf of the ALS community, I want to say a profuse thank you to Senator Braun and his dedicated team for their tireless work on behalf of the ALS community. The Senator's leadership and efforts are so very much appreciated by the ALS community. Too often we are forgotten and not spoken for in such a busy world.

I also appreciate your willingness to accommodate my need to be virtual because of the challenges of travel, the physical toll it takes on me and the stress it places on my family especially my wife, Sandra. Each year, I wonder whether it will be my last opportunity to engage

with Congress because most people living with ALS live only two to five years post-diagnosis. I want to express my sincere gratitude to the Committee for the bipartisan support to have this hearing today to discuss how we can unlock hope and accelerate access to therapies for people with rare, progressive diseases like ALS.

ALS is a disease that is 160 years old. Let me repeat that: For 160 years, ALS has killed everyone diagnosed with it. That is simply unacceptable. ALS is a relentless and progressive neurodegenerative disorder that takes away your ability to talk, to walk, to care for yourself and, ultimately, to breathe. For those who have not been diagnosed, it is hard to imagine what living with ALS is like but I can tell you that it is brutally horrific for me, my family and loved ones. ALS has many unmet medical needs including no effective treatment so it is 100% fatal. ALS and the lack of a cure or even real treatment that can help with the progression highlights the urgency for new treatments and why legislation such as the Promising Pathway Act is essential for the ALS community.

Today, under current FDA standards, it can take 15 years or more for effective drugs to move from preclinical work to approval. Drug sponsors must show substantial evidence of safety and efficacy. In the meantime, many people who have rapidly progressive terminal conditions including ALS die and have no viable treatment options or hope available to them.
ALS remains a challenging and enigmatic neurodegenerative disease, and there is much that is not yet understood about it. While some progress has been made in recent years, including better understanding some genetic aspects of the disease, many questions and scientific mysteries persist. It is important to recognize that ALS is not a single disease but a group of disorders characterized by the progressive degeneration of motor neurons in the brain and spinal cord. This is known as heterogeneity and it makes it incredibly challenging to pinpoint a single cause or treatment strategy that applies to all cases.

For the majority of ALS cases, the exact cause is still unknown. Researchers have explored various hypotheses but no single cause has been identified. ALS is a complex and multifaceted disease for which much remains to be understood. While scientific progress is slowly being

made, there is still no definitive answer to the cause of ALS, and effective treatments remain elusive.

This is exactly why legislation such as the Promising Pathway Act is critical for people living with ALS and can make a real difference. This legislation is building a foundation for the future so that in the next few years we will have a system that allows faster access to promising drugs for people with rapidly progressing terminal diseases.

The PPA tackles the important issue of expedited access for drugs that treat certain very serious conditions where there is an unmet need and death will result without effective treatments. Today, existing FDA pathways are not suited for such circumstances. Drug approvals for serious, complicated conditions take many years to weave through various trial phases including in some cases multiple phase three trials plus lengthy negotiations with the FDA prior to even filing for approval. The PPA offers the prospect of cutting five or more years off the timeframe for marketing efficacious therapies. That timeframe is enormous for rapidly progressing terminal diseases.

Current FDA approval pathways take far too long to help those currently suffering from such diseases. Even the existing FDA expedited pathways are insufficient. For example, the FDA's "accelerated approval" pathway allows for drug approval without evidence of direct clinical benefit in certain circumstances if a drug's effect on a biomarker (a biological measurement) is likely to predict clinical benefit. However, over 95% of ALS cases do not have an accepted biomarker.

Other existing pathways such as expanded access programs or right to try are very important, but they have significant limitations especially in regards to financing and scope. While there is NIH funding for expanded access programs because of the ACT for ALS that many in this room helped pass in 2021, many such programs are outside of NIH funding and dependent on

financing by the manufacturer. The same is true for Right to Try - this program is completely dependent on the willingness and financial capacity of a manufacturer to provide access to a treatment.

The PPA affords patients access to therapies that have shown promise of safety and efficacy while the process of gathering additional evidence of efficacy proceeds. The PPA requires the FDA to withdraw provisional approval if such evidence is not provided. The PPA also preserves efficacy standards for final drug approval. We support efforts to bring safe, promising therapies to more people living with terminal diagnoses pending full FDA approval. The provisions in the Promising Pathway Act provide such a pathway.

The PPA does adjust the FDA's "substantial evidence" of efficacy standard for drug approval for certain limited serious conditions. This lowering is very intentional. The showing of relevant early evidence of positive therapeutic outcome based on adequate and well-controlled investigations is based in science. The key is that PPA approval is merely provisional. It affords early access to promising drugs to people with extremely serious conditions who are willing to take risks. It allows additional evidence about a drug's efficacy to be collected during the short two-year provisional approval windows. Provisional approval can occur only if a drug has been shown to be safe. Required patient registries enable much broader data collection about a drug's efficacy and safety than can occur in traditional, double-blinded, randomized, placebo-controlled trials, which in the case of ALS, may only involve 100-200 people. In rare diseases, it can be hard to even find enough people to conduct a meaningful trial.

Importantly, under the PPA, the FDA maintains meaningful authority to collect data and withdraw provisional approval based on safety or efficacy. Moreover, drug sponsors presumably want to obtain full approval of any provisionally approved drug. Other than allowing the use of real-world evidence to supplement an application, the PPA does not alter current FDA standards for full drug approval in any way.

I believe that the Promising Pathway Act is common sense legislation with many safeguards that would enable early access to promising drugs for those who have no other options and who

otherwise face certain death. It is simply impossible to run a traditional clinical trial for too many rare & fatal diseases.

The ALS story is slowly changing and with measures such as the Promising Pathway Act we can make much needed & faster changes that finally get treatments to the community that allow people, including me, the chance to watch our families grow up, thrive and not be faced with a death sentence.

Thank you for your time & thank you for allowing me to be a part of this important discussion.

October 26, 2023

Senate Aging Committee Hearing

My name is Maureen. I'm 50 years of age and I live in Shelton, Pennsylvania.

I have lived with Galactosemia for my entire life.

Shortly after my birth in 1972, I began to show the classic hallmark signs of failure to thrive. Jaundice, repeated vomiting and weight loss. Seven days later, I was diagnosed as having classic galactosemia upon release from the hospital.

My mom and dad were given a 32 page booklet entitled A Parents Guide to a Galactose Restricted Diet. They were instructed to follow this booklet as I would need to be on a lactose free, dairy free diet for the rest of my life at that time. The only treatment for galactosemia. I doubt my parents knew that many more challenges would lie ahead in the following years to come then just for having me follow a dairy free diet.

It seemed like everything was working fine for me at the time, but I was getting older and it made me feel very left out when I could not eat the same way as my peers. Without the modern advances we have in nutrition today, I cannot tell you how isolating this was for me. There were many social events that I could not go to. My mom tried so hard, always sending me to school with a special treat – not just enough for me but for everyone to share. As a child this was really difficult.

I also could not process information the same way. I was always a low average student, and math was always my most difficult subject and still is today, but not in the way other people say that. I struggle with making change, leaving tips at restaurants, figuring out percents when stores have a percentage off sale. I cannot process it at the moment. Basic life circumstances became a struggle and only when I met other people living with Galactosemia did I realize that the comprehension issues were similar for all of us.

Just as I was slow academically, I was also slow in developing physically. While my friends were going through puberty and talking about it, I was not having any of these issues or normal signs such as late development and still looking like I was in grade school physically as opposed to being in high school. This continued the sense of isolation that having galactosemia makes me feel. After going through puberty, I began to have unusual symptoms such as hot flashes, mood swings and night sweats. After about a year of experiencing these symptoms and having blood work, I was diagnosed at the age of 18 as having premature ovarian insufficiency. Which is it a direct result of Galactosemia. This is something that I continue to struggle with today.

As a result of this diagnoses, I became very reclusive. I wanted no part of dating or socializing like any other 18 year old would be interested in the impact of POI. Secondary to having galactosemia, this was very difficult in my 20s. I just wanted to be like any other woman my

age, socializing and having fun. However, I was depressed and had a difficult time making friends and meeting new people. There were many nights where I cried myself to sleep. At a church event in 1999, I met a man named Bill who showed interest in me and started spending time with him. I was very apprehensive about getting involved in a relationship, even though I was 26 years old. The fear of falling for someone only to have to tell him that I was infertile and taking a chance on losing this relationship weighed heavy on my mind. However, I finally got the nerve up to tell him. Bill is a pharmacist and his response was priceless, not caring about my diagnosis and instead advising me to take my calcium because I was such a calcium slacker. What a huge weight off my shoulders and we celebrated our 21 years of marriage this past May.

I was told long ago that having galactosemia was like looking at everyone at a party through a glass window and watching others being a part of eating foods I could not have. I could see them through the window and through the glass, but could not break it or join them. The same is true for infertility. I can see moms and children through the glass, but cannot experience what it is truly like to be a mom. All my life I longed to be on the other side of that window.

There could finally be a treatment for people like me. And even if it is too late for me, it could work for younger ones living the way I grew up. I spoke at the Patient Focused Drug Development meeting, but our community never heard from FDA after that. They had no questions, no clarifications and that made us worry they had not taken the time to learn from our work before reviewing a drug. Will they understand that speech issues don't matter to us the same way as cognition and developmental delays do? Some of us have even more scary symptoms than the ones I have had to live with, like seizures, kidney issues, tremors, cataracts, neurological impairments, and intellectual impairments.

Will they understand that if they ask for another trial, our community won't have enough patients for another trial? Will they understand that if the drug is approved for something else rare, our doctors have seen the improvements in our community and will want to prescribe it for us too. The drug is already being studied in other rare diseases. These days we have to fight for approval but then fight insurance too. The Galactosemia Foundation is working hard on both of these things and I hope you can help us. Today a bill is being introduced in the House by Representatives Dunn and Matsui that will help us with the insurance side. I would like my Senator and the others in the room to look at this bill too. Please help us with this bill.

I'm trying to learn about what places like FDA and CMS and Congress can mean to me and to the others whose lives are impacted by diseases like Galactosemia. I don't pretend to understand it all. But I know even one person can make a difference and I want to help the little girls with Galactosemia going through the isolation, the puberty, the depression, the fear, the inability to understand and process. If all of you can take my story and help them, it will mean so much.

Margaret Plews-Ogan, MD
Brodie Professor of Medicine
University of Virginia
Public Witness Written Testimony
Committee on Aging
United States Senate
October 26, 2023

Chairman Casey, Ranking Member Braun, members of the committee,

Thank you for the opportunity to present this testimony. The testimony I give here today is reflective of my own views and is not intended to reflect the position(s) of the University of Virginia.

My name is Margaret Plews-Ogan and I am first and foremost the wife and caregiver to my husband Jim. We are both physicians. On December 2nd,2021 our lives cracked open. Jim was diagnosed with ALS. At the time, we were both busy clinician - scholars. Our lives were full and engaging, with meaningful work, close family and a community of friends. We were runners, and loved camping, hiking and exploring the world. We were activists, focusing on improving the care of vulnerable populations. With this diagnosis, our lives were completely upended.

What I remember from medical school about ALS is that it is the diagnosis a physician dreads more than any other. Why? ALS is a disease that robs a person of almost everything essential to living our lives– the ability to move, to communicate, to eat and drink, and eventually to breathe. But the double-edged cruelty is that awareness and cognition are left intact. Persons living with ALS can feel each loss and fear the next one, every moment. ALS is 100% fatal. No one has ever survived. The average life expectancy after diagnosis is 2-5 years. Eighty-five years after the diagnosis was made famous by baseball legend Lou Gehrig, only a few minimally effective treatments exist, these aimed only to slow the course. When given this diagnosis, patients commonly hear: "go home, hug your loved ones and get your affairs in order."

People worry, I think, about giving patients false hope. But they clearly do not understand the devastation of having no hope, of simply waiting for the inevitable decline.

Having no hope was not an option for our family, so, like many ALS families, we got moving. We read, we got involved in advocacy, we investigated clinical trials and new treatments. As physicians, neither of us were naive about ALS. But to be diagnosed with a disease that has been around for 150 years, and has one, perhaps two, minimally effective treatment options, was shocking.

One unacceptable reality we faced was that the disease moves faster than the FDA. We learned that the one option in the pipeline that had good evidence for efficacy, AMX0035, was initially denied approval by the FDA because they wanted an additional, confirmatory, Phase III trial. This drug is a combination of two drugs that had been on the market for many years, one that was over the counter! The combination, AMX0035, had excellent safety and substantial evidence of efficacy in a Phase II/III trial. The only way for us to obtain the medication was to get the one component, Tudca, online and the other component from a specialty pharmacy in New Jersey off label. And because it had not yet been approved, it cost around $1500-$3000/month. Most of our friends in the ALS community could not afford this. After advocacy from the ALS community the FDA took another look at the efficacy data and finally approved it, over two years after the results of the clinical trial were known. What does that two years mean for an ALS patient?

Two years ago, Jim was running races. He was starting a new integrated care network for children across the state of Virginia. He was standing up a new program at UVA to care for medically complex children. He had a thriving pediatric practice full of kids and parents who adored him. Today he struggles to feed himself, he is confined to a wheelchair, he cannot roll over in bed, or brush his teeth, or put in his contacts, or even scratch an itch. He is losing his ability to speak. Inside the body that is failing him, Jim is the same brilliant, compassionate, creative, loving human being. The courage he displays every day is stunning. I am Jim's primary caregiver. The nights are the toughest. Every time Jim needs to move to adjust his vent mask, to pull up the covers, or to turn to get pressure off his hip or shoulder, I need to do that for him, and he needs to somehow communicate that need. Were it not for the support of our amazing grown children, extended family, neighbors and dear friends, I'm not sure what we would do. What do you think our life will be like in just 6 months? One thing I know...Jim needs to be here. He's got a new grandbaby, and a wedding to attend!

ALS is 100% fatal. No one survives. As a physician one of my areas of expertise is reducing errors in medicine. Classically, physicians, and frankly most human beings, are more afraid of doing something that might hurt someone than we are of NOT doing something that might help someone. But this isn't rational. Until I had this experience of watching helplessly as my husband lost the ability to use his hands, then his legs, then his voice, I don't think I fully appreciated the fact that doing nothing in the face of a 100% fatal disease, delaying approval until the ultimate confirmatory trial is completed, is much worse than *doing something that might help* (allowing patients with a disease like ALS access to therapeutics that are safe and have promise...not a guarantee, but promise of efficacy). The standard FDA pathways do not give the FDA a way to appropriately weight the devastation caused by denial or non-action in a rapidly progressive 100% fatal disease like ALS. So, when the FDA failed to approve AMX0035, not because of any safety issues, but because they wanted another Phase III trial to *confirm* efficacy, it was devastating.

Jim and I are both old enough to have lived through the AIDS crisis. When I started residency there were no treatments, and the medical wards were filled with AIDS patients who were dying no matter what we did. With an influx of funding our understanding of the disease

progressed, and therapies began to emerge. The accelerated pathway was created so that these emerging therapies could get to the patients quickly. I watched as each new therapy, one by one, turned the disease around. Almost immediately, patients started living longer. The earliest therapies were less effective and had more side effects, but they saved people's lives while drugs were added, and combined together into cocktails. Patients and their loved ones fought for the opportunity to start these drugs. The side effects paled when the alternative was certain death and the suffering that preceded it. Those who survived are grateful to this day to have had the opportunity for early access to lifesaving medication.

It is the same in the ALS community now. We are fighting for the early access to safe and promising therapies. Like HIV, we anticipate therapies will build on each other, be combined in cocktails, and we will see ALS turn into a manageable and eventually curable disease. We will happily participate in registries to help you gather the necessary confirmatory data. The Promising Pathway Act is our ongoing hope for early access to the many promising therapies that are on the near horizon. This is not false hope. It is real hope. You have the opportunity, in this congress, to make the PPA a reality. You have the power to change the landscape of ALS, transforming it into a manageable, and eventually a curable, disease. We need your urgent action. We are counting on you.

Witness Testimony
Anish Bhatnagar, MD
Chief Executive Officer, Soleno Therapeutics

Chairman Casey, Ranking Member Braun, and Honorable Members of the U.S. Senate Special Committee on Aging, I am honored to testify at today's hearing. Thank you for inviting me.

I am a physician by training. My 25-year career, almost entirely at small companies has involved developing treatments for cancer, and neurological, psychiatric, cardiovascular and other diseases and for the last several years, rare diseases.

None of my work, including that on lifesaving cancer drugs, has been as meaningful as working with this amazing community of families who have children and adults with Prader Willi syndrome (PWS). While the regulatory challenges across therapeutic areas are similar, there is a much more disproportionate impact on patients with rare diseases. A similar disproportionate impact is seen on small companies like ours, which do a large proportion of the high-risk work. We have a single lead program, and our survival as a company is determined by the progress on that program. Our ability to raise money and continue our work depends prominently on regulatory clarity. If the minutes of an FDA meeting do not clearly state a path forward or if a company receives inconsistent feedback, it could be the difference between having money to carry out a pivotal trial or giving up on a drug to treat a disease that has no options.

Speaking of diseases with no options, PWS is a rare and life-threatening genetic condition which occurs randomly and affects 10-20,000 patients in the United States. Children with PWS are often recognized within a few weeks of birth because newborns with PWS have a constellation of symptoms that raise suspicion for the condition, including low muscle tone (they are floppy babies) and complete lack of desire to feed – which is remarkable, considering what comes later in life for these individuals. Children will be prescribed growth hormone – which may normalize their stature, improve body composition, developmental milestones and cognition – but will not do anything for the hallmark symptom of the disease, hyperphagia. By the age of 3 to 4 years, children will start to show more of an interest in food, which increases over time until they ultimately develop the hallmark symptom of hyperphagia – an insatiable desire to eat, the brain telling you that you are starving, even as you eat. Individuals affected by PWS never feel full and are constantly focused on one thing - food, and how to get it. Left unsupervised, they have the potential to literally eat themselves to death – much like a situation described by a mother of a teenager with PWS who ran away from home, begged strangers at a restaurant for food, ate enough that his stomach ruptured, and he passed away. The only remedy for hyperphagia today is to restrict access to food – closed kitchens, locked refrigerators and pantries, motion activated cameras and alarms. Families live in the constant fear of problematic behaviors resulting in extreme outcomes such as 911 calls from school, visits to ERs, police intervention and, in many situations, the need to be cared for in an institutionalized setting. Unaffected siblings will often have PTSD, and families have trouble staying together. And invariably, there is need for constant supervision for life.

Numerous drugs have been tested to treat hyperphagia in PWS in late-stage trials, each one of them has failed and many companies have been dissolved. Our drug, DCCR, is a once-a-day pill which was evaluated in an approval-directed study from 2018 through 2020, ending a few months after the start of

the Covid-19 pandemic. The study missed its primary endpoint, but analysis of the pre-Covid data showed statistical significance in favor of DCCR. Long term data, now up to 4 years in some patients, and comparisons to the natural history of the disease show statistical significance as well as clinically meaningful improvements with the drug. We have heard from families and physicians that children on DCCR have significantly improved academic performance, participate in varsity sports and extracurricular activities, go on dates, have sleepovers, go to prom without parents having to supervise them – essentially, they can live their lives as typical kids/young adults. We have been asked to generate additional controlled data before submitting a marketing application for DCCR. We have just completed that study, which shows highly statistically significant and clinically meaningful benefits of DCCR, and we hope to submit an NDA to the FDA next year.

We need a regulatory framework that recognizes the novel, complex and heart-breaking nature of diseases such as PWS. We cannot continue to apply the same regulatory paradigm to all diseases and all drugs – context must play a role. It is amazing to see new options available for people with ALS, and the first approval of a drug for Friedrich's Ataxia. But there are also diseases like Barth syndrome, where a drug with promising data may not have a path forward and the program may shut down. Regulatory delays such as our 3+ year back-and-forth with the FDA, have real-life impacts. For companies such as ours, programs will be cut, and some will even have to shut their doors. Every day, every week, every month, every year – symptoms will worsen, sometimes in irreversible manners, and patients may even die as they wait for treatments.

The FDA is and needs to remain the premier regulatory body of its kind in the world. What is desirable is a rigorous regulatory process, but one that balances the risk of approving a drug with the risk of having no treatments available for a desperate population. The Promising Pathway Act is a significant step in the right direction. Time-limited provisional approval would allow patients the ability to access potentially life-changing treatments as additional meaningful data is generated to justify their use. Availability of such treatments would be driven by clinically relevant data, and final approval would come only upon rigorous analysis of data generated from natural history studies and/or patient registries.

In closing, I truly appreciate the opportunity to share Soleno's story and highlight the significant unmet need for rare disease communities, and, in particular, the PWS community. Thank you Chairman Casey, Ranking Member Braun, and members of the Committee for your time. I look forward to your questions and discussion.

Subcommittee on Aging
Hearing on "Unlocking Hope: Access to Therapies for People with Rare, Progressive, and Serious Diseases"

October 26, 2023

Holly Fernandez Lynch, JD, MBe, Assistant Professor of Medical Ethics and Law, Perelman School of Medicine and Carey Law School, University of Pennsylvania

SUMMARY

- FDA already has and exercises substantial regulatory flexibility to approve promising drugs for rare, serious diseases. Where it needs additional adjustment is in requiring rigorous follow-up studies after approval to confirm these drugs are truly beneficial.
- The Promising Pathway Act would set the bar for provisional approval and later confirmation of drug benefit too low, resulting in more drugs on the market, but not necessarily more drugs *that work* to treat people with rare, serious diseases.
- Weak approval standards inhibit development of evidence that all patients need to guide treatment decisions and risk interfering with development of other possibly better drugs.
- Patient registries have limited ability to demonstrate drug effectiveness because they lack randomization and blinding; observed differences in outcomes may therefore result not from the drug, but from other differences between patients. This is especially true when the disease is heterogenous, its natural history is not well understood, or a drug's effect is small.
- The Promising Pathway Act faces additional shortcomings as currently drafted, including lack of clarity about how a drug moves from provisional to traditional approval and requirements for provisional approval to be renewed.
- FDA and NIH have undertaken a variety of efforts, including recent initiatives, to support scientific advancement in rare disease drug development and to reduce regulatory burden.
- This committee can help facilitate the goal of improving access to effective rare disease treatments by: (1) ensuring funding for rare disease research and efforts to promote clinical trial accessibility; (2) encouraging use of FDA's expanded access pathway; and (3) clarifying that FDA has the authority to require and enforce post-market efficacy studies whenever it approves a drug with uncertain benefit, in order to ensure patients, clinicians, and payers all have the confirmatory evidence they need.

Senator Casey, Ranking Member Braun, and distinguished Members of the Committee, thank you for convening this important hearing and inviting me to testify. I am grateful for the opportunity to submit written comments in addition to my hearing testimony to inform a goal we all share: helping patients with rare, serious diseases live better and survive longer.

BIOGRAPHY

My name is Holly Fernandez Lynch. I am a bioethicist and attorney by training. I'm also an assistant professor of medical ethics and law at the University of Pennsylvania, which has asked me to note that opinions expressed in this testimony do not necessarily represent those of the University of Pennsylvania Health System or the Perelman School of Medicine. My remarks also should not be attributed to the National Academies committee on which I currently serve, focused on accelerating treatments and improving quality of life for people living with amyotrophic lateral sclerosis (ALS), or to any other organization with which I am affiliated. I receive research funding from Arnold Ventures to study issues relevant to this hearing, but no funder has played a role in preparing this testimony.

I obtained my JD and master's degree in bioethics from the University of Pennsylvania in 2006. I worked as an associate attorney in the pharmaceutical and biotechnology practice group at Hogan Lovells (then Hogan & Hartson), where I was trained in FDA law and policy and gained exposure to the world of clinical research and regulation and FDA approval standards. I then served as a bioethicist in the Human Subjects Protection Branch at the National Institutes of Health (NIH) Division of AIDS. There, I helped address ethical challenges arising in US and global HIV prevention and treatment research. I next served as a senior policy and research analyst supporting President Obama's Commission for the Study of Bioethical Issues, where I worked on reports addressing historical research ethics abuses and improving modern research protections. Immediately before returning to Penn, I served as the executive director of the Petrie-Flom Center, a health policy and bioethics research program at Harvard Law School, teaching and mentoring students and leading research to improve clinical trial participation, conduct, and oversight, among a variety of other projects.

I joined the faculty at Penn in 2017, with a primary appointment in the medical school and secondary appointment in the law school; I have recently been promoted to associate professor, effective July 2024. I also serve in several national leadership roles, including President-elect of the board of directors for the American Society of Law, Medicine, and Ethics and board director for Public Responsibility in Medicine & Research. I founded and co-chair the Consortium to Advance Effective Research Ethics Oversight, an organization that aims to define, measure, and improve the quality of Institutional Review Boards (IRBs) responsible for protecting the rights and welfare of research participants. In addition, I served as a member of the US Department of Health and Human Services Secretary's Advisory Committee on Human Research Protections (SACHRP), offering expert advice and recommendations on government research regulations and policy. Finally, I am an active member of the Compassionate Use and Preapproval Access Working Group at the NYU's Grossman School of Medicine.

Informed by this experience, my scholarship focuses on FDA drug approval policy, access to investigational medicines before FDA approval, and clinical research ethics, regulation, and oversight. **The overarching question that drives my research is this: how should we balance speed and certainty in decisions that affect access to new drugs?** This question raises important ethical issues regarding respect for autonomy, informed decision-making, avoidance of exploitation, and promotion of benefit for individual patients and broader populations, both in the present and the future. The question is also informed and affected by legal levers that influence what sort of evidence is generated and when. I have published extensively in this space and would be happy to provide copies of relevant articles.[1–14]

Although I have bioethics and legal expertise that I hope this committee will find useful, I have no immediate personal stake in the outcome of this hearing, as I am not myself facing a rare, serious disease. I recognize that some believe lived experience is the only credential relevant to these policy issues and I certainly agree that personal experience is valuable in this context.[15] However, the sad reality is that rare, serious diseases are not rare in the aggregate. Any one of us could find ourselves and our loved ones affected at any time. We all have an interest in these important issues and I care about them deeply, for the sake of all who are suffering today and all who may be suffering tomorrow.

MY KEY MESSAGE TO THE COMMITTEE

With the help and guidance of some tremendous advocates, my work has led me to better understand the deep challenges facing the community of people living with and affected by ALS, as well as other rare and life-threatening diseases that lack good treatment options. From the "Right to Try"[16] to the "Promising Pathway Act," I have seen patients and advocates seek legislative solutions that they hope will provide speedier access to new drugs, emphasizing their willingness to accept great uncertainty and risk in pursuit of something – anything – that will work. I understand these approaches and why they seem attractive. However, I accepted the Committee's invitation to testify because I believe we must be wary of unintended consequences in efforts to promote access to unproven drugs.

My key message is that we must avoid approaches that displace the essential goal of getting patients more drugs *that work* with the deflated goal of simply getting them more drugs. That is the risk posed by the Promising Pathway Act.

FDA'S EXISTING REGULATORY FLEXIBILITY

To be clear, **I support regulatory flexibility in FDA drug approvals.** By statute, FDA must determine that new drugs are safe and effective – a standard that requires both scientific assessment and policy judgment.[17] The real question is whether a drug is safe and effective *enough*, given the disease at hand. Context matters and it is reasonable to accept less certainty about a drug to treat ALS or a fatal pediatric disorder than a drug to treat migraines.

With that in mind, it is essential to acknowledge that **FDA already has tremendous regulatory flexibility for serious diseases with unmet treatment needs – and the agency often uses it.** Importantly, however, regulatory flexibility does not mean that every drug is or should be approved.

Perhaps the most well-known type of flexibility available to FDA is accelerated approval, which allows certain drugs to be approved based on measures other than those directly

assessing how a patient feels, functions, or survives. Accelerated approvals are granted based on a reasonable prediction of benefit supported by a drug's impact on unproven surrogate or intermediate endpoints, such as reduction in certain biomarkers in the blood or brain. They are followed by required post-market trials to confirm whether the predicted benefit is real; if benefit is not confirmed, FDA may utilize an expedited process to withdraw approval. Accelerated approvals are on the rise, including outside oncology and in the neurodegenerative disease space.[18,19] However, more than a third of accelerated approvals have incomplete confirmatory trials, and a third of those are past their due dates, with uncertainty dragging on for patients – including for very pricey drugs.[18] In addition to delays, the quality of confirmatory trials is often questionable and it can be difficult to withdraw approvals even when confirmatory trial results fail to show benefit.[5,20] These problems challenge the accelerated approval compromise, which is intended to provide speedy access to promising drugs now with evidence of benefit later.

Beyond accelerated approval, FDA also has other types of flexibility. Most importantly, **the agency can and does approve drugs even when trials fail to show benefit on pre-specified endpoints**. For example, FDA approved Biogen's Qalsody (tofersen), a drug to treat a rare genetic type of ALS, even though the trial did not meet its primary or secondary endpoints. The agency has also approved drugs for other rare diseases despite failed trials, including an ultra-rare connective tissue disorder called fibrodysplasia ossificans progressive (FOP) and Duchenne's muscular dystrophy.[21] In fact, 10% of the drugs FDA approved between 2018-2021 had pivotal trials with null findings.[22] I also want to be clear that FDA does not require a demonstrated survival benefit for drug approval, nor does it require that benefit be demonstrated in all study participants, although these are misconceptions I often hear; demonstrated or likely functional benefit in a subgroup of the trial population can also suffice, especially if the trial was well-designed to measure that outcome.

Finally, **FDA has demonstrated an increased willingness to approve drugs based on just one pivotal trial rather than the gold standard of at least two adequate and well-controlled clinical investigations**. In 2022, 65% of drug approvals were supported by a single efficacy study,[23] including Amylyx's ALS drug, Relyvrio (sodium phenylbutyrate and taurursodiol), which the European Medicines Agency (EMA) has refused to approve until it can

review results of an ongoing Phase 3 trial given uncertainty about the drug's benefit. Moreover, FDA is not demanding perfection from the single studies supporting these approvals; they are often not randomized, without concurrent controls, and lack results with exceptionally strong statistical significance.[24]

Importantly, **when FDA grants early approval to drugs with uncertain benefit outside the accelerated approval pathway, it does not require companies to complete additional studies to ensure that benefit is confirmed**.[2] It is that disconnect between early approval and confirmation of efficacy that especially concerns me.[2] Unfortunately, I fear **the Promising Pathway Act would inadvertently exacerbate the problem**.

PRIMARY CONCERNS REGARDING THE PROMISING PATHWAY ACT

The proposed Promising Pathway Act would create a new category of "provisional approval" for drugs intended to treat, prevent, or diagnose a serious or life-threatening disease or condition, followed by required patient registries that FDA would be required to review annually to assess the drug's "side effect profile" in relation to its benefit.

Especially because I know many have worked hard on this piece of legislation, let me start with the bill's strengths. First, it would impose automatic expiration dates on provisionally approved drugs, with 2-year terms that may be renewed for a total maximum period of 8 years. That's helpful because **it is a step in the right direction to limit how long drugs with uncertain benefit are allowed to remain on the market**. Second, the bill would require that further data be collected from all patients receiving a provisionally approved drug. Although the approach the bill takes to that data collection has shortcomings as described below, it is at least an important acknowledgment that **uncertain approvals should always be followed with additional evidence**. Third, the bill would require specific informed consent from patients prescribed a provisionally approved drug, acknowledging that it did not undergo the usual process for FDA approval, and explicit acknowledgment of provisional approval status in all drug labeling and promotional materials. Both steps would help **draw patient and clinician attention to relevant shortcomings in the evidence supporting the drug**, an improvement

over current approaches that may lead to confusion over the evidence supporting accelerated approval drugs or those approved through other types of regulatory flexibility.[25]

Despite these strengths, the bill raises important concerns, including several that leading experts in FDA pharmaceutical law, policy, and ethics shared with Senator Braun's office in 2020 in the context of this bill's predecessor, the Conditional Approval Act.[26] **In sum, the Promising Pathway Act would set the bar for both provisional approval and later confirmation of drug benefit far too low.**

THE PROBLEM WITH WEAK APPROVAL STANDARDS

Rather than the current evidentiary standard for drug approval, which requires "substantial evidence" of effectiveness, **the Promising Pathway Act would allow approval based on "relevant early evidence" from "adequate and well-controlled investigations, including early-stage clinical investigations" to establish that the drug provides "a positive therapeutic outcome," a much lower standard**. The phrases "relevant early evidence" and "positive therapeutic outcome" are not further defined and it is unclear what the lower evidentiary bound might be. Could relevant early evidence come from Phase 1 trials or unplanned post-hoc analyses? What drugs couldn't be approved on this standard?

Unfortunately, many drugs look promising in early development or based on various unplanned subgroup analyses, only to fail to demonstrate benefit in later studies. To take one example, in dexpramipexole's Phase 2 trial, ALS patients receiving the highest dose saw almost 50% slower decline in muscle function than those receiving placebo, although other results were marginal. In the Phase 3 trial conducted in nearly 1000 ALS patients across 11 countries, however, the drug was not effective in slowing loss of muscle function or improving survival.[27]

In another salient example, BrainStorm's investigational stem cell therapy for ALS, debamestrocel (branded NurOwn), missed all primary and secondary endpoints in its Phase 3 trial by a very wide margin. Given these results, FDA refused to file the company's biologics license application, but the company nonetheless filed over protest. At a recent advisory

committee meeting, FDA explained that in addition to failure on pre-specified endpoints, biomarker data did not provide evidence of NurOwn's clinical effect and there was a survival imbalance: more patients who received the drug died than those who received placebo. The agency also noted serious product quality deficiencies and manufacturing concerns, such that even if the product were effective, it was not clear the company could produce it consistently for future patients. The company pointed to additional analyses suggesting a possible treatment effect in some patients with earlier disease, but FDA statisticians explained that unplanned subgroup analyses have a "high risk of obtaining false positive results . . . and break randomization that may result in imbalance in measured and unmeasured baseline prognostic factors, which leads to confounding."[28] In other words, any benefit they show may not be real.

Ultimately, the advisory committee voted 17-1 (with 1 abstention) that the data presented did not demonstrate substantial evidence of effectiveness. Notably, the committee included a patient living with ALS, who voted with the majority against approval. In addition, the ALS Association (ALSA), the largest patient advocacy funder of BrainStorm's NurOwn program, declined to endorse the drug after the company refused to provide a full data package to undergo the Association's independent peer review process. ALSA explained that "[t]he amazing testimonials we have seen online do not align with the data that BrainStorm has shared with us or has been published in peer-reviewed publications."[29]

Last week, BrainStorm withdrew its NurOwn application and stated that it plans to conduct another Phase 3 trial to follow up on the exploratory subgroup analyses. Even though the drug remains unapproved, the company can use FDA's expanded access pathway to provide patients with NurOwn for treatment use while this next trial is being planned; it can also provide the drug via expanded access to patients who do not qualify for the trial once it is up and running. In addition, FDA allows recovery of direct costs for the provision of expanded access drugs[30,31] and there are other mechanisms for covering expanded access expenses specifically in the context of ALS.[10]

To some, NurOwn is the poster child for why the Promising Pathway Act is needed. A drug that may help some patients has not been able to meet the current statutory standard for

approval. But I think what the NurOwn example shows is just the opposite: the current approval standard must be maintained.[32] Even with all the flexibility that FDA has – and has shown in prior rare disease drug approvals, including for ALS – it could not find anything in the NurOwn data to hang its hat on because the evidence wasn't there. Why bother conducting efficacy trials simply to ignore their results? **Rare disease patients deserve better than to be treated like second-class citizens, sold drugs not even shown to be likely to work.**

It is certainly understandable for individual patients to be willing to risk substantial uncertainty for themselves before better evidence comes available, especially when they have no time to lose, and I support their right to do so via expanded access. However, **weakened approval standards affect all patients**. Sometimes I hear advocates seeking approval of a new drug say, "if other patients don't want to take it, they don't have to" – indeed, that's just what some have said about NurOwn. And it's true. But the issue is far more complex.

One of FDA's most important roles is to incentivize companies to produce information that patients and clinicians need to meaningfully guide their treatment decisions.[33] Under the Food, Drug, and Cosmetic Act, companies cannot sell their drugs – and therefore cannot profit – until they generate strong enough evidence to convince FDA the drug is safe and effective. As a result, companies seek to generate the evidence that FDA demands. If FDA demands less, patients and clinicians will have less, even if they really want and need more.

One must look only as far as the dietary supplement industry to see how this plays out. Unlike drugs, dietary supplements can be marketed without evidence of safety or effectiveness. As a result, we simply lack that evidence – and any meaningful innovation.[32] Imagine if what you had available to treat your life-threatening illness was rows and rows of products, none of which you knew worked. **More does not always mean better.**

This is especially true when we consider the opportunity costs. Even when there are no proven treatment options for a life-threatening disease, the choice about whether to try an uncertain drug has important tradeoffs. Side effects described as mild can cause substantial discomfort – is time spent dealing with diarrhea, nausea, headaches, extremely dry skin, or dry

mouth worth it for a drug that might not work? Surely for some, the answer will be yes. But how are others to make those decisions without information to guide them? Patients may also have to decide whether to incur hefty financial costs for an unproven drug – or whether to take a provisionally approved drug instead of enrolling in a trial of one that might be better. That latter choice is particularly salient because if patients seek unproven but approved drugs rather than choosing to participate in research to study new alternatives, it will be difficult to study those alternatives and improve the field. In this way, **weak FDA approval standards can entrench poor treatment options, leaving future patients no better off than patients today**.[1,5,8]

FDA's existing expansive regulatory flexibility raises many of these same concerns. However, **the response should not be to further weaken approval standards – at the very least, it should be to shore up the ability to collect rigorous, high-quality data after approval.**[2] Unfortunately, patient registries do not meet that bar. The Promising Pathway Act asks them to do more than they are capable of.

THE PROBLEM WITH PATIENT REGISTRIES

Because the Promising Pathway Act does not require any additional studies following provisional approval beyond a patient registry, and because it directs FDA to allow use of real world evidence to fulfill follow-up requirements and support applications, the bill appears to contemplate registry data serving as the exclusive support to move a drug from provisional to traditional approval. However, for several reasons, **registries are limited in their ability to demonstrate a drug's effectiveness, making this one of the most important concerns about the bill**.

Most importantly, **registries do not involve randomization or blinding, and they often lack a concurrent control group**. In addition, they often fail to include confounding patient and medical center variables that could influence outcomes.[34] Patients who are prescribed and choose to take a provisionally approved drug – the patients who would be followed under the Promising Pathway Act – are likely to be meaningfully different from those who do not. For example, they may be healthier or perhaps sicker, they may have different comorbidities, they may be taking

different concomitant medications, they may have different access to care, services, and treatment, and they may be more optimistic about a drug's likelihood of working. Similarly, physicians who prescribe a provisionally approved drug are likely to engage in treatment behaviors that differ from their non-prescribing colleagues. Patients who are enrolled in an open label trial in which they know they are receiving the active treatment of interest, and the physicians treating them, often report positive outcomes that can be difficult to evaluate. These challenges are exactly why randomized, blinded study designs are so valuable, even if observational data are available from patients who are not taking the drug of interest. **Randomization and blinding help make sure that the only difference between patients, including relevant differences that may be difficult to predict or measure, is whether they are receiving the investigational drug.** This, in turn, allows any differences in outcomes to be causally attributed to the drug.

Sometimes an external control group can address these challenges, for example relying on data collected from patients in the control group of an earlier study or natural history data for comparison. FDA has explained that "if the natural history of a disease is well-defined and the disease is known not to improve in the absence of an intervention or with available therapies," historical information can potentially serve as a control group, if available.[35] However, **when a disease is heterogenous with regard to its clinical presentation, severity, prognosis, speed of progression, and other factors, when its natural history is not well understood, and when a drug's effect size is likely only small or moderate, randomization is essential to proving whether a drug works**. Without it, the risk of bias and confounders is too great – in other words, it becomes impossible to know if it is the drug that caused the effect, or if it is one of the many other differences in background conditions between the patients.

Unfortunately, many rare diseases lack strong natural history studies and face the kind of heterogeneity within and across patients that makes reliance on external control groups unreliable. In ALS, for example, "plateaus and small reversals are common, especially over brief intervals," such that stable disease for a short period of time should not be interpreted as a treatment effect.[36] In contrast, large, sustained ALS reversals are rare – yet that type of large

drug benefit likely would be clear from an early phase trial and not just a registry, potentially supporting traditional rather than provisional approval.

To be clear, the type of real world data generated by registries can be important to tracking safety, evaluating the outcomes achieved for a wider range of patients facing a wider range of circumstances than are typically included in clinical trials, and gathering data over a longer period of time. Accordingly, I do not mean to suggest that registries are never helpful – they can be. In fact, because they can be specifically designed to collect certain types of information, they can be better sources of real world data than electronic health records (EHRs) and payer claims data, which are primarily intended for other uses and therefore may not be fit for purpose.[37] The problem is simply that – **even for rare diseases – registries typically cannot substitute for rigorous, prospective, randomized trials when we're trying to determine whether a drug in fact works**.

With that substantial limitation in mind, it is also important to be aware of two additional challenges facing registries. First, having distinct registries for individual drugs can prevent them from being used for important comparative effectiveness research due to differences in the data collected. A single unified registry with consistent data requirements would be most helpful. Second, registries rely on clinicians to input the relevant data during routine clinical practice, a time consuming and uncompensated task that can result in major gaps in data collection and quality. Registries linked to EHRs and claims data therefore can be preferable to any single source on its own, and registries required by payers are most likely to have complete data.

ADDITIONAL CONCERNS REGARDING THE PROMISING PATHWAY ACT

Although the most foundational concerns with the Promising Pathway Act are the dual concerns of weakened standards for approval and insufficient requirements to confirm benefit, the bill presents several additional issues:

- The bill proposes to shorten the time for FDA review of provisional approval applications to only 90 days. However, even if review occurs on a rolling basis, **90 days is likely not**

enough time for FDA's scientists to adequately assess the relevant data, including with regard to possible safety concerns. Drugs granted priority review designation must be reviewed within 6 months, a timeframe that already places tremendous pressure on reviewers, especially given numerous unfilled positions at FDA. Moreover, available evidence indicates that post-market safety events are more common for drugs that were approved near their regulatory deadline.[38,39]

- The bill discusses several ways that provisional approval could be rescinded or withdrawn, e.g., due to side effects or passing expiration dates. However, **it is not clear how a drug could move from provisional approval to traditional approval**. It appears the bill contemplates this happening as a result of real world evidence generated by the required registry, but that is insufficient, for the reasons noted above.

- Relatedly, **the bill would problematically require FDA to consider waiving requirements for adequate and well-controlled studies when deciding whether a provisionally approved drug should move to traditional approval**. This means a drug could move to traditional approval with substantial uncertainty about whether it works and for whom.

- The bill takes the Food, Drug, and Cosmetic Act's existing language regarding "substantial evidence" of effectiveness and instead uses that same language in the context of describing the evidence of safety needed to support provisional approval, resulting in text that is very difficult to parse. Specifically, the bill calls for "substantial evidence of *safety* for the drug, such that there is evidence . . . to evaluate the *safety* of the drug involved, on the basis of which it could fairly and responsibly be concluded that the drug will have the *effect* it purports or is represented to have . . . ." (emphasis added). However, **evidence regarding safety has nothing to do with whether the drug will have its purported effect**.

- The bill discusses provisional approval based on "scientifically substantiated surrogates," seemingly without recognizing that FDA can already grant accelerated approval (with more concrete post-market study requirements than a patient registry) based on these unvalidated surrogate endpoints.

- The bill notes that approved researchers and medical professionals may access registry data for public health research in a de-identified, aggregated manner. However, **it does not indicate who may be denied access and on what grounds**. For example, it may be important for sponsors developing competing drugs to have access to the data. In addition, aggregated data may obscure key insights that can only be seen through individual level data, which could also be de-identified. Payers should also have access to registry data to support their decisions about coverage of provisionally approved drugs.

- The bill assumes that provisional approval may be renewed up to 3 times, for a total of 8 years. However, it offers **no description of what will be needed to grant these renewals**.

- Although the bill acknowledges that provisional approval will be based on less certain evidence, it expects payers to cover provisionally approved drugs as they do drugs approved on traditional standards of evidence. For Medicare, which has only very limited ability to negotiate price under the Inflation Reduction Act, that would mean paying whatever price the sponsor sets, despite substantial uncertainty.

EFFORTS TO ADDRESS CHALLENGES IN RARE DISEASE DRUG DEVELOPMENT

Although the Promising Pathway Act is not the right way forward, there are a number of other opportunities to meaningfully improve rare disease drug development. **The most important of these are upstream from FDA**, including support for scientific advancement in understanding these diseases so that sponsors are able to target the right mechanisms and conduct trials that ask the right questions through the right designs most likely to identify drugs that work. **Too often, the problem facing rare disease patients is not that FDA is standing in the way of good drugs – but rather that there are no good drugs at all.**

In addition to the wide-ranging flexibility FDA already exercises in drug approval, it has also undertaken several initiatives to address scientific bottlenecks and regulatory barriers arising

in the rare disease context, especially over the past year. Importantly, FDA is making these changes within their existing statutory authority without legislative change. For example:

- FDA's **"Support for clinical Trials Advancing Rare disease Therapeutics" (START) program**, informally described as Operation Warp Speed for rare diseases,[40,41] will be piloted with companies developing gene therapies to address rare or serious pediatric diseases or drugs to treat rare neurodegenerative conditions. The Center for Biologics Evaluation and Research (CBER) and the Center for Drug Evaluation and Research (CDER) will each select 3 sponsors to begin the program in 2024. The companies will obtain frequent advice and ad hoc communication with FDA staff to address product-specific development issues, such as study design, choice of control group, and selection of patient population. The hypothesis is that speeding response times – and helping sponsors recognize when they should be asking questions – will speed drug development times and help avoid problems that could inhibit approval down the road, especially for sponsors with less FDA experience. In addition, CBER's director, Peter Marks, has encouraged accelerated approvals for biologics, sought to help companies address manufacturing challenges for biologics early in development, and acknowledged the need for flexibility around what trials will be feasible in rare disease.[40]

- As announced last fall, CBER and CDER established a **Rare Disease Endpoint Advancement (RDEA) Pilot Program** to support novel efficacy endpoint development for drugs to treat rare diseases, through close collaboration between FDA and sponsors.[42] The pilot will include sponsors with an "active investigational new drug (IND) or pre-IND for the rare disease, or sponsors who do not yet have an active development program but have, or are initiating, a natural history study where the proposed endpoint is intended to be studied."

- Early in 2023, FDA launched another pilot program, called **"Split Real Time Application Review" (STAR)**, which seeks to allow earlier patient access to therapies that address an unmet medical need by shortening the time from the date an application is submitted to the action date.[43] The program applies to supplemental drug and biologics applications proposing new uses of approved therapies to address unmet medical need when clinical evidence

indicates the drug may demonstrate substantial improvement over available therapies. FDA will begin to review data once it receives a Part 1 submission including, among other things, all components of the efficacy supplement except for final clinical study reports. The sponsor must then submit clinical study reports and integrated summaries of safety and effectiveness as a Part 2 submission within 3 months. Because FDA will begin reviewing the data sooner, decisions will ideally move more quickly. However, unlike the Promising Pathway Act, the STAR program does not change the relevant PDUFA date, the clock for which would start with the Part 2 submission, nor would it apply to products with no prior approvals.

Although each of these programs needs to be assessed following their pilots, they demonstrate FDA's efforts to be responsive to the needs of the rare disease community, especially when considered alongside the expansive exercise of regulatory flexibility described above.

In addition, FDA has developed a **5-year action plan for rare neurodegenerative diseases**, including ALS, which it published last year in response to a directive from the Accelerating Access to Critical Therapies for ALS Act, or "ACT for ALS."[44] ACT for ALS also directed grant funding for scientific research using data from expanded access to investigational ALS drugs; development of a public-private partnership for rare neurodegenerative diseases including both NIH and FDA; and an additional grant program focused on characterizing neurodegenerative diseases and their natural history, identifying molecular targets, and increasing the efficiency and productivity of clinical development of therapies.

As part of FDA's action plan, it developed an inter-center **Rare Neurodegenerative Diseases Task Force** intended to coordinate efforts toward advancing science and drug development for rare neurodegenerative diseases and developed an **ALS Science Strategy** to address challenges to ALS drug development. That strategy focuses on **improving characterization of ALS disease pathogenesis and natural history, facilitating access to clinical trials including through decentralized models, encouraging the incorporation of expanded access into clinical development programs, enhancing trial infrastructure and agility, facilitating data sharing, and exploring innovative trial designs including novel statistical approaches for small populations**. Note that each of these areas focuses attention on

improving the science rather than weaking approval standards, with the explicit intention that improvements in ALS science will also benefit other rare neurodegenerative diseases. A variety of other scientific efforts are also underway, including **NIH's Therapeutics for Rare and Neglected Diseases (TRND) Program**, which is leading an effort to screen existing compounds for potential repurposing to treat rare and neglected diseases and working to develop a "gene therapy toolbox" that can help address obstacles in manufacturing and delivery.[45]

CONCLUSION AND RECOMMENDATIONS

The terrible reality is that many patients, both children and adults, are facing serious and life-threatening diseases without good treatment options. However, that is not because FDA is blocking access or refusing to exercise its substantial flexibility to approve new drugs. Instead, it is because in too many areas, the science has not caught up to the need. **Addressing that scientific gap should be the focus of our attention.**

In the meantime, I recognize patients need both evidence and access. This committee might facilitate that goal in several ways:

1. **Ensuring funding both for rare disease drug research and efforts to promote clinical trial accessibility**, so that every patient who wants to participate in a clinical trial can do so.

2. **Supporting efforts to encourage the provision of investigational drugs to patients unable to participate in clinical trials through FDA's expanded access pathway.**[8]

3. **Clarifying that FDA has the authority to require post-market efficacy studies even for drugs approved outside the accelerated approval pathway, encouraging FDA to vigorously enforce post-market study requirements, and supporting FDA when it seeks to rescind approvals for drugs that fail to confirm benefit**. Importantly, these steps may ease agency concerns about granting early approvals in specific cases, adding flexibility.[2]

* * *

Thank you for inviting me to testify and for your commitment and attention to these critical issues for all patients and families that are or will be affected by rare, serious diseases.

Acknowledgments

Thank you to Dr. Reshma Ramachandran, MD, MPP, MHS, Assistant Professor of Medicine at Yale School of Medicine, co-director of the Yale Collaboration for Regulatory Rigor, Integrity, and Transparency, and chair of the Doctors for America FDA Task Force for assistance in preparing this testimony. All views expressed are my own.

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Written Testimony of Keith Desserich
Chairman and Co-Founder
"Unlocking Hope: Access to Therapies for People with Rare, Progressive and Serious Diseases"
United States Senate Special Committee on Aging
October 26, 2023

Thank you Chairman Casey, Ranking Member Braun and distinguished members of the Committee for the opportunity to discuss the Promising Pathway Act, something I consider vital to our efforts to find the "homerun cure" for cancer.

As you stated, I am a father. My daughter, Elena, fought a cancer called DIPG brain cancer when she was 6-years-old. Like thousands of families before us, they told us we had no hope, there were no trials available and to go home and make memories. Sadly, she understood this as well, fully aware until her last day that there was nothing we could do. You see, with DIPG, each day you see your children lose something. One day it was he ability to see out of her left eye, the next her ability to speak, then her ability to walk, until one day it is her ability to breathe, swallow or her heartbeat. Yet the brain is untouched in a particularly cruel cancer that progresses within weeks. Many experts regard this as the "cancer they fear most." Other experts see in it the chance to advance strategies like no other cancer does. Universally it is known as a "homerun cure" cancer.

We wrote about this one day during her battle in a blog ending simply with the words "the cure starts now" and with it started a cause as we were joined by hundreds of families and researchers that changed the course of their careers. Contrary to our wishes, this blog became a bestselling book translated to 22 languages, leading to the calling that my wife and I inherited. We have made it our mission to focus on these homerun, rare cancers and by building tools such as linked registries, intelligent patient tools, strategic research, centers of excellence and virtual hospitals that today are being used as models for other cancers. In the nearly 17 years since she lost her fight, we have partnered with 129 hospitals in 17 countries to invest in over $30 million in research and support through 135 projects.

I come here with hope. Hope for a new way to fight cancer. I believe that the FDA is well-intentioned, but in the end, no one expects this type of devastating cancer – let alone afflicting your children. Instead, I believe there is much confusion inherited from bureaucracy. And whether by regulation or guidance clarity, I argue that the system is broken and the status quo will not do.

It is important to note that Expanded Access, or Compassionate Use is not an alternative for the Promising Pathway Act. I know this not only from dealing with the loss of my daughter but also in calls with over 200 families per year asking for help in their final days.

With DIPG, a patient is frequently given only two weeks after progression to act. Expanded Access requires four levels of approval:

- 24 hours for the family or patient to react to the news
- 3 days for the doctor to determine a strategy and complete an application

- 2 weeks for the Internal Review Board to approve the methodology
- 3 days for the pharmaceutical company to respond
- 1-30 days for the FDA to render approval

That's at least a week after our child dies.

Expanded Access and Compassionate Use is a "wild west" strategy to medicine sadly predicated on your doctor's ability to craft a bureaucratic narrative to satisfy both their IRB and the FDA.

Then there is Right to Try. Slightly better with a two-level approval process, it still lacks data transparency to patients and families in an annual report model that only submits to the FDA.

The current models just don't work. They assume that "terminal" means "months to live", they assume patients are not intelligent enough to make decisions for themselves, they assume that data in less than ideal situations are worthless, and they assume that every patient is an adult.

The reality is that we don't get doctors that understand the system, we don't get a call back on the weekend and not one of these acts were designed for pediatric terminal diseases.

The Promising Pathway Act is different.

- It offers an alternative to the FDA-mandated unethical practice of trials giving the wrong drug to the wrong patients for pediatric terminal diseases. It is estimated that 1,040 children die each year from cancer. Right now, nearly every therapy designed for pediatric cancer is guided through a three-phase adult trial before we get to try it on terminally diagnosed children. Sadly enough, some of these cancers don't even affect adults, meaning that we either misapply a trial on the wrong patients or, worse yet, the drug company simply gives up. Now remember that some of our biggest advances in cancer started with pediatric cancer. You want to know why we can't advance a cure? This is why.
- It preserves critical data on outlier participants in a trial and retains it for the use by the FDA, the drug companies, the researcher AND the patients - in any third-party registry of substance, thus improving transparency.
- It addresses insurance coverage and financial burden in ways neither previous alternative has.
- It advances innovative therapies that may be impossible to subject to current trial design. Keep in mind that trials for "rare" cancers "rarely" ever achieve full accruals, leading us to either give up on good ideas or enrolling children in older trials that we already know don't work. PPA could be another model on how we could save countless lives.

PPA is not for all patients. The language is careful to consider the definition of "terminal" and does not create a shortcut to trials as it may be alleged.

It is also not lost on me the value of a clinical trial. But what is often lost on many others is the value of a QUICK and EFFICIENT clinical trial. Unfortunately, with rare pediatric cancers, we have to consider both this, and sadly in their final days – we also have to consider compassion. At any point there are roughly 200,000 people fighting a terminal disease. For them, PPA could be a lifeline to treatments they may never see before they die.

I'm a big believer in personal initiative but in this case, we may be able to go NO FURTHER unless government gets out of the way. The Promising Pathway Act is how we do this. Families are desperate for another chance: a chance at seeing their children go to kindergarten, a chance to see their child get a driver's license, a chance to see them graduate from high school, a chance to see them go to college, a chance to see them get married – a chance to see them grow up.

PPA may be the single biggest piece of legislation that costs nearly nothing, but may change everything about how we win against cancer.

Questions for the Record

U.S. Senate Special Committee on Aging
"Unlocking Hope: Access to Therapies for People with Rare, Progressive, and Serious Diseases"
October 26, 2023
Questions for the Record
Brian Wallach

Ranking Member Mike Braun

Question:

At the end of the October 26th Senate Special Committee on Aging titled "*Unlocking Hope: Access to Therapies for People with Rare, Progressive, and Serious Diseases,*" Chairman Casey cited the following excerpt from Holly Fernandez Lynch's testimony:

> "It is certainly understandable for individual patients to be willing to risk substantial uncertainty for themselves before better evidence comes available, especially when they have no time to lose, and I support their right to do so via expanded access. However, weakened approval standards affect all patients."

Chairman Casey then asked Mrs. Fernandez Lynch to talk about how regulators and policymakers should balance the needs of patients when not all patients have the same needs or risk tolerance.

Mrs. Fernandez Lynch provided the following response:

> "One of the things that I've often heard, in the context of discussing Promising Pathway, is 'if patients don't want to take a provisionally approved drug, then of course, they don't have to.' That is absolutely true. But it becomes more complicated, because when you lower FDA approval standards, that tells industry, 'this is the bar that you have to meet.' When that bar is lowered, then industry responds accordingly. And what that does is push back to patients and clinicians the need to make decisions without evidence. Some people may have that high risk tolerance, but not everybody will. That's why I think the dietary supplement example is so salient. Dietary supplements do not have to show safety and effectiveness, so industry does not demonstrate that. That's not what people who are facing these terrible diseases need.
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> "The other challenge is that, when standards are low and you allow other products on the market that have not demonstrated that they are beneficial, it complicates the development of potentially better drugs. It makes it difficult to accrue those studies.

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> "FDA has to account in its public health responsibilities not only for the interests of patients today but also the broader population of patients, which is why I am encouraging the Committee to draw on what we've heard about challenges to the expanded access pathway. I think that is the avenue that really does need to be improved to provide this balance: allowing patients today who have high risk tolerance to take unproven medicines while we continue to gather rigorous evidence. Unfortunately, patient registries are not going to get us there because they are not randomized and not controlled. They are not going to be able to answer these questions in the way that patients need to make autonomous, informed decisions about their treatment."

Ranking Member Braun asks that you respond to Chairman Casey's initial question and provide any commentary you feel necessary regarding Mrs. Fernandez Lynch's original response.

Response:

Thank you for the opportunity to respond to Mrs. Fernandez Lynch. I think it is important to make clear that the provisional approval pathway does not, in any way, lower the standard for full FDA approval, for either safety or efficacy. For an investigational treatment to be able to use the provisional approval pathway it has to complete a Phase 2 trial so that it is shown to be safe. That is the same standard for the Expanded Access Program created by ACT for ALS. The reason why EAP is not able to meet the full need of the ALS community is because there is a limit to how much funding Congress can appropriate under ACT for ALS. While ACT for ALS was an amazing step forward, there is still a need for the provisional approval pathway under the PPA.

This is why I was perplexed by Mrs. Fernandez Lynch's testimony. Her response is based on an assumption that the Promising Pathways Act will lower scientific standards for new therapies and that is inaccurate. In particular, I was frustrated by her testimony about dietary supplements as they have nothing to do with a treatment going through the clinical trials process. If you intend to respect people living with ALS and their autonomy, it is a no-brainer to pass the Promising Pathways Act. It has no effect on the standards for FDA approval. Instead, it allows people living with ALS, who can't access EAP and do not qualify for clinical trials, to have the ability to access a safe, promising treatment. That should be our collective goal as ALS is still 100% fatal despite the progress we have seen over the last five years.

U.S. Senate Special Committee on Aging
"Unlocking Hope: Access to Therapies for People with Rare, Progressive, and Serious Diseases"
October 26, 2023
Questions for the Record
Dr. Margaret Plews-Ogan

Ranking Member Mike Braun

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> "One of the things that I've often heard, in the context of discussing Promising Pathway, is 'if patients don't want to take a provisionally approved drug, then of course, they don't have to.' That is absolutely true. But it becomes more complicated, because when you lower FDA approval standards, that tells industry, 'this is the bar that you have to meet.' When that bar is lowered, then industry responds accordingly. And what that does is push back to patients and clinicians the need to make decisions without evidence. Some people may have that high risk tolerance, but not everybody will. That's why I think the dietary supplement example is so salient. Dietary supplements do not have to show safety and effectiveness, so industry does not demonstrate that. That's not what people who are facing these terrible diseases need.
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> "FDA has to account in its public health responsibilities not only for the interests of patients today but also the broader population of patients, which is why I am encouraging the Committee to draw on what we've heard about challenges to the expanded access pathway. I think that is the avenue that really does need to be improved to provide this balance: allowing patients today who have high risk tolerance to take unproven medicines while we continue to gather rigorous evidence. Unfortunately, patient registries are not going to get us there because they are not randomized and not controlled. They are not going to be able to answer these questions in the way that patients need to make autonomous, informed decisions about their treatment."

Ranking Member Braun asks that you respond to Chairman Casey's initial question, and provide any commentary you feel necessary regarding Mrs. Fernandez Lynch's original response.

Response:

Requested Additional Written Testimony
US Senate Special Committee on Aging Hearing on October 26th 2023
Dr. Margaret Plews-Ogan MD MS
December 8th, 2023

Introduction

Ranking member Braun, thank you for the opportunity to add written testimony to my oral testimony offered on October 26th. Below is my response to your request. I attempt to clarify the strength of the PPA, and to address the common misconceptions or overgeneralizations that we heard during oral testimony. The opinions expressed here reflect my own views and are not intended to reflect the position(s) of the University of Virginia.

Concern about risk posed to patients

Some appear concerned that the PPA will pose unacceptable risk to patients, and that some patients are more risk tolerant than others. Risk should be separated into risk of a drug being harmful, and risk of a drug not being effective. Just to be clear, we are not suggesting any change to the current safety standard, and the PPA would have the same safety standards as other pathways.. The FDA process involves early trials to *establish safety*, then Phase II trials to *confirm safety* and establish potential efficacy, and then Phase III trials to confirm *efficacy.* Phase III confirmatory trials can take an additional 4-8 years. The time it takes for Phase III confirmatory trials to confirm *efficacy* is time we do not have. We need, and deserve, a reliable, equitable, predictable pathway to access safe, promising therapies when safety has been established, early evidence for effectiveness has been established (ie after phase II), and the effectiveness of the drug is being confirmed. The PPA is a conditional approval pathway, and confirmatory evidence would be required of all drugs in order to achieve final approval. So what we are really discussing is a provisional approval pathway for drugs to treat disease like ALS, a universally fatal rapidly progressive disease, while the confirmatory evidence for effectiveness is being gathered for final approval. The insinuated risk of approving a therapy that has limited effectiveness is a mis-appropriated risk when the only other option is death.

The slippery slope argument

Some who are against the PPA will invoke the "slippery slope" argument, suggesting that the PPA would lead to a wild west of ineffective drugs like dietary supplements! This argument fails to acknowledge that the PPA is designed to address a very specific subset of diseases like ALS, which is universally fatal, rapidly progressive, with no alternatives. Dietary supplements should NEVER be invoked as an applicable corollary to this situation, and it belies a lack of understanding of the relevant circumstance to which the PPA would apply. It also fails to acknowledge that this is a conditional approval pathway, that safety has been established and that there is promising evidence for efficacy, and that confirmatory evidence of efficacy is required prior to final approval of any drug. Allowing a conditional approval pathway for these kinds of diseases will not change the landscape of FDA standards. First, it is small subset of diseases that would qualify for this pathway. Second, this is conditional approval, and final approval will depend upon providing the appropriate confirmatory evidence of efficacy, as required by the FDA. If that evidence is not provided within a specified timeline the drug's conditional approval will be removed under the PPA, so the legislation is actually stronger than current FDA practice.

Balancing certainty and speed

Balancing certainty and speed is fundamental to why we need a new pathway. Unfortunately, many people are afraid of putting drugs *provisionally* on the market that end up not being as efficacious as initially hoped. But in the case of the universally fatal disease, that in my opinion is not the worst error to be made. Instead, the worst mistake we can make is to *not* approve a drug that actually could have made a positive impact.

As much as I appreciate the academic concerns of ethicists, the stance that people with a rapidly progressive fatal disease need protection from themselves is an intolerably paternalistic view. There is a reason that patients, family members and their doctors who are directly facing fatal diseases are agitating for change. It is not because they are hysterical. It is because they, more than someone removed from the experience, are aware of the proper balance. Unlike the person removed from the experience, they cannot minimize, or deny, or delay. It does not make them less rational. It simply makes their thought process more grounded in reality. That is why people might say to someone who is simply studying a disease or a problem rather than living it "come here, for a moment, walk in my shoes". It is to inform rational decision-making, to help that person or entity make better, more wise, decisions. That is why we and others with proximity to the diseases that the PPA would address come to the Senate hearing to tell their story, not to get sympathy, but to inform your decision-making, your balancing question. This balance is not the same for every circumstance. That is why the Promising Pathways Act is designed to apply to only those diseases that are serious and life-threatening, rapidly progressive and terminal, with no other options. For those diseases, the balance can and should be different. I would therefore implore bioethicists to adapt their balance question to account for the particular circumstances faced by those with rapidly progressive terminal diseases, and begin to align their goals to take that lived experience into account. Surely the system can move beyond a one size fits all approach, and be nuanced enough to cope with these vastly different circumstances.

In fact, if I were the FDA, I would welcome a pathway for these rapidly progressive fatal diseases that allowed me to *provisionally* approve *safe and promising* therapies, and then remove them from the market if it became clear through confirmatory evidence, that they were not effective. It would help me to manage the uncertainty in a more measured, reasonable way than being forced to make a decision that is permanent in the midst of some uncertainty. That is why the Promising Pathways Act is a provisional approval pathway and is designed to apply only to those diseases that are rapidly progressive and terminal, with no other options. For those diseases—for people like Jim—the balance should tip toward speed of access while certainty of efficacy is being established.

Removing conditionally approved drugs that fail confirmatory trials

The PPA requires confirmatory evidence if the drug is to move to final approval. That timeline is 8 years at most. Conditionally approved drugs that are found to be ineffective in confirmatory studies would be removed from the market. If they are found to be effective, then we would have the happy circumstance of being able to compare the new drug to previously approved therapies. This is exactly the pattern we followed when moving from the early treatments of other diseases, like HIV, where the early treatments were marginally effective, and we were gradually able to create newer drugs, and combinations of drugs, that fully controlled the disease. But those early drugs prolonged lives, and created the first generation of survivors.

There are those who doubt that the FDA can fulfill its role of removing drugs that have been conditionally approved if they do not provide confirmatory evidence of efficacy. The PPA actually addresses this problem (thereby improving upon the accelerated approval pathway). It creates firm timelines for drug companies to provide confirmatory evidence or face withdrawal of approval. And it specifies penalties if the company fails to create the required registries designed to collect important follow up data. This will give important "teeth" to the FDA. In fact, in a 2021 article in Health Affairs blog (Health Affairs Blog, August 18, 2021. DOI: 10.1377/hblog20210812.337699) it was suggested that to "fix" the accelerated pathway there might be 7 essential steps. The PPA puts in place three out of the seven suggestions. The remaining suggestions primarily have to do with payment, which is generally beyond the purview of the PPA. However, the PPA does take one important step toward a health system that is truly focused on fair, predictable, accountable care of patients, and that is the requirement that insurance companies not deny coverage for these drugs solely on the basis of their conditional approval. Like drugs approved under any other FDA pathway, insurance companies must treat these approvals like any other. This will put the argument about cost of drugs squarely where it should be, which is between the drug companies and the insurance companies, and will prevent insurance companies from scuttling this responsibility off to the patients.

The worry that the PPA would change the FDA standards for the broader population

Some express concerns that the PPA would change FDA approval standards for the broader population. This is a fundamental misunderstanding of the PPA. This pathway does not apply to a broader population of patients. It is specific to a narrow set of diseases like ALS, a uniformly fatal disease, with no alternatives. It is also a conditional approval pathway that gives patients with serious fatal diseases early access to therapies while the evidence for final approval is being confirmed. It would not change the fundamental approval standards of the FDA.

Existing pathways at the FDA are insufficient.

There are those that suggest that current pathways, including accelerated approval, expanded access, and right to try, are sufficient to address our needs. This is untrue.

The accelerated approval pathway is not available to diseases like ALS, which except for a very small subset of cases related to a specific gene, does not have an accepted biomarker.

Expanded access is an important program, but the access it provides is highly variable, unpredictable, and ultimately cannot and will not provide fair and equitable early access to promising therapies for all

patients. It depends completely on the drug company's willingness to extend themselves, and upon funding to support the manufacturing of the drug and the maintenance of the expanded access program. There is no uniformity or predictability to access, for how long or to whom. It is a necessary program, but it is no replacement for a reliable, standardized conditional approval process, where the data collection can be standardized and the process is predictable, for the patients, for the physicians treating the patients, and for the companies developing and manufacturing the drug.

The Right Try program is also often invoked as a currently existing solution to the problem of early access to promising therapies. This is simply not true. Right to Try is intended to be an end stage, rescue program, one that applies after all other options are exhausted. But what does it mean to "exhaust all options" in ALS? Is it once you are on a ventilator? Once you reach the end stages of ALS, any of the drugs meant to preserve neurons are useless. Until we have a therapeutic that can undo that neuronal damage, a program like right to try is problematic. The name of the game to prolong life right now is to stop or significantly slow the disease *before* neurons are destroyed.

Patient registries

A registry, well designed and maintained, with critical data being collected from patients in the registry, can and will provide meaningful, actionable data to discern efficacy, and will be a more robust set of data than we currently have for any existing pathway to discern any safety issues that develop. The registry can and should be designed as we currently design an open label extension or a well-designed observational study. As drugs are approved and added to the treatment options, head-to-head trials can be designed to sort out which drugs work most effectively. Other diseases have used this approach very successfully, adapting designs as more drugs became available and the goal became discerning which drug or combination of drugs worked better. Some express concern about whether these registries (we can call them observational studies or open label studies) will actually be done by the drug companies. To address this concern, the PPA has both a stick and a carrot…monetary penalties and requirements for re-approval, to assure compliance. Finally, these registries will allow the FDA to have better data on safety than it has on drugs approved through other pathways, as the registry will be a failsafe mode of gathering data on side effects as the drugs are used by more people. Right now, after approval, drug safety data are only gathered through voluntary reporting from treating physicians, an unreliable and slow means of identifying safety issues. The registries will make that process transparent and much more reliable.

U.S. Senate Special Committee on Aging
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October 26, 2023
Questions for the Record
Dr. Anish Bhatnagar

Ranking Member Mike Braun

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Ranking Member Braun asks that you respond to Chairman Casey's initial question, and provide any commentary you feel necessary regarding Mrs. Fernandez Lynch's original response.

Response:

With over identified 10,000 rare diseases,[1] it is invariably true that many conditions present in heterogenous and complex ways - impacting multiple organ systems and affecting the patient population in different manners. Given the complex and heterogenous nature of rare diseases, it is not surprising that patients and caregivers have different needs to address variable symptoms as well as different levels of risk tolerance.

Congress has correctly granted the Food and Drug Administration (FDA) the authority to regulate and ensure the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices. Congress also recognized the importance of elevating the patient perspective with PDUFA V [PL 112-144], which established the FDA's Patient-focused Drug Development (PFDD) initiative; PDUFA VI [PL 115–52], which required guidance on the Benefit-Risk Assessment for New Drug and Biological Products; and the 21st Century Cures Act (Cures Act) [PL 114–255], which directed the FDA to commission the following report: "FDA Assessment of Use of Patient Experience Data in Regulatory Decision-Making."[2] The PFDD framework at the FDA is a crucial tool to understanding, incorporating, and elevating the patient perspective in drug development and decision-making – as the FDA acknowledged: "patients with chronic serious disease are experts on what it is like to live with their condition, and we have learned that they want to be as active as possible in the work to develop and evaluate new treatments."[3]

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[1] Lamoreaux et. al, *The Power of Being Counted,* Published May 27, 2022, https://rare-x.org/wpcontent/uploads/2022/05/be-counted-052722-WEB.pdf

[2] Eastern Research Group, Inc., *Assessment of the Use of Patient Experience Data in Regulatory Decision-Making Final Report,* Published June 18, 2021, https://www.fda.gov/media/150405/download?attachment

[3] Testimony of Janet Woodcock, M.D., Peter Marks, M.D., and Jeffrey Shuren, M.D., J.D., U.S. FDA Center Directors

Regulation and policy therefore need to be made and applied with context. The variability of the disease presentation, symptoms, and progression necessitate appropriate regulatory flexibility in the availability and application of approval pathways. Only 5% of the over 10,000 identified rare diseases have an FDA-approved treatment – the other 95% will not have one for the foreseeable future if we do not consider the utility of novel approval pathways and other tools. An example is

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a condition like Prader-Willi syndrome, with a prevalence rate of between 10,000 to 20,000 individuals in the United States,[4]

The currently available tools, such as Expanded Access, are impractical when it comes to scaling up to appropriately meet the needs of communities – generally, the Expanded Access program is ideal if operationalized for a small number patients at a few centers. Expanded Access is fundamentally a clinical trial, and its associated complexity does not lend it to be a tool for wider access. Another currently available tool – the Accelerated Approval Pathway (AAP) – can be useful at accelerating access to safe and effective therapies. However, the AAP is useful only in a narrow construct, which has proven to be very difficult to apply to rare diseases as only 15 out of the 70 orphan drugs approved via the AAP between 2008 to 2021 were for non-oncology conditions.[5]

Not every clinical trial is (or can be) randomized or controlled given the size and heterogeneity of disease conditions. Provisional approval, such as with the proposed Promising Pathway Act, does not necessarily mean lowering regulatory standards. Provisional approval provides a framework for regulators to use while considering very consequential questions of access to drugs for rare, serious diseases. The mere existence of a regulatory tool does not mean automatic approval, and one would expect the FDA to use it judiciously with the same regulatory discretion it applies to other expedited approval pathways.

Joint Testimony Before the United States Senate Committee on Health, Education, Labor and Pensions, March 21, 2017, https://www.help.senate.gov/imo/media/doc/JointTestimony.pdf

[4] Bohonowych et. al, "The Global Prader–Willi Syndrome Registry: Development, Launch, and Early Demographics," Published September 14, 2019, 10.3390/genes10090713

[5] Monge, MD, PhD, et. al, "Use of US Food and Drug Administration Expedited Drug Development and Review Programs by Orphan and Nonorphan Novel Drugs Approved From 2008 to 2021," Published November 1, 2022, 10.1001/jamanetworkopen.2022.39336

December 8, 2023

Dear Senators Casey and Blumenthal,

Thank you for the opportunity to provide additional information following my written testimony and participation in the October 26 hearing. I have included responses to each of your questions below and would be happy to discuss these issues further at any time.

Respectfully,



Holly Fernandez Lynch, JD, MBE
Assistant Professor of Medical Ethics and Law
Perelman School of Medicine and Carey Law School
University of Pennsylvania

U.S. Senate Special Committee on Aging
"Unlocking Hope: Access to Therapies for People with Rare, Progressive, and Serious Diseases"
October 26, 2023
Questions for the Record
Holly Fernandez Lynch

Chairman Robert P. Casey, Jr.

Question:

What are the FDA's standards for approving new drugs? Does the Promising Pathway Act change those standards? If so, how so, and what would the implications be of that change?

Response:

The Federal Food, Drug, and Cosmetic Act (FDCA), which sets the statutory standard for drug approval, requires that sponsors submit to FDA "full reports of investigations" to show their drug is "safe for use" and "effective in use."[1]

In terms of safety, FDA may not grant approval if the sponsor submits: (1) inadequate tests or insufficient information to determine the drug is safe for use under labeled conditions; or (2)

results that show the drug is unsafe or do not show the drug is safe for use under labeled conditions.

In terms of efficacy, FDA may not grant approval if the application lacks "substantial evidence" that the drug will have the purported effect under labeled conditions. The statute defines substantial evidence as consisting of "adequate and well-controlled investigations" on the basis of which experts could fairly conclude the drug will have its purported effect. This standard may be satisfied in several ways: (1) at least 2 adequate and well-controlled investigations; (2) 1 adequate and well-controlled investigation plus "confirmatory evidence," including tests of the agent in related populations or indications, convincing evidence of the drug's mechanism of action in treating the indication in question, or additional data from natural history of the disease, among other approaches; or (3) 1 statistically very persuasive study, such as a large multi-central trial with results that are highly statistically significant.[2,3]

In addition to these variations in the quantity of evidence that may be accepted to demonstrate a drug's effectiveness, FDA has flexibility regarding the type of evidence that may support approval. Traditional FDA approval is based on a demonstration of benefit on clinical endpoints that directly measure how a patient feels, functions, or survives. In contrast, under the accelerated approval pathway, FDA can approve drugs for serious and life-threatening conditions with unmet treatment need based on unvalidated surrogate endpoints or intermediate clinical endpoints deemed reasonably likely to predict clinical benefit, such as reduction in certain proteins in the brain, blood, or spinal fluid. Because these endpoints have not yet been confirmed as valid measures of clinical benefit, accelerated approval involves a compromise: early approval with some uncertainty, followed by required post-market studies to further examine effectiveness. If those post-market studies fail to confirm a drug's benefit, FDA can follow an expedited path to withdraw approval. However, post-market studies are often delayed and may rely on weak study designs due to the challenges of continued trials after a product receives FDA approval and becomes available on the market.[4,5] This is related to a key concern under the Promising Pathway Act, as explained below.

Overall, FDA has substantial regulatory flexibility in approving new drugs, which it routinely exercises. Nearly 300 drug applications have been granted accelerated approval since 1992, with a quarter of those between 2020 and 2021 (none of which were for COVID-19).[6] Moreover, a recent review of FDA approvals of novel therapeutic agents found that between the periods 1995-1997 and 2015-2017, the proportion of approvals supported by at least two pivotal trials declined from 81% to 53%;[7] in 2022, 65% of drug approvals were supported by only a single efficacy study.[8] Over half of approved orphan drugs (designated for treatment of a rare disease) were supported by trials lasting less than one year and about one-third were approved based on trials lasting 6 months or less.[7] In addition, FDA can and does approve drugs even when trials fail to show benefit on pre-specified endpoints; 10% of the drugs FDA approved between 20182021 had pivotal trials with null findings.[9] More broadly, FDA guidance acknowledges that for serious diseases, the agency may accept weaker trial designs and endpoints, fewer trials, or less statistical confidence, pointing to perceived patient "willingness to accept less certainty about effectiveness in return for earlier access to much needed medicines."[2]

Despite this expansive regulatory flexibility, the Promising Pathway Act (PPA) would amend the FDCA to unnecessarily and problematically weaken FDA's drug approval standard. Rather than the current "substantial evidence" standard, the PPA would allow provisional approval of drugs intended to treat, prevent, or diagnose a serious or life-threatening disease or condition based on "relevant early evidence" from "adequate and well-controlled investigations, including early-stage clinical investigations" to establish that the drug provides "a positive therapeutic outcome," a much lower standard. This language clearly contemplates approval based on Phase 2 trials, which primarily measure safety in the intended patient population and offer only preliminary assessments of efficacy. However, it could also support approval based on Phase 1 trials that first test a drug in people or on statistically problematic post-hoc (unplanned) analyses. This is concerning because drugs that look promising in early development or based on unplanned analyses of subsets of trial participants often fail to have their benefit confirmed in later studies.[10–12]

The PPA's solution for weak provisional approval is two-fold – but inadequate. First, provisional approval would be time-limited, with an initial 2-year approval period, renewable for up to 8 years total. Second, the PPA would require that treated patients participate in "an observational registry" until either the drug is granted traditional approval or provisional approval is rescinded. Under such a registry, information will be collected about patients taking the drug. However, registries do not involve randomization or blinding, and they lack concurrent control groups of patients not taking the drug to provide data for comparison, all of which are critical design features that help make clear whether any benefits experienced by patients are due to the drug and not something else.[13–15] These design features are especially important when a disease is heterogenous in how it affects patients (e.g., some people living with ALS are "fast progressors" and some are "slow progressors"); its natural history is not well understood (e.g., people living with ALS may experience plateaus or reversals in their progression, over the short term[16]); or a drug's effect size is modest (e.g., a slowing of progression as measured by the slope of decline on a functional rating scale over a few months). Each of these factors, which are common, can substantially impair the ability to meaningfully interpret observational data. Yet the PPA does not require any additional studies beyond the registry and instead directs FDA to allow use of real-world evidence (such as a registry study) to fulfill follow-up requirements and support applications for traditional approval. It also directs FDA to "consider the option to waive requirements for adequate and well-controlled studies" when determining whether a provisionally approved drug should move to traditional approval. Accordingly, the bill appears to contemplate registry data serving as the exclusive mechanism to confirm drug benefit, even though registries are usually incapable of demonstrating a drug's effectiveness, even for rare diseases. This is one of the PPA's most worrisome shortcomings, explaining why both the time-limited nature of provisional approval and the registry requirement are insufficient to assuage concerns about weakened standards.

One implication of amending FDA's approval standard as the PPA proposes is that more drugs may be allowed on the market, but these drugs will not be supported by the evidence necessary to guide patients and clinicians in their treatment decisions. Even dying patients need evidence about whether a drug works and for whom, as well as how to use effective drugs to maximize benefit and minimize risk. Even for ostensibly safe drugs, unpleasant side effects may be worthwhile only for drugs that offer real benefit. One need only look as far as the dietary supplement industry to see the impact of lax regulatory standards. Imagine if what you had

available to treat your life-threatening illness was rows of products none of which you knew worked at all, let alone which was most appropriate for you or how it should be taken to maximize effect. Simply having more drugs available is not the same as having good drugs. The goal must be to get patients drugs that are proven to work.

Another critical implication of the PPA's proposal is that weak approval standards can entrench poor treatments by making it difficult to study potentially better options.[17] When an unproven drug becomes available to patients through FDA approval, it can reduce their willingness to enroll in subsequent trials, especially because approval often signals that a drug is worth trying. To enroll patients, then, it may be necessary to compare new drugs to approved yet unproven products, making it much harder to interpret trial results. As described by one of my colleagues with decades of industry experience as a biotech investor, "if the market is flooded with half-baked ideas of drugs," they become "background noise and truly impede accrual of patients into clinical trials," while also interfering with "generating evidence that is meaningful, and in support of more conventional approvals of truly promising agents." This investor also explained why industry may oppose the PPA approach: "industry would absolutely want to know that its efforts to follow a more robust pathway provide it with the appropriate advantage in gaining approvals and ultimate success in the market." This suggests that provisional approval is likely not to speed the development of good drugs, but rather to stand in the way of that critical goal. This leaves future patients no better off than those facing terrible diseases today.[4,18,19]

Question:

What changes, if any, would you recommend to the FDA's expanded access to make it work better for patients seeking access to investigational therapies?

Response:

FDA's expanded access pathway (sometimes called "compassionate use") allows patients with serious and life-threatening conditions to be treated with investigational drugs outside clinical trials if they lack comparable or satisfactory treatment alternatives, the likely benefits of the investigational drug outweigh the risks, and the provision of expanded access would not interfere with the drug's clinical investigations needed to support marketing approval.[20] Expanded access can be provided to single patients, including for emergency use, as well as to intermediate sized and even larger patient populations; if the expanded access request is for more than a single patient, FDA requires somewhat stronger evidence of potential benefit.

Sponsors are under no legal obligation to provide expanded access; company participation is completely voluntary (and the same is true under state and federal "right to try" laws). If a physician agrees that a patient is a good candidate for expanded access to a particular investigational product, they must get the company to agree to provide it. In addition, both FDA and an institutional review board (IRB) must sign off on the request.[20] Companies are allowed to charge for the direct costs of making the expanded access drug available but they may not profit. When expanded access is offered, most companies provide the drug for free, recognizing that patients are unlikely to be able to pay out of pocket and insurers will not cover investigational

products. However, not every company has the resources to do so, especially smaller start-up companies lacking any approved products.

FDA approves nearly every expanded access request it receives, especially for single patients,[21] and typically does so on an expedited basis. FDA has undertaken several steps to improve use of the expanded access pathway, including offering streamlined submission forms for physicians estimated to take only an hour to complete and allowing IRB approval of single patient expanded access requests by a designated IRB member rather than requiring full board review.[22] In addition, FDA's Oncology Center of Excellence launched "Project Facilitate" to help oncology health care providers and regulatory professionals submit expanded access requests.[23–25]

While FDA makes its data public, it is unclear how many expanded access requests companies receive, as they are not required to report this information. Companies are required by law to at least post their expanded access policies on a publicly accessible website,[26] although their policy may be not to provide expanded access, for a variety of reasons. Companies may face several challenges when considering these requests, such as how to ensure fairness between patients making requests when not all requests will be granted, as well as fairness between patients pursuing expanded access and those participating in trials who may be randomized not to receive the drug of interest. Companies may also have limited supply of the drug, limited human resource capacity to manage requests, and limited funds. In addition, they may be concerned that patients will experience adverse events that will impede clinical development, although FDA has often sought to clarify that it recognizes patients outside trials differ in important ways. Perhaps most importantly, companies may worry about their bottom line: they are for-profit businesses and the pathway both to profit and to benefiting as many patients as possible is to get the drug approved as expeditiously as possible. Anything else may be seen as a distraction, even if a company has adequate resources to provide the investigational drug to expanded access patients for free. In terms of the speed of securing expanded access in the event a sponsor says yes, the bulk of time is spent negotiating terms and requirements between companies and treatment sites.

In recognition of some of these challenges and in response to advocacy from patients, the Accelerating Clinical Therapeutics for ALS Act (ACT for ALS), passed at the end of 2021, included a provision intended to promote expanded access by offering funding for research use of expanded access data collected for drugs being studied in Phase 3 trials and developed by small businesses.[27] NIH announced in October 2023 the three projects that had been selected for funding, including an expanded access protocol with 100 patients for a drug comprised of drinkable gold nanoparticles hypothesized to protect nerve cells; an expanded access protocol with 200 patients for a drug designed to activate a protein expressed in motor neurons; and an expanded access protocol with 40 patients who would not otherwise be eligible for ALS trials due to reduced pulmonary function for a cell therapy intended to improve respiratory function and survival.[28]

It is unclear how successful the ACT for ALS program will be, both in promoting substantial patient access to expanded access drugs and in generating useful data.[27] Although some companies have included expanded access data in their regulatory submissions or in support of payer coverage determinations,[29–31] the quality of expanded access data are often lacking in important ways, given the heterogeneity of patients unable to participate in trials and lack of

randomization, a control group, or other features of rigorous design.[32] In several ways, the concerns about relying on expanded access data are similar to the concerns about registries noted above.

Overall, it is unclear how common expanded access should be, given that these drugs are by definition not yet proven to be safe or effective. However, the pathway is an important option for seriously ill patients unable to participate in trials who lack good treatment alternatives. Therefore, ensuring that expanded access is fairly and equitably accessible and minimizing unnecessary burdens and hurdles are important goals, especially in contrast to alternatives that would instead weaken FDA approval standards. Several possible approaches could help improve the expanded access pathway to treatment use of investigational drugs:

1. Ensure that all physicians whose patients could benefit from expanded access are aware of the pathway and know how to navigate it. This is especially important outside major academic medical centers, where clinicians may not be running trials, may be less familiar with the research pipeline, and may be less aware of this approach.

2. Enforce existing requirements for companies to post their expanded access policies (whether to provide expanded access or not) on a public website, and additionally require that those policies be filed with FDA.

3. Improve transparency regarding the number and types of requests received by companies, the demographics of patients seeking expanded access, whether requests are granted, and on what basis. In addition, this information should be reported annually to FDA and FDA should be required to post aggregated data publicly.

4. Make Project Facilitate a broader program across FDA's drug and biologics centers, rather than leaving it exclusively within the Oncology Center of Excellence.

5. Further streamline IRB review requirements for expanded access, including acceptance of FDA forms without requiring additional protocol documents, providing a standard informed consent document, and reducing administrative burden on clinicians and IRBs associated with continuing reviews.

6. If the ACT for ALS approach works well to produce useful evidence after its initial piloting, consider extending disease-agnostic funding for the approach without limitation to ALS.

7. Promote efforts to make data collection from expanded access patients as low burden on clinicians as possible, while promoting systematic data collection and ensuring adequate funding support for these efforts. Simply demanding that clinicians gather more data without resources to do so could result in reluctance to use the expanded access pathway. With adequate resources, however, rigorous data collection and reporting should be required.

8. Offer guidance – both in general and for specific drugs – about FDA requirements for expanded access data to be acceptable in supporting approvals, including of label expansions to additional patient populations. This approach may encourage company willingness to offer expanded access through provision of an economic incentive.

9. Encourage companies to plan for expanded access when budgeting their clinical development programs and explore options for defraying the costs. For example, in some European countries, companies may charge for compassionate use with the possibility of various clawbacks depending on outcomes.[33,34]

10. Examine the pros and cons of tying FDA's "fast track" and "priority review" designations to sponsor willingness to offer expanded access programs, as an incentive to making it available.

Whatever reforms may be adopted, it is essential to recognize that expanded access is working reasonably well at present to both protect the integrity of clinical trials and to avoid the exploitation of desperate patients. Overall, expanded access should never be viewed as a substitute for well-designed clinical trials.

Question:

Are there changes to the Accelerated Approval pathway Congress should consider to help advance therapies for rare diseases?

Response:

Accelerated approval is available to all serious and life-threatening diseases with unmet treatment needs, whether common or rare. The primary challenge to use of the pathway is whether there is an acceptable surrogate or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. Unfortunately, this is sometimes not the case – although FDA has been willing to accept questionable surrogate endpoints to support accelerated approvals in the past,[35] such as levels of dystrophin or microdystrophin in Duchenne's muscular dystrophy[36] and beta-amyloid plaque for Alzheimer's disease. Some surrogate endpoints used to support accelerated approval in oncology are also not consistently correlated with clinical outcomes but nonetheless continue to be accepted by FDA.[37–39] Importantly, the availability of acceptable surrogates is a scientific issue, not one that requires further legislative adjustment of the accelerated approval pathway itself. Instead, it requires supporting the scientific development of appropriate endpoints, both through adequate research funding and regulatory support. FDA is making progress in this domain through its Rare Disease Endpoint Advancement program, discussed in detail below.[40]

Rather than being used too infrequently, the primary question facing accelerated approval is whether its central compromise is being upheld: early approval despite uncertainty, followed by later confirmation of benefit or withdrawal. Accordingly, the most important needed reforms are those that focus on ensuring confirmatory studies are rigorous and completed on time, and that when they fail to confirm drug benefit, approvals are quickly withdrawn.[4,5]

The Food and Drug Omnibus Reform Act (FDORA) passed in December 2022 addressed several of these concerns, including by affirming FDA's authority to require confirmatory studies to be underway prior to granting accelerated approval, which has been shown to speed both transition to full approval or withdrawal, when needed.[41,42] FDORA also required additional reporting on the status of post-market studies to ensure they are progressing appropriately and that adjustments can be made if needed. Finally, the law streamlined the approach to expedited withdrawal.

Additional useful reforms might include adding an automatic expiration date for accelerated approvals to encourage timely completion of confirmatory studies and improving informed consent so that patients understand when a drug they have been prescribed has not been traditionally approved, which in turn may improve willingness to participate in confirmatory studies. Both of these provisions are included in the PPA and would be worth extracting for application to accelerated approval. Another important reform might be to require FDA and companies to reach explicit prior agreement about the results needed in confirmatory studies in order to retain approval, as well as results that will result in withdrawal.[43]

For its part, FDA has also independently implemented several important changes around accelerated approval. As noted in FDORA, the agency has emphasized that confirmatory studies will typically be expected to be well underway prior to accelerated approval. Although some rare disease groups have expressed concern about this approach, it is an important step toward addressing the key challenge that occurs once a drug gets marketing approval: it becomes very difficult to enroll subsequent rigorous trials. Relatedly, FDA's Oncology Center of Excellence has recently issued a draft guidance that encourages a "one-trial" approach for accelerated approval, in which the sponsor conducts a randomized controlled trial to support accelerated approval, with longer-term follow-up in the same trial to fulfill the post-marketing requirement to verify clinical benefit. The benefit of this approach, including for rare disease, is that it "maintains efficiency in drug development and can provide early access to a drug using the accelerated approval pathway, while ensuring that a postmarketing trial is fully accrued and well underway to verify longer term benefit in a timely fashion."[44] This approach should be encouraged beyond oncology as well.

More recently, FDA has expressed increasing willingness to use the accelerated approval pathway for gene therapies and other rare disease drugs.[45] The concern now, as noted above, is ensuring both that the selected surrogate endpoints are scientifically reasonable and that this approach does not result in dangling approvals that fail to confirm benefit.

Question:

How should the FDA take into account the risk tolerance of individual patients vs. the risk to public health when considering approving an investigational drug?

Response:

It is reasonable for FDA – as it currently does – to acknowledge that patient populations facing serious and life-threatening diseases and conditions often have a heightened tolerance for risk and uncertainty. This is why FDA offers the expanded access program, described previously, and why it is willing to exercise substantial regulatory flexibility, including through the accelerated approval pathway.

However, it is critical that FDA not grant marketing approval to a drug simply because patients are willing to try it. As noted above, that is bad for patients today who need evidence to guide their treatment decisions, as well as bad for patients tomorrow because it inhibits the ability and incentive to study potentially better treatment options.[19] Weak approval standards harm all patients. As a public health agency, FDA must consider what is in the best interests of populations, which is maintaining reasonably high standards for approval, and when flexibility is offered, ensuring that benefit is confirmed after approval rapidly and rigorously. If rigorous clinical development is protected and approval standards are maintained, then individual patient risk tolerance should be accommodated through expanded access.

Question:

What do you see as the biggest challenges slowing or preventing safe and effective therapies from reaching patients as quickly as possible? How would you recommend addressing those challenges?

Response:

The reason many serious and life-threatening diseases currently lack good treatment options is not because FDA is standing in the way but rather because there are crucial gaps in scientific understanding upstream from the regulatory approval process. Therefore, the strongest path forward is to address scientific bottlenecks.

FDA and others have already taken important steps in this direction and need adequate funding to continue this trajectory. For example, FDA recently launched "Support for Clinical Trials Advancing Rare disease Therapeutics" (START), a pilot program informally dubbed "Operation Warp Speed for rare diseases," which will provide real-time advice to companies starting early in drug development to speed successful trials and address manufacturing issues.[46,47] The agency has also established the Rare Disease Endpoint Advancement (RDEA) pilot program to support novel efficacy endpoint development for drugs to treat rare diseases.[40] In addition, FDA's Action Plan for Rare Neurodegenerative Diseases and its ALS Science Strategy emphasize improved scientific understanding of rare disease through characterizing disease development and natural history, facilitating access to clinical trial participation through decentralized models, enhancing trial infrastructure, adopting innovative trial designs to support the development of better drugs and novel statistical approaches for small populations, and incorporating expanded access into clinical development programs.[48] Importantly, these efforts – all of which are described in more detail below – focus attention on improving science rather than weakening approval standards.[49]

Congress can help ensure that safe and effective therapies reach patients as quickly as possible by:

- Ensuring robust funding for rare disease research, including efforts to improve prevention, speed of diagnosis, and biomarker development, as well as grant programs to support development of promising drugs by small companies with limited capital.

- Providing FDA with sufficient funding to support the agency's current pilot programs, expansion of those programs, and efforts to offer nuanced regulatory guidance for rare disease drug development.

Question:

Why is it so important to have strong efficacy data for new drugs? What are the implications for patients and for future drug development if the efficacy data are limited at the time of approval? Are there historical examples of these implications when drugs were approved with limited efficacy data?

Response:

As noted above, ensuring that there is strong efficacy data for all drugs available on the market will allow patients and their clinicians to make well-informed decisions about benefit-risk tradeoffs, which are important even for patients facing serious and life-threatening diseases. Without strong efficacy data, it will not be clear which patients should be prescribed which drugs, or how they should be used to maximize benefit. These data are therefore essential to promoting patient autonomy.

Weak approval standards also inhibit the development of potentially better drugs.[50] This happens in several ways. First, once a product is approved, even with weak evidence, it can reduce willingness to participate in confirmatory studies of that drug or studies of other drugs, often because patients and doctors may not be aware of the weak evidence supporting approval or because they are unwilling to undertake the burdens of participation, including randomization to something other than the drug of interest, even if it is not yet proven beneficial. Second, even if patients are willing to participate in subsequent trials, they may insist on being offered the approved drug in a control group or as part of baseline therapy offered to all patients. This, in turn, makes it much harder to interpret trial results; it will also likely require bigger trials, which are more expensive and especially difficult for rare diseases. Third, investment in the disease area may be negatively impacted by weak approval standards, despite common claims to the contrary. This is in part because of the difficulties running additional trials just described, and also because sponsors want to be sure that if they develop a better drug, it will gain a market advantage. However, with weak approval standards, it may not be clear to patients and clinicians which drugs should be preferred. Relatedly, to the extent that weak approval standards encourage companies to invest in a given disease area, the result is not likely to be the development of better products, but rather simply more products that have not been proven to work or that offer minimal benefit. For all of these reasons, both the National Organization for Rare Disorders (NORD) and the Pharmaceutical Research and

Manufacturers of America (PhRMA) have indicated they do not support the Promising Pathway Act.[51,52]

The strongest example demonstrating concerns about the impact of weak approval standards arises in Duchenne's muscular dystrophy (described more fully below). FDA's first drug approval for DMD was granted in 2016, in part based on publicly acknowledged consideration of the company's financial solvency, despite serious concerns about evidence of benefit; FDA's scientific reviewers recommended against approval and were overruled by agency leadership.[53] Since then, the sponsor has not completed required confirmatory studies for its 3 initial DMD drugs and was recently granted another controversial approval for the first DMD gene therapy, with a confirmatory trial that failed to meet its primary endpoints. Each of these drugs came with extraordinarily high price tags, ranging from $300,000 to $3.2M. What have these weak approval standards gotten DMD patients? Several approved drugs, none of which have been proven to work.

Question:

The FDA has several opportunities to hear from patients and experts during the drug development and review process, including Patient-Focused Drug Development meetings and Advisory Committee meetings. What are the benefits and limitations of soliciting external feedback in these contexts?

Response:

As central stakeholders, it is important for FDA to hear from the patients affected by their regulatory decisions. Patient input is most helpful in understanding what study designs will be feasible or overly burdensome for participants, which study endpoints will provide evidence that can meaningfully inform patient decisions (including patient reported outcomes), and what study results will reflect improvement in patient lives. This input is especially valuable early in drug development when studies are being designed.

Once studies are complete, patient input can also be helpful in evaluating whether statistically significant changes in designated endpoints are in fact clinically relevant. For example, a study might demonstrate a statistically significant change in score on a functional rating scale, but the magnitude of that change may be imperceptible to patients – or it may be that even a small change could be quite impactful and patient perspectives can help explain why.

Where patient input is more challenging is when it simply emphasizes the lack of good treatment options or articulates a willingness to accept substantial uncertainty about benefits and risks. These factors might result in advocacy for weakened approval standards, raising all of the concerns noted above. As FDA incorporates patient perspectives, it must adhere to its statutory standards for approval, account for the diversity of patient opinion and avoid generalization about patient preferences, consider the interests of both current and future patients,[19] help patients and the public understand the rationale for its decisions, and resist a "something is better than nothing" mindset.[54]

Beyond Patient-Focused Dug Development activities, FDA uses advisory committees to seek recommendations from independent experts, including scientists, clinicians, patient representatives, and consumer representatives, on issues regarding specific drugs (both approval and withdrawal) and broader policy decisions. In addition to providing critical outside perspectives to agency officials from both advisors and public comments, advisory committee meetings offer an important opportunity to promote transparency and trust in FDA decisions and the reasoning behind those decisions, since meetings and relevant materials are open to the public.[55] Despite these important benefits, there are number of changes that could improve the advisory committee process.

First, it is important for patients and advocates to understand that advisory committee meetings are resource intensive for FDA review staff and leadership. Therefore, they should be reserved for matters about which there are genuine questions about the scientific evidence and application of regulatory standards, such as whether to accept a novel surrogate endpoint, whether additional or different evidence should be required, how to handle challenging study results, and what additional study requirements should be imposed after approval. When the scientific evidence clearly does not meet the standard for drug approval, advisory committee meetings are not needed and not helpful. Relatedly, it is important for patients and advocates to recognize the difference between the opportunity to be heard and authority to determine the outcome. Patients may share their views, including in favor of a drug's approval, but in the event that FDA determines the evidence does not support approval, this does not mean patients have been ignored.

Second, FDA should undertake several steps to make sure the advisory committee process is working to its strongest potential. Importantly, FDA's use of advisory committees to guide product approval questions has declined dramatically in recent years: 50% of newly approved drugs received advisory committee review before approval in 2010, compared to only 6% in 2021.[55] This means there is reduced opportunity for independent expert advice and transparency about FDA decisions. FDA should therefore issue clear guidance about when and why it will convene advisory committees.[55] This will help avoid more ad hoc approaches, which may be perceived as using advisory committees to generate public support for weak approvals or as avoiding advisory committees that may challenge controversial FDA decisions. It should also adopt a standardized question structure centered around the specific regulatory decision to avoid the perception or reality of seeking to influence the advisors' discussion and votes.[55]

When selecting advisors to serve on committees, FDA should rigorously avoid including individuals with conflicts of interest. Although FDA does have conflict of interest policies for advisory committee members, it frequently grants waivers to allow committee service based on perceived unique expertise. For example, in FY22 and FY23 to date, FDA held a combined total of 90 advisory committee meetings and issued 46 conflict waivers.[56] However, rather than allowing conflicted individuals with unique expertise to serve as voting members of advisory committees, FDA should offer alternatives such as allowing an expert presentation or encouraging submission of public comments. In addition, FDA should require all public commenters – especially those given time to speak during advisory committee meetings – to disclose their conflicts, including any relationships with industry. This is currently encouraged but not required.

Senator Richard Blumenthal

Question:

I have heard from concerned patients and their families who suffer from rare diseases such as Duchenne muscular dystrophy and Barth syndrome who feel as though FDA reviews rare disease treatments and therapies arbitrarily and without sufficient flexibility. This is especially true when the patient population is extremely small, making it more difficult for sponsors to conduct adequate and well-controlled clinical trials. They are also concerned that FDA fails to take into account the life-changing impact that even modest benefits can confer to patients, especially when a disease is terminal and there are no other treatments or therapies available.

Response:

It is understandable that patients and families suffering from rare, serious diseases are frustrated with the pace of progress. However, taking the DMD example as instructive, we can see that FDA has in fact exhibited tremendous flexibility – often more than is justified by the scientific evidence:

- In 2016, FDA granted accelerated approval to eteplirsen (Exondys 51) for DMD, against the recommendation of its advisory committee and FDA's own scientific staff. A single, small clinical trial showed that eteplirsen led to a small increase in the protein dystrophin, which became the surrogate endpoint supporting the drug's accelerated approval. However, this same study showed no improvement in clinical progression measured by a functional 6-minute walk test. In other words, although the drug was clearly active in the body, the impact of that activity may not produce even modest benefits that are discernable to patients.[36] In a letter accompanying the FDA approval press release, then CDER director Janet Woodcock stated "flexibility is warranted because of the life-threatening nature of the disease; the lack of available therapy; the fact that the intended population is a small subset of an already rare disease; and the fact that this is a life-limiting disease of children."[57]

- Increased dystrophin still has not been validated as a measure of clinical benefit in DMD, i.e., improvement in how a patient feels, functions, or survives. Nevertheless, FDA has awarded three more approvals for similar DMD drugs using this same surrogate endpoint. Confirmation of clinical benefit for all four treatments remains pending, with none of the required confirmatory trials yet completed.[36]

- More recently, in June 2023, FDA approved the first gene therapy for DMD, called Elevidys, with leadership again overruling the reviewing scientists. The drug is intended to work through the production of a new, genetically-engineered protein called microdystrophin. While the drug successfully increases levels of this protein, it is another unvalidated surrogate endpoint: we don't know whether micro-dystrophin will improve

function in children with DMD or what levels of micro-dystrophin would be needed to do so. The only randomized, double-blinded, placebo-controlled study of the drug failed to show any correlation between the expression of micro-dystrophin in patients who received the drug and functional outcomes.[36] Following the drug's initial accelerated approval, the sponsor completed a pivotal study examining clinical endpoints, including motor function. That pivotal study failed to meet its primary endpoint (patients treated with the gene therapy experienced a 2.6 point increase in a motor function measure, but those on placebo experienced a 1.9 point increase, a difference likely to be explained by chance). The sponsor has emphasized improvement on two secondary endpoints, both of which demonstrated improvement of about half a second compared to placebo in the time to rise from the floor and the 10-meter distance test, changes unlikely to be noticeable to anyone in day-to-day life. Nevertheless, it appears likely that FDA will convert the drug to traditional approval, including for a broader age range of patients.[58] Notably, patients who receive this gene therapy will likely not be able to enroll in clinical trials for other similar vector-based gene therapies or be able to receive a future FDA-approved vectorbased gene therapy, precluding the possibility of receiving a better treatment should one become available.[36] In addition, the sponsor priced Elevidys at $3.2M.

As this example demonstrates, along with many others (such as FDA's August 2023 approval of palovarotene for fibrodysplasia ossificans progressive, a rare bone disorder, despite a trial that failed to demonstrate benefit on prespecified endpoints[59]), FDA is not withholding approvals out of concern that benefits are too small. To the contrary, FDA is exercising substantial regulatory flexibility, especially for rare diseases, to approve drugs despite uncertainty about whether they work at all.

Question:

How would you characterize FDA's review of rare disease drug applications? Do you believe FDA uses its discretion appropriately in making decisions based on rare disease drugs? In your view, and generally speaking, when FDA fails to approve a rare disease drug application, what is their reasoning, and is it justified?

Response:

As noted above, FDA's review of rare disease drug applications has been remarkable for its flexibility. The agency has been willing to accept very small trials (as is often appropriate in rare diseases), very short trials,[7] and a great deal of uncertainty about drugs allowed on the market, approving most new drugs before they approved by any other global regulator. To share additional examples, consider two ALS drugs recently granted approval:

<u>Relyvrio (sodium phenylbutyrate and taurursodiol): traditional approval, 2022</u>[60]

- Amylyx, Relyvrio's sponsor, published results of its Phase 2 double-blind, placebocontrolled, randomized CENTAUR trial in September 2020, reporting a small but statistically significant slowing of functional decline. This was an exciting result, but Phase 2 trials are still in the early phase and typically need to be confirmed; in many cases, positive Phase 2 results are not replicated in later studies.

- Amylyx contemplated an immediate application for marketing approval based on CENTAUR's results, but FDA sought data from an additional placebo-controlled trial. Amylyx moved forward with its Phase 3 PHOENIX trial.
- In September 2021, following substantial patient advocacy, FDA indicated a willingness to accept Amylyx's marketing application without waiting for Phase 3 data. The application included data from an open-label extension (OLE) of the CENTAUR study, during which all study participants received Relyvrio. Based on those data, Amylyx reported a survival benefit of about 6.5 months in patients who received the drug earlier than those initially randomized to the placebo group.
- In March 2022, FDA called an advisory committee meeting to discuss the Relyvrio application. The agency raised concerns about the statistical analysis methodology used in CENTAUR, noted the result was not "exceptionally persuasive" (the usual standard for approval based on just one study), questioned the statistical interpretability of the survival benefit seen in the OLE,[61] and indicated that the data may be insufficient to support approval without completion of the PHOENIX trial. The advisory committee voted 4-6, with only a minority agreeing that the data established a conclusion of effectiveness.
- Amylyx then provided additional analysis from individual responders in the CENTAUR study and from the OLE, as well as biomarker data from a study of Relyvrio in patients with Alzheimer's disease or mild cognitive impairment. In September 2022, FDA again called the advisory committee, but in briefing documents indicated that the additional data did not appear to provide persuasive or independent substantiation of effectiveness. At this second meeting, FDA's Office of Neuroscience director delivered a presentation emphasizing FDA's regulatory flexibility, while continuing to express skepticism as to whether the available data supporting Relyvrio satisfied the substantial evidence standard for drug approval. After Amylyx's CEO was pressed to agree to voluntary withdrawal if the PHOENIX trial did not show drug benefit, the advisory committee voted 7-2, with the majority now agreeing that the available evidence of effectiveness was sufficient to support approval, considering the unmet need in ALS and the seriousness of the disease, as well as the status of the ongoing Phase 3 trial.[43]
- On September 29, 2022, FDA announced Relyvrio's approval, while acknowledging "a degree of residual uncertainty about the evidence of effectiveness that exceeds that which might typically remain following a conclusion that substantial evidence of effectiveness has been demonstrated."[62]
- In contrast to FDA's decision, Relyvrio has now received two negative opinions from the European regulator, which is refusing to approve while the Phase 3 trial remains pending, based on similar concerns about the adequacy of available evidence.[63]
- Some advocates have suggested that Relyvrio is an example of how the Promising Pathway Act could be helpful by encouraging FDA to grant approval earlier than it did. However, that is the wrong conclusion. The fact that FDA was willing to approve the drug at all prior to completion of the PHOENIX trial, given serious questions about the product's effectiveness, is a testament to FDA's expansive flexibility.

<u>Qalsody (toferson): accelerated approval, 2023</u>

- Qalsody, a therapy for a rare subtype of ALS caused by a mutation in the SOD1 gene, was studied in the Phase 3 VALOR study. In that study, reported in late 2021, the drug failed to meet the primary endpoint of statistically significant change in functional rating

score from baseline to week 28. The company later published combined analyses of 12month VALOR data and the accompanying OLE, reporting that earlier initiation slowed decline in patients.[64]

- The VALOR results also demonstrated that the drug could reduce the plasma concentration of a protein called neurofilament light chain (NfL) compared to placebo. Reduction in NfL is an unvalidated surrogate marker that had never before supported an FDA approval.[64]
- At a March 2022 advisory committee meeting, the advisors voted unanimously that reduction in NfL is reasonably likely to predict clinical benefit, thus supporting accelerated approval. However, the panel voted 5-3 that the available clinical data did not provide substantial evidence of effectiveness for traditional approval.[65]
- FDA granted the drug accelerated approval in April 2023. This pathway requires confirmatory studies to be conducted after approval. However, given the extremely rare nature of SOD1-ALS and very small pool of eligible patients, FDA recognized that conducting another trial in symptomatic patients would not be feasible. Therefore, it was willing accept an alternative study of the drug in pre-symptomatic SOD1 positive individuals in satisfaction of the requirements.[66]
- Here we see another example of the sorts of flexibility FDA has been willing to extend in the context of rare disease, approving a drug that failed to demonstrate clinical benefit, accepting a novel endpoint, and allowing an alternative approach to the required confirmatory study.

In terms of whether FDA uses its discretion appropriately in making decisions about rare disease drugs, my worry is not that FDA is insufficiently flexible. However, there are a few questions worth considering:

Question:

Are different offices and divisions at FDA taking consistent approaches to flexibility – or explaining why different approaches are appropriate?

Response:

It is a common claim that some parts of FDA are more flexible than others. Traditionally, the oncology group has had a reputation for flexibility, the neurology group has had several recent approvals that suggest the same is increasingly true there, and the leader of the Center for Biologics Evaluation and Research (CBER) has made several public statements emphasizing a new era for flexibility in the approval of gene therapies and other biologics, especially for rare diseases. Other groups may be perceived as less flexible, when in fact, the reality may be that the science is less promising. Clarifying the agency's approach to regulatory flexibility across the board may be useful.

Question:

Is there a disconnect between FDA's scientific reviewers and its office, division, and center directors, with higher-level leaders more willing to exert flexibility, leading to confusing messaging and experiences for sponsors?

Response:

This is also a common claim and source of frustration, which should be examined more closely.

Question:

Across both domains – inconsistency between FDA offices and inconsistency between reviewers and senior leaders – how should inconsistency be resolved, i.e., with more or less flexibility?

Response:

Regulatory flexibility can be appropriate so long as (1) initial approval standards remain reasonably high, such that there is a defensible expectation that benefit will be confirmed later; and (2) benefit is in fact confirmed later. At present, I am concerned that flexible approvals are being granted even when these conditions are not satisfied. It is especially concerning that FDA does not require confirmatory studies other than for drugs that receive accelerated approval, despite residual uncertainty that often remains for drugs granted traditional approval, and that existing confirmatory study requirements are often weak and weakly enforced. To the extent that FDA is moving towards greater regulatory flexibility, the agency's post-marketing study requirements should increase proportionately.[5]

Finally, you asked about the reasoning provided when FDA refuses to approve a rare disease drug application, and whether these refusals are justified. In my opinion, they are. Another example will be instructive here:

- In 2020, BrainStorm reported the results of its Phase 3 trial of NurOwn, an investigational stem cell therapy being developed for treatment of ALS.[67] The drug missed all primary and secondary endpoints by a wide margin, and there was a modest excess in deaths in those treated with NurOwn. The company parsed the data in several ways that were not initially planned (post-hoc analyses), looking for some signal of benefit, an approach that is appropriate to generate hypotheses to inform additional trials but not as confirmation of efficacy due to various scientific and statistical weaknesses.
- FDA rejected the company's marketing application twice before BrainStorm decided to "file over protest." In the 3 years since the Phase 3 results were reported, BrainStorm has conducted several additional analyses of existing data but gathered no new data.
- After extensive advocacy, including from study participants with anecdotal claims of benefit, FDA agreed to hold an advisory committee meeting to discuss the drug. At the meeting and in briefing documents, FDA reiterated numerous concerns about NurOwn's efficacy and safety, as well as about BrainStorm's ability to consistently manufacture the drug. FDA noted that the drug failed to meet any of its pre-specified endpoints and

explained that, contrary to the company's claims, purported shortcomings of the measurement tool used to assess patient function could not explain the study's negative results. Although the company suggested that biomarker data support benefit, FDA explained that the available results ran in the opposite direction of what would support efficacy. FDA also reiterated important concerns that the drug may hasten death relative to placebo.[68]

- Given these extensive concerns about both safety and effectiveness, it was clear that FDA was almost certain to reject the marketing application, which BrainStorm decided to withdraw soon after the advisory committee meeting. The company has now committed to conducting a new pivotal study.
- In this example, FDA offered incredible clarity about its concerns regarding the drug, which were not at all about magnitude of benefit but rather about the fact that the drug had not shown any benefit at all. Many in the patient community found FDA's reasoning convincing and agreed that the drug needs further study. Many others, however, insist that any positive signal of benefit – even based on post-hoc analyses of smaller, unplanned patient subgroups – should support approval for a disease as serious as ALS. However, that approach would fill the market with snake oil and harm patients in all the ways described in response to earlier questions.[69]

Ultimately, the reasons that FDA refuses to approve a drug are that the drug has not been shown to work (or be likely to work) on any reasonable analysis of the available data, the drug raises substantial safety concerns, or both. Given the tremendous flexibility FDA often exercises in approving new drugs, when it refuses to approve one (or even to file an application), there is generally a very good scientific reason to support that judgment. I recognize that there are examples arising in Barth Syndrome, ARG1-D, and other rare diseases where patient advocates and others feel that FDA's decisions have not been adequately justified. These diseases are outside my specific areas of expertise, but it is important to acknowledge that there may be communication challenges or inconsistencies that need to be addressed, per the points raised above. As a rule, however, FDA is simply not refusing to approve good drugs. Unfortunately, the problem is too often the lack of good drugs ready for FDA approval.

Question:

How can we work to better improve the rare disease drug review process without sacrificing drug safety and efficacy?

Response:

The most important way to achieve this goal is to ensure that FDA and sponsors are able to meet early and often to agree on an appropriate clinical development plan as these drugs begin and proceed through human trials. This means coordination and collaboration on appropriately designed trials and the development and selection of endpoints capable of demonstrating safety and effectiveness. Both of these steps are currently being pursued by FDA as part of the "Support for Clinical Trials Advancing Rare disease Therapeutics" (START) and Rare Disease Endpoint Advancement (RDEA) pilot programs. It is essential to ensure that FDA has adequate resources

to provide this level of engagement and support to sponsors pursuing rare disease drug development.

Importantly, by the time studies are completed and FDA is considering a submitted application for marketing approval, the data are what they are – and if they fail to clearly demonstrate benefit, the review can be far more challenging. Rather than pushing FDA to weaken its approval standards in these cases, the focus should be on producing the highest quality science to inform regulatory decisions.

Question:

The ACT for ALS was an important step forward in getting new treatments to patients with a disease as devastating as ALS. The law was also intended to target other rare neurodegenerative diseases, such as spinocerebellar ataxia (SCA). Can you discuss what the ACT for ALS Act mandated? Did it create any new drug approval pathways? Did it provide FDA with new flexibilities? Overall, how did it seek to usher in new treatments for ALS and other rare neurodegenerative diseases?

Response:

ACT for ALS has five central components: (1) grants for research use of data from expanded access to ALS drugs, which have begun to be awarded, as described above;[27,70] (2) a new public-private partnership to advance understanding of neurodegenerative diseases and foster development of treatments, which was announced in 2022 as the Critical Path for Rare Neurodegenerative Diseases (CP-RND); (3) a required 5-year FDA action plan to foster drug development and facilitate access to investigational drugs for ALS and other neurodegenerative diseases, which has already been published;[48] (4) an FDA rare neurodegenerative disease grant program to be administered by the Office of Orphan Products Development focused on characterizing these diseases and their natural history, identifying molecular targets, and improving clinical development through use of innovative trial designs and trial networks; and (5) a Government Accountability Office (GAO) report to Congress analyzing both of the law's grant programs. To accomplish these tasks, the law authorized $100M in appropriations for each fiscal year from 2022-2026. It does not, however, specify how those funds will be allocated across the law's components or between its two grant programs.

ACT for ALS did not create any new drug approval pathways or provide FDA with new flexibilities; such changes are not needed and would not be helpful, for all the reasons described throughout these responses. Instead, the law focused on supporting the science needed for the development of meaningful, proven treatments. This is exactly the right approach. We will continue to see many therapeutic candidates fail until there is a better understanding of these diseases, their causes, how they progress, and what biological processes should be targeted to slow progression or even prevent disease occurrence. It is also critical to facilitate clinical trials, including by supporting patients who volunteer to participate in them.

As part of FDA's action plan,[48] it developed an inter-center Rare Neurodegenerative Diseases Task Force intended to coordinate efforts toward advancing science and drug development for

rare neurodegenerative diseases. It also developed an ALS Science Strategy to address specific challenges to ALS drug development. That strategy focuses on improving characterization of ALS disease pathogenesis and natural history, facilitating access to clinical trials including through decentralized models, encouraging the incorporation of expanded access into clinical development programs, enhancing trial infrastructure and agility, facilitating data sharing, and exploring innovative trial designs including novel statistical approaches for small populations. Again, these are exactly the sorts of approaches that will speed the development of safe and effective treatments that patients with rare disease desperately need. There are no shortcuts in the science, but supporting high quality science will avoid critical wasted time and effort on drugs that fail to work.

Question:

How can the federal government support and encourage increased investment in the development of new treatments for rare and progressive diseases?

Response:

Rare disease drug development faces unique challenges on the US market-based model, given that small patient populations make the conduct of clinical trials more difficult and limit the profit scale that companies can anticipate from their investment. It is notable, however, that the Orphan Drug Act, which provides financial incentives to rare disease drug developers in the form of tax breaks and market exclusivity, has produced substantial investment in rare disease without any change to FDA's approval standard. It is critical that we not forget that lesson: lowering FDA's approval standard for rare disease drugs will not result in increased investment in drugs that work.

Instead, the federal government can encourage increased investment in strong treatments for rare diseases by:

(1) Increasing funding for basic science research, research to understand these diseases as clearly as possible, and research to develop appropriate endpoints. These early, essential scientific steps will improve predictability for industry so they can be more confident in their ability to develop drugs that work and will be clearly approvable, rather than wasting time and resources on investments unlikely to pan out. Additional federal funding should be provided to support research into novel trial designs and statistical approaches that may be useful in the context of rare disease, as well as research to address manufacturing challenges that often arise for biological drugs, many of which are being developed for rare diseases.

(2) Increasing funding for FDA's efforts to give clear guidance to rare disease drug companies very early in development and throughout the process (e.g., the START program), which will also serve to minimize uncertainty and maximize the likelihood of developing good treatment options that are proven to be safe and effective.

(3) Supporting mechanisms for the federal government to play a greater role in directly developing rare disease drugs. There are a number of ways this could work, for example, calling on ARPA-H to engage in efforts to repurpose drugs that may be promising for rare diseases (in support of existing NIH work in this domain) and to play a significant role in late-stage research and development and commercialization of these products. The traditional model has been for the government to support basic research, which industry then builds on and commercializes. But when industry is not interested in particular disease markets, the federal government can step in, which will also promote scientific rigor through oversight of clinical trial design and endpoints. These approaches reflect what the government did successfully via BARDA and Operation Warp Speed during the COVID-19 pandemic and it could be replicated for rare disease. This "public option" could also help address some of the staggering prices that companies attach to rare disease drugs, ostensibly to recoup their investment.

Question:

Can you explain how the support for clinical trials advancing rare disease therapeutics (START) program at FDA may be beneficial for companies as they go through the development process? What are some of the most common challenges that the START program can help address?

Response:

The START Pilot Program was formally announced in September 2023, with the goal to "further accelerate the pace of development of novel drug and biological products that are intended to address an unmet medical need as a treatment for a rare disease."[71] FDA already offers formal meetings to sponsors at several designated timepoints but the process can take weeks or months, potentially delaying key decisions or making it difficult to course correct if FDA flags issues that need to be resolved. In contrast, START will be available to selected product development programs that would benefit from "enhanced communications" with FDA. Through "more rapid, ad-hoc communications" with the agency (emails and videoconference responses within days), the program will provide "a mechanism for addressing clinical development issues that otherwise would delay or prevent a promising novel drug or biological product from progressing" to the pivotal trial stage (i.e., the key trial needed to support a marketing application) or to the stage at which sponsors meet with FDA immediately before submitting a marketing application. START program communications will address issues with specific programmatic needs for individual products, such as study design, choice of control group, choice of patient population, endpoint selection to support approval, statistical methodology, use of nonclinical information, or product characterization. Each of these issues can raise challenges for rare disease drug developers, especially given small population sizes available for trial enrollment, associated statistical challenges, and open questions about how many of these diseases develop and progress that can make it difficult to select appropriate endpoints. Compounding these issues is that many rare disease drug developers are small companies without much prior experience or understanding of FDA requirements and expectations.

This increased communication between FDA reviewers and sponsors is intended to help generate high quality data to support marketing applications. The approach is likely to be beneficial for

selected companies because they will have FDA experts on "speed-dial" to make sure they are not making choices that will ultimately waste time, generate insufficient evidence, or otherwise impede approval of drugs likely to help patients. Notably, the approach is inspired by the collaborative engagement that made Operation Warp Speed so successful.

At present, START is not available to all rare disease drug sponsors. To be eligible, a sponsor must have a product currently in clinical trials with an active Investigational New Drug (IND) Application. Eligible products regulated by CBER must be "a gene or cellular therapy intended to address an unmet medical need as a treatment for a rare disease or serious condition, which is likely to lead to significant disability or death within the first decade of life." Eligible products regulated by CDER must be "intended to treat rare neurodegenerative conditions, including those of rare genetic metabolic type." FDA will select up to 3 participants for each Center; following evaluation of the pilot, FDA may consider a second iteration of the program. If successful, additional resources could help the program expand to more sponsors developing drugs to treat serious diseases with unmet need.[47] CBER director Peter Marks has noted that expansion of the program will require dozens of new FDA employees, but that if the program is successful, benefits will be obvious to industry and Congress in the form of potential reductions in development time by 25-50%, which will benefit patients by getting drugs to them more quickly, as well as industry.[72]

START is just one of several initiatives FDA is undertaking to support rare disease drug development. For example, CDER's Accelerating Rare disease Cures (ARC) program is taking a multi-pronged approach, including a program called "Learning and Education to Advance and Empower Rare Disease Drug Developers" (LEADER 3D). As part of this program, the agency is seeking stakeholder feedback to identify knowledge gaps in rare disease drug development and develop resources to inform stakeholders who design and conduct rare disease drug development programs on regulatory considerations in clinical trial design.[47] ARC reports that some emerging themes of this outreach to date include the potential need to clarify "the importance and use of natural history studies, establishing novel endpoints for rare disease regulatory submissions, and leveraging real-world evidence for regulatory submissions[.]"[47] In addition, ARC supports scientific and regulatory initiatives, such as platforms to facilitate natural history studies, methods to construct novel endpoints, disease and drug modeling, approaches to dose-selection, and novel statistical approaches with the potential to increase trial efficiency.[49]

In another approach, FDA announced the Rare Disease Endpoint Advancement (RDEA) Pilot Program in 2022, which supports novel endpoint efficacy development for sponsors with an active IND or pre-IND for a rare disease, as well as sponsors who are initiating a rare disease natural history study where the proposed endpoint is intended to be studied. As part of RDEA, selected sponsors will have greater interaction with interdisciplinary FDA experts in endpoint development and the associated clinical review division, promoting innovation and building FDA staff capacity to facilitate novel endpoint development to evaluate the efficacy of rare disease therapies. FDA will select up to one RDEA proposal per quarter during the pilot phase of the program, which may also expand in the future if the program is successful and resources are available to support it.

* * *

Thank you again for the opportunity to engage on these important issues. FDA has shown itself to be tremendously flexible in support of rare disease drug development and approval. What is needed now are concerted efforts to support scientific advancement through funding and regulatory engagement – not revisions to weaken drug approval standards.

Please let me know if you have any other questions or if further discussion would be helpful.

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U.S. Senate Special Committee on Aging
"Unlocking Hope: Access to Therapies for People with Rare, Progressive, and Serious Diseases"
October 26, 2023
Questions for the Record
Keith Desserich

Ranking Member Mike Braun

Question:

At the end of the October 26th Senate Special Committee on Aging titled "*Unlocking Hope: Access to Therapies for People with Rare, Progressive, and Serious Diseases,*" Chairman Casey cited the following excerpt from Holly Fernandez Lynch's testimony:

> "It is certainly understandable for individual patients to be willing to risk substantial uncertainty for themselves before better evidence comes available, especially when they have no time to lose, and I support their right to do so via expanded access. However, weakened approval standards affect all patients."

Chairman Casey then asked Mrs. Fernandez Lynch to talk about how regulators and policymakers should balance the needs of patients when not all patients have the same needs or risk tolerance.

Mrs. Fernandez Lynch provided the following response:

> "One of the things that I've often heard, in the context of discussing Promising Pathway, is 'if patients don't want to take a provisionally approved drug, then of course, they don't have to.' That is absolutely true. But it becomes more complicated, because when you lower FDA approval standards, that tells industry, 'this is the bar that you have to meet.' When that bar is lowered, then industry responds accordingly. And what that does is push back to patients and clinicians the need to make decisions without evidence. Some people may have that high risk tolerance, but not everybody will. That's why I think the dietary supplement example is so salient. Dietary supplements do not have to show safety and effectiveness, so industry does not demonstrate that. That's not what people who are facing these terrible diseases need.
>
> "The other challenge is that, when standards are low and you allow other products on the market that have not demonstrated that they are beneficial, it complicates the development of potentially better drugs. It makes it difficult to accrue those studies. Then you might also find yourself having to test new interventions against interventions that have not yet been proven to work. So you can't quite tell, are patients benefitting from this new drug? Or is it that neither of these drugs are beneficial? You can entrench drugs that don't actually benefit patients.

> "FDA has to account in its public health responsibilities not only for the interests of patients today but also the broader population of patients, which is why I am encouraging the Committee to draw on what we've heard about challenges to the expanded access pathway. I think that is the avenue that really does need to be improved to provide this balance: allowing patients today who have high risk tolerance to take unproven medicines while we continue to gather rigorous evidence. Unfortunately, patient registries are not going to get us there because they are not randomized and not controlled. They are not going to be able to answer these questions in the way that patients need to make autonomous, informed decisions about their treatment."

Ranking Member Braun asks that you respond to Chairman Casey's initial question and provide any commentary you feel necessary regarding Mrs. Fernandez Lynch's original response.

Response:

When others propose that the Promising Pathway Act "lowers standards" we are making the assumption that there are both alternative treatments and adequate biomarkers on a specific terminal diagnosis. For the pediatric terminal disease community, we also make the assumption that trials are available for their categories of affliction. Ultimately all three of these assumptions are flawed and incorrect. The Promising Pathway Act does not lower standards for any non-terminal or even terminal diseases that have existing clinical trials. It is specific to those cases where we do not have alternatives or even the patient data to determine benchmarks.

In the hundreds of cases I've directly worked with over the years of DIPG and DMG, no current FDA option (Expanded Access, Right to Try or Accelerated Approval) has either responded quick enough or provided the necessary options to patients to even provide an option for care.

Additionally, no current FDA access option provides the transparent data abilities that the PPA offers through the third-party registry framework. Instead we operate often blindly with care, jeopardizing both patient outcomes and losing valuable data that may, in fact, help future FDA considerations. A third-party registry allows for patients, researchers and industry to judge patterns of both care and response. Keep in mind that the standard for independent registries in PPA doesn't allow for all registries, thus voiding the "well-controlled" and "randomized" argument. It requires that they must attain certain standards and the registries that would comply are already being used for clinical trials in many terminal diseases – some even to satisfy other FDA requests in ongoing approvals.

Statements for the Record



MADELINE ADAMS

Birmingham, AL

Madeline was a spunky 3 year old when she was diagnosed with an inoperable brain tumor called, DIPG. With NO existing medical treatment options specific to her cancer, Madeline underwent radiation and was allowed into drug trials intended for other cancers. She battled for 11 months, ultimately losing her ability to swallow and breath and dying a slow and merciless death.

Why the Promising Pathway Act is Important to our Family: The Promising Pathway Act is important to our family because it will open up new drug approval pathways to help give hope to families of children like Madeline who have little to no treatments options, and no time to wait for one to breakthrough.

Elizabeth and Patrick Adams

Parents of Madeline

[redacted]

Dear Members of Senate Special Committee on Aging:

My name is Walker Burger. I am 34 years old and live in Montgomery, Alabama. I am a participant in the Tazpower Study battling Barth syndrome.

Before the Tazpower study, Barth syndrome controlled my life. I was exhausted with a poor quality of life. With the drug, I am living the life I always dreamed about. The improvements that I've seen in my strength, energy and general quality of life is something I could only dream about before. The study drug Elamipretide has made it my reality.

Diagnosed with cardiomyopathy and low muscle tone as an infant, I was nineteen years old when I was finally diagnosed with Barth syndrome.

Growing up, I participated in Boy Scouts, earning Eagle. Some physical activities, such as hiking, had to be modified. I was driven around at summer camp to save my limited energy. When walking, I had to stop and rest two or three times every quarter mile. I was out of breath and my legs ached. After a week at summer camp, it took several days to recover.

After graduating from college, I was able to work full-time, but I had no energy to do anything else. It was hard to be in my twenties with no energy!

In August of 2017, I enrolled in the TAZPOWER study. My life has dramatically changed since beginning the drug therapy.
My daily life is so different than just a few years ago. I am happier and more pleasant to be around, enjoying life more. I like exercising. I walk one mile without taking a break – that's four times longer than before -- and this also happens to be the best part of my day.

In summary, if someone were to ask me today "Walker, do you have Barth syndrome?" I would say "No, I HAD Barth syndrome." I am thankful for this new quality of life. I look forward to seeing how much the drug Elamipretide can help others.

I am now most fearful that the drug will be taken away. Without FDA approval, I could lose access to the drug that has literately changed my life. I cannot imagine returning to the poor quality of life with no energy, pain and constant fatigue.

Please help encourage the FDA to fairly examine the findings of the study. The well being of all Barth syndrome patients depend on the drug's approval.

Sincerely,
Walker Burger
Barth syndrome Patient and TAZ Power Study Patient

Sent from my iPad

Jan P. | Alabama

Age: 69
Year of Diagnosis: 2019
Type: Limb Onset, Sporadic

We Can't Wait

Any chance to slow Progression with the chance of living longer would be worth taking

If we don't try we will never know!

If there is positive improvement after 1st or 2nd trial I am in favor of letting us try it

If you consider that I have spent my life's work helping others in the community to not being able to walk or use arms or hands, very significant. Our whole family has been impacted!

Grandchildren and children are heartbroken, we had so many plans

There is no treatment!

Find a treatment that will give us some hope!! **There have been many trials that have shown promise and yet we are denied.** Fund the research like many other diseases and make it a priority, not another hundred years of waiting!!

Paul K. | Alabama



Age: 79
Year of Diagnosis: 2009
Type: Bulbar Onset

Highly anticipated particularly Neuron stem cell therapy. ALS patients should be put on a diaphragm Pacer as soon as diagnosed. I was and it has been my life saver treatment. Why does the ALS and MDA not recommend that instead of Cpap or Trilogy.? It works 24-7 without the inconvenience of carrying a machine and mask every where you go.

Not at all worried about side effects of a new drug as long as it is shown to be tolerated and not kill the patient.

Cannot walk, talk very poorly and have trouble communicating with my Love ones , friends and fellow workers.

Horribly! I cannot help at all do the things I use to do, and my wife has to do them or hire them out.

The devastation it brings on a family and the person that has ALS.

Create a drug or vaccine that stops ALS and cures a patient. Just like you did for Covid-19 in operation warp speed. You have the brain power and funding and do it now.

Christie G. | Alabama



Age:
Year of Diagnosis: 2021
Type: Bulbar Onset

ALS progresses rapidly, my dad was diagnosed and passed away all within the same week. If we could have slowed down this disease even by weeks, I think we could have had proper research and treatment set up without my dad spending his last days in the hospital. **If someone said " hey we think this therapy or new medicine might ease your symptoms but here are the potential side effects..." we would have tried it, what would be the negative side of that? The benefits would far outweigh the decision to not to.**

We just want to make sure it's safe before anyone with ALS starts a trial stage there's a difference between wanting a experimental treatment not approved yet and one that's been tested. It's a peace of mind moving forward.

My dad lived with symptoms for about a year and was never properly diagnosed. The tremors, weight loss and not being able to eat he never knew why. Little by little day to day it was always something debilitating, he loved planting trees, working out in the garden but that was all stripped away rather quickly with his muscle loss. He stopped going out, missed family dinners, holidays and most importantly doing things that he was passionate about. My dad would say...but we had one last Christmas together and I was able to spend that day with my grandchildren before the final stages. This disease is like no other, to be trapped in a body with no way to live your life not even fully but just with good quality and good health day to day. It's a scary thing to go through.

Seeing someone you love suffer is heartbreaking, I felt helpless I couldn't do anything to ease my dads' symptoms. I can say it's mentally and emotionally draining. For my mom especially.

How rapid this disease progresses and how hard it is to get a proper diagnosis in some places. My dad shouldn't have suffered as long as he did with no answers from multiple doctors, hospitals and tests. Awareness is detrimental.

We need treatments, we need a way to help people living with a debilitating disease life their best most comfortable life. If you could imagine being trapped in your body but you mind was aware of mostly everything going on the pain, the tremors, not being to eat, wasting away physically, no one should have to suffer through that. Treatment or therapy to ease symptoms to help those living with this disease that should be the steps moving forward.

David C. | Sanford

Age: 65
Year of Diagnosis: 2018
Type: Limb Onset



We Can't Wait

A few months only extends the suffering.

My balance is compromised, and the therapy is not worth the risk.

If it is showing significant positive results in animal studies, I would definitely be interested in NU 9.

It has taken my ability to walk, speak, and have trouble swallowing. Limited income. Can't get disability. I'm a self-employed carpenter still doing what I can. The bills are overwhelming. The stress does not help the disease. It to much for my wife to handle. I will not consider a feeding tube or breathing machine. I **do not want to extend my life because it will be too much on my wife.** If motor neuron diseases were a virus, we'd have a cure.

It's been devastating..

I wish the public had more knowledge of the disease. Then maybe there would be more funding and more support. More pressure on the FDA.

There are drugs on the market right now to help upper motor neuron disease. **But they are being held up because of the FDA. Why? I would be willing to be a part of an animal study if it shows positive results.** NU 9

People are dying with no hope. The FDA doesn't seem to care. Give us a little hope and opportunity. Any opportunity and hope is better than nothing.



C. Szabo-Cassella FSHD Testimonial

October 25, 2023

Dear Chairman Casey, Ranking Member Braun, and Honorable Members of the U.S. Senate Special Committee on Aging:

My name is Claire Szabo-Cassella, and I live with a disease called Facioscapulohumeral Muscular Dystrophy, or FSHD.

If Covid-19 taught us anything, it's that effective treatments for a disease can be found quickly when awareness, political leadership, and science come together to find a cure. I implore each Congressperson to recognize the dire need for a cure for FSHD, and to garner the necessary resources to meet the unmet medical needs of the over 870,000 individuals, like myself, who are struggling with this debilitating form of muscular dystrophy.

FSHD is a progressive disease that attacks one's life on all levels - physically, emotionally, spiritually, and financially. Since age 50, I have needed an ever-increasing amount of caregiving, intensive physical therapy, and specialized equipment, all of which I have had to resource without insurance coverage in many cases. Disability was denied to me, which is mind boggling. Now, age 59, I am unable to work due to the severity of my disease, and have had to resort to GoFundMe fundraisers.

Claire Szabo-Cassella

Red Scooter Diaries
www.redscooterdiaries.com
Recommendations.
Reflections.
Access Advocacy.

Ph: (503) 619-9664

October 18, 2023

[redacted]

Re: Promising Pathways Hearing – October 26, 2023

Good morning Senators Braun, Gillibrand, and Kelly:

My name is Michelle Lorenz. I am an Arizona resident whose mother died of a rare disease called Amyloidosis. I am also a patient advocate in the ALS community that led the fight to pass the ACT for ALS. Thanks to each of you for co-sponsoring and helping pass that legislation.

I am writing today to share my family's story with amyloidosis and to share my opinion why the Promising Pathways Act is desperately needed for people with imminently fatal, heterogeneous rare diseases. If the committee is allowing in-person testimony, I am also requesting an opportunity to speak.

I. Three Rare Diseases where Therapies Work but the FDA Denied Approval

Following you will find the powerful evidence that was presented at AdComs for ALS, Amyloidosis and Duchenne Muscular Dystrophy (DMD) therapies – all which would have easily met the PPA standard of review. The FDA incorrectly held that these therapies didn't meet the current statutory standards for approval.

Perhaps most egregious, the FDA blatantly ignored the Real World Data and Real World Evidence as specified in 21st Century Cures et al. Multiple people in the trial and their world-renowned physicians testified that these investigative therapies improved how the patients "felt functioned and survived" – which is supposed to be the legal standard to evaluate whether a therapy has a clinically meaningful effect. The expertise of these physicians exceeded those of AdCom members and far exceeded the expertise of anyone in the FDA. Nonetheless, these lesser qualified people

ignored the clinical trial data, testimony and clinical observations of top disease specialists with hundreds of years of expertise.

Promising Pathways is necessary to improve early access to therapies as each of these therapies had **"relevant early evidence of a positive therapeutic outcome"** years ago, and at a minimum, these therapies could have been approved in the last year if PPA were the law.

People are dying waiting, while therapies that work are stuck in bureaucratic red tape – despite evidence that people slowed or halted lethal rare disease progression. Some people even regained function. But the FDA said some evidence is not enough for approval.

These three therapies exemplify why we need the Promising Pathways Act for imminently life-threatening, rare heterogeneous diseases.

I. <u>ATTR Amyloidosis – Patisiran by Alnylam Therapeutics</u>

Amyloidosis is a fatal, heterogeneous rare disease. My mother died of amyloidosis in 2003. It took nearly a decade to receive a diagnosis. At the time she died, there were no disease modifying treatments. But her hematologist tried various off-label therapies in an attempt to give her a chance to live longer -- even though there were no peer-reviewed data showing that they might be effective in her disease. Sadly, the FDA does not act with the same urgency or compassion as my mom's hematologist did.

Amyloidosis is a systemic disease wherein amyloid proteins misfold and aggregate, then deposit in organs throughout the body, where they cause those organs to dysfunction. There are 30 different types of proteins that misfold. In addition to those 30 different types of proteins, there is genetic heterogeneity as well. ATTR amyloidosis can be wild type or inherited. Of the inherited types, there are 150+ variants. The most common variant (V122i) affects 4% of African Americans. The graphic below illustrates the heterogeneity. The average lifespan for someone diagnosed with ATTR cardiomyopathy is 2.5 to 5.5 years. The drug at issue, Patisiran, was developed for all subtypes of ATTR amyloidosis.

	Examples of Heterogeneity of Amyloidosis - 30+ Types					
Heterogeneity	Amyloidosis - not hereditary				h-ATTR - 150+ variants	
	AL (primary)	**AA (secondary)**	**ALECT2**	**ATTR WT**	**ATTR V122i**	**ATTR V30M**
Amyloid Protein	Monoclonal Immunoglobin Light Chain	**Serum** Amyloid A	LECT2	Transthyretin (Wild Type)	Transthyretin (inherited)	Transthyretin (inherited)
Common Ethnicity	ANY	ANY	**Mexican** Chinese (Han) Punjabi Egyptian Pakistani Sudanese Indigenous First Nation	ANY	**African American** West African Caribbean	ANY Portuguese Brazilian* Japanese Swedish**
Cause	Bone Marrow Disorder	Chronic Inflammatory Diseases	Possibly Digenic ?	Aging ?	**Genetic**	**Genetic**
Frequency Cardiac Involvement	Often	Some	Rarely	≈ 100%	≈ 100%	Rarely
Main Organ Involvement	Heart Kidney Nerves	Kidney Liver	Kidney Liver	Heart	Heart	Nerves
Possible Other Organ Involvement	GI Edema CTS Tongue Nails Purpura	GI Heart Spleen Edema Thyroid Autonomic Nerves	Spleen Adrenals Parathyroid Gallbladder Pancreas GI Prostate Ovaries & Fallopian Tubes	CTS Biceps Nerves Bladder Spine	Kidney Liver Spleen Nerves Spine CTS Biceps GI Ocular	Kidney Liver Spleen Thyroid Spine CTS Biceps GI Ocular
ICD-10 Codes	E85.81 AL	E85.3 AA	**E85.89** (Other)	E85.82 ATTR-WT	**E85.0 non-neuropathic inherited**	E85.1 neuropathic inherited

Patisiran is a gene silencing drug that interferes with the production of an abnormal form of the transthyretin protein. Patisiran targets and reduces production of the TTR protein in the liver via the RNAi pathway. In 2018, Patisiran was first approved for the treatment of the subtypes of ATTR amyloidosis that affect the nerves (ATTR-PN). Some people with both peripheral neuropathy and cardiomyopathy demonstrated improvement in their heart failure symptoms and their ability to function. These changes were consistent with the Phase 3 trial data and real world experiences of people in EAP who got Patisiran.

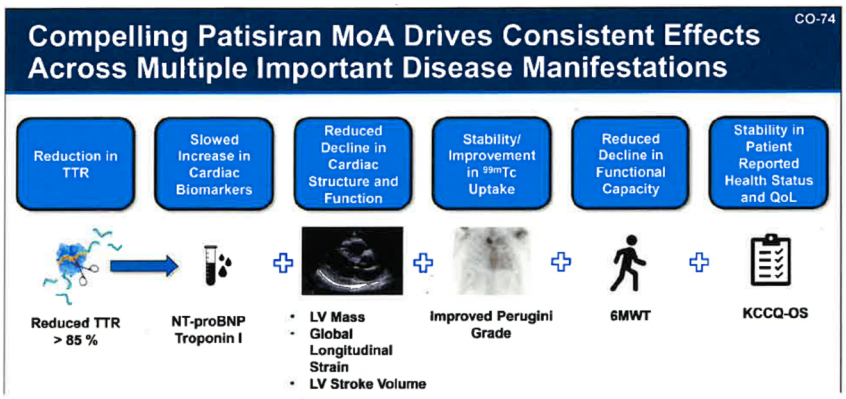
In 2023, Alnylam sought approval for both the wild type and hereditary subtypes of ATTR that cause heart failure aka cardiomyopathy (ATTR-CM). The Cardiovascular and Renal Drugs Advisory Committee meeting (CRDAC) met on September 13, 2023. Despite the positive AdCom recommendation of 9-3, on October 8, 2023, the FDA refused to approve Patisiran for people with ATTR-CM.

At the AdCom, several world-renowned amyloidosis specialists joined Alnylam in presenting the results of the Phase 3 cardiomyopathy trial called APOLLO-B.

- Ron Witteles, MD – Stanford University Cardiologist. founder & co-director of the Stanford Amyloid Center. He is the author of 399 peer-reviewed publications, 243 of which relate to amyloidosis.
- John Berk, MD – Boston University Cardiologist & Assistant Director of the Amyloidosis Center with specific expertise in ATTR. He is also on the editorial board of "Amyloid: the journal of protein folding disorders." He has over 300 peer- reviewed publications, 216 of which relate to amyloidosis.
- Brian Drachman, MD – Penn's Associate Chief of Cardiovascular Medicine, Penn Presbyterian Medical Center Co-Director, Amyloidosis Program who has treated 850 amyloidosis patients.
- John Spertus, MD MPH – St Luke's Heart Institute at the University of Missouri-Kansas City. Dr. Spertus designed the clinical outcome assessment called the KCCQ that was used in the Patisiran trial. It assesses improvements in the quality of life of people with ATTR-and other types of heart failure.

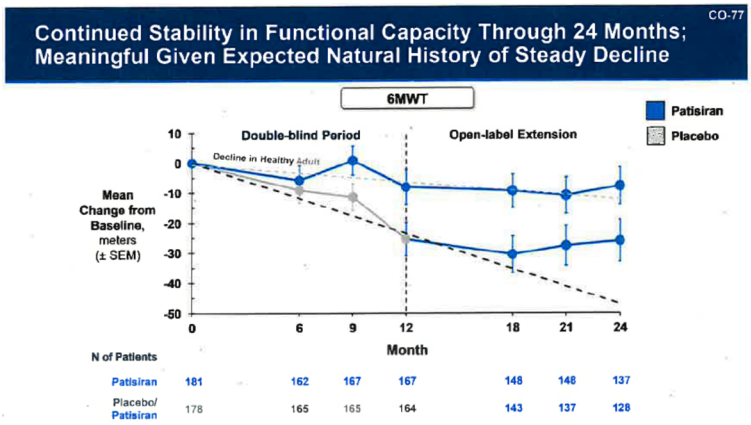
The Patisiran trial met its primary endpoint which was based on a timed six-minute walk test. People on Patisiran had a 62% reduction in their rate of decline and preserved function on that test through the 24 month Open-Label-Extension. Patisiran also met its key secondary endpoint with improvements in the KCCQ quality of life questionnaire (aka Patient Reported Outcome measure).

Patisiran also had a clinically meaningful impact on multiple biomarkers. It caused an 85% reduction in the pathogenic TTR protein. It impacted cardiology biomarkers, NT-proBNP and Troponin I. It also impacted radiographic biomarkers. Dr. Ron Witteles reviewed these clinically meaningful changes in the Alnylam graphic below. He said: "Patisiran has favorable effects on the very methods by which patients are assessed clinically and monitored in the real world. Patisiran is shown benefitting across each and every one of these elements with a remarkable consistency and it's particularly impressive to see such consistency of benefit in just 12 months."



At 1:36:45 into the AdCom, Dr. Ron Witteles shared his clinical perspective after caring for amyloidosis patients over the past 16 years at Stanford's Amyloidosis clinics, one of the world's pre-eminent amyloidosis clinics. He spoke about the "unrelenting loss of function" and lack of effective treatment options. . While the Patisiran Apollo B trial met its primary and secondary endpoints, Dr. Witteles shared the clinically meaningful impact of that data when comparing the Patisiran arm with the placebo crossover arm:

> When I look at this data as a clinician, if I'm talking to a patient with a disease who is going to have a slope like this and we can pretty clearly flatten that slope to the age related decline, that matters.... The fact that it is an inexorable decline is not in question. The fact that we can slow this decline by, depending on the outcome that you're looking at, some 60-odd-percent, it's clinically meaningful and with patients living longer we expect that as you have curves diverging, this benefit is only going to accumulate and matter more over time.



But then he also added:

> Of course, more important than what I think is what my patients want. Time and time again, patients say their quality of life is the most important goal of therapy. What they're most afraid of losing. Now, don't get me wrong, longevity is important as well but for most patients, death is not the most feared outcome. My patients with the disease who are most commonly in 70s and 80s and have other comorbidities know they're not going to live forever. They're not training for the next marathon. What they want is to be comfortable with their activities of daily living and activities that matter to them: taking a walk with a spouse or walking around the home and spending time with grandchildren.
>
> By the time that the patients start therapy, they have substantial limitations due to age, other comorbidities or the progression of the disease itself. For such patients, even what a healthy 50 or 60 year old, might consider a small delta, can be clinically meaningful and life altering. As I review the data from Apollo B, I see important benefits on exercise capacity and quality of life that speak directly to the goals of treatment that I know are most meaningful to my patients.... when you're talking about the patient population who already has significant limitations, the clinical importance for patients is clear.

During clarifying questions, Dr. John Berk said:

> "While we don't have longitudinal data that extends beyond 2 years of cardiomyopathy data. I can say to you quite bluntly, **this is life changing**. To me, as a physician who has cared for these patients over time, it's hard to share with you exactly how satisfying it is. I will tell you just by clinical scenarios, there's a 42 year old woman that was just involved in a TTR gene silencing trial... In that trial, she had remarkable sensory and motor improvement. The moving part of this is at the age of 42, she's facing the time at which her mother died despite a liver transplant, has two young children she's hoping to mother and see through graduations.

> And she was so moved by the marked effect on her life and outcome, her ability to look forward, that she had to give me a hug and I'm not a huggable person."

If an amyloidosis specialist opines that Patisiran's impact is life-changing for his patients, how does this not meet the "substantial evidence" threshold for approval?

Similarly, another amyloidosis specialist, Dr. Drachman, commented on the unmet need in amyloidosis. He said that despite being on Tafamidis, the only approved ATTR-CM therapy: **"people get worse and they die."** He opined that adding a drug that will suppress over 85% of the precursor protein should only benefit patients in the long term. He added that waiting for patients to deteriorate will result in "**irreversible damage** that will never be recovered."

During the Open Public Comment section, other PIs offered testimony. Nitasha Sarswat MD is an amyloidosis at the University of Chicago. She has been practicing as an advanced heart failure and transplant cardiologist for about 10 years. She participated in many TTR clinical trials and advocated or Patisiran approval:

> We have already seen a significant improvement in our patients' lives with neuropathy alone and in those with both cardiomyopathy and neuropathy. ... Additionally as a cardiologist, the idea that the drug actually improves blood flow to the body and potentially end organ function is a very exciting one. These patients want to run after their grandchildren and go for walks. We need another treatment for patients to attack this disease from the initial point as this disease causes such morbidity & mortality. I've had several patients from the Apollo B trial and in the early access Patisiran trial that have attributed their ability to go on vacations, stay out of the hospital and be more active. I have a particular 74 year old patient male who was having trouble visiting his wife in the rehab facility after her hip fracture. Once he started the early access program, he's been able to make it there; he's been able to walk, see her and enjoy their life together, and help her recover. This is the case for patients in general who have all felt better on Patisiran.

Rebecca Hung MD PhD was a PI at Vanderbilt's Amyloidosis Clinic, a major regional center for amyloidosis. They are treating over 240 TTR patients and enrolled 15 people in the Apollo B Patisiran trial and 8 more in EAP. These are her comments in support of approval:

> Of our initial 5 patients all ambulatory at enrollment, three were randomized to placebo, Of those 3, 2 have died directly related to TTR... Two randomized to Patisiran have both had atrial arrhythmias that required ablations but remain ambulatory with relatively preserved 6 minute walk, BNP and renal function..
> As part of the EAP, we added 8 patients who met criteria.... I recently saw one of those patients, a 79-year old man. He and his wife drive from Indiana to Nashville every three weeks for his infusions. They felt he had no quality of life on standard of care Tafamidis. His wife told me, unprompted, that I think the infusions saved his life. Prior to coming to Vanderbilt, he was hospitalized almost bi-weekly for heart failure. Since starting Patisiran he's required no augmentation in his maintenance diuretic and has had no readmissions for heart failure. He's more active, while obviously still limited, but doing things he and his wife report he could not do two years ago. His most recent ProBNP was at an all-time low. And the six-minute walk remains preserved over the 16 month we have been seeing him....

> At Vanderbilt, we have observed the expected decline in 6mwalk and QOL that continues to be the natural history of TTR cardiomyopathy – even on Tafamidis. Our patients have seen additional stabilization or improvement in symptoms and quality of life with the addition of Patisiran.

The totality of the evidence from these esteemed amyloidosis specialists – alone – SHOULD be enough to meet the substantial evidence threshold. The fact that the FDA found that it doesn't further buttresses the need for the Promising Pathways Act.

In addition to the trial investigators who testified in support of approval, 8 people who participated in the trial also shared their real world experiences. The Patisiran Open Public Hearing testimony starts at 5:01 in the AdCom. Their real world experiences are powerful proof about how Patisiran improved how they felt, functioned and survived. Yet, the healthy members of the FDA and biostatisticians who have never treated a dying patient supplanted their opinions about what is "clinically meaningful" over the opinions of patients and their world-class specialized amyloidosis cardiologists.

Given the mountain of evidence and the act that the trial met its endpoints, the FDA still didn't find that this met the "substantial evidence threshold for approval. These patients are our parents and grandparents. If the FDA can't exercise its promised regulatory flexibility for this aging senior population with a critical unmet need, it's clear that we must change the laws so our most vulnerable populations are given every chance to thrive.

If Promising Pathways were the law, this evidence would have easily met the standard of proof of "early evidence of efficacy."

II. ALS Therapy – NurOwn by Brainstorm Cell Therapeutics

As the Chair Braun knows, ALS is a 100% fatal disease with a critical unmet need. A mesenchymal stem cell therapy called NurOwn has been helping people with ALS halt their progression and regain function since its early Phase 1 and Phase 2 trials. The subsequent Phase 3 trial showed NurOwn met the legal standard of "substantial evidence" for some people earlier in ALS progression. In the Phase 3 trial:

- NurOwn met its pre-specified endpoints for people with scores ≥35 on the 48 point subjective and lawed functional scale. Een though this sample size was so small
- In post hoc analysis, NurOwn showed a clinically meaningful and statistically significant impact on people ≥27 on the 48 point scale.
- First in class biomarker data showed NurOwn had a biological impact across the disease spectrum and only on people in the NurOwn arm.
- Real world data from the trial, EAP and Right to Try demonstrated that NurOwn improved how people felt and functioned.

There is ample real world evidence and patient experiences proving NurOwn works. Please see the attached Public Comments filed in support of approval at the NurOwn AdCom, and include these Public Comments in the Congressional record for this hearing. Please also refer to the public testimony of these patients and Dr. Tony Windebank. Here is the link to the AdCom video.

Dr. Tony Windebank from Mayo Clinic was a PI in the Phase 2 and Phase 3 trial. With his 40 years of experience, Dr. Windebank shared his clinical observations and those of other PIs in the trial who had decades of ALS expertise. Dr Windebank summarized the "compelling data and shared his opinion regarding why NurOwn should be approved.

> "While it is clear that not everyone responds to the treatment, there are clearly a SIGNIFICANT NUMBER who do. I have clearly seen some people STABILIZE in a way that I have NEVER seen IN ANY OTHER TRIAL."

He further commented on the cyclic pattern of stabilization then decline he observed in the people who received additional doses in Expanded Access after the Phase 3 trial was over.

> In the small number of people who participated in EAP & received 6-9 treatments, there were people who STABILIZED while on treatment in the trial. In the interval before they were in the EAP -- which was over a year or more in some cases -- these participants deteriorated... then again STABILIZED in the additional treatment period.
>
> There were also SOME WHO IMPROVED THEIR SCORE FROM BASELINE ... something that is rarely seen. I should stress that other investigators who have been working 'hands on' with the participants in the trial have seen similar responses....

The opinions of the esteemed neurologists and the large amount of real world data and evidence was never discussed by anyone at the Advisory Committee meeting. This is the substantial evidence of efficacy that would support approval if Promising Pathways were the law.

More importantly, in the NurOwn trial, to receive the intrathecal therapy, people must have approximately a teaspoon of CSF removed before NurOwn is injected. This CSF could be a gold mine for researchers. ALS currently doesn't have any validated biomarkers but desperately needs them given our flawed clinical outcome assessment tool. If Promising Pathways were the law and NurOwn had a pathway to approval with post-marketing commitments, this CSF from thousands of people with ALS could help advance the science of ALS – and likely many other neurodegenerative diseases with a critical unmet need.

Please see my Public Comment filed for the NurOwn AdCom on September 27, 2023. Please include it as part of the Congressional record for the Senate Special Committee on Aging. It establishes the evidence that proves NurOwn works, and why we need the Promising Pathways Act to ensure 32,000 Americans with ALS don't die waiting while promising clinical drugs are stuck in the regulatory pipeline.

III. Duchenne Muscular Dystrophy

Attached is CBER's Advisory Committee meeting for Sarepta's gene therapy to help boys with Duchenne Muscular Dystrophy (DMD). Please take the time to listen to the parents and sub-specialized expert pediatric neurologists who treated these boys with DMD. The FDA only approved this therapy for boys who are 4-5 years old. Other boys with DMD are dying waiting for approval.

Beginning at 3:36:40 is the Open Public Hearing portion of the Sarepta AdCom on May 12, 2023. The parents showed probative video of real world evidence about how their boys with DMD functioned before and after Sarepta's therapy. They offered testimony about how clinically meaningful a few points of function are on the subjective clinical outcome assessment used for the trial endpoints.

Tearful parents compared the DMD natural history and how their sons had lost function without the therapy in comparison with those who were enjoying their childhood because of how the therapy helped them. One family had one son who qualified for the trial and one son who didn't. Now with the FDA's decision to only approve it for some, this inhumanity is foisted upon many families who have more than one son battling this horrific pediatric muscular dystrophy.

Other tearful parents shared their sons' improvements on a split screen compared to their friends' sons who were losing precious function every month. As one parent said, "Time equals muscle." One mother showed the graves of the boys with DMD who died waiting for access to Sarepta's therapy.

The parents' testimony was compelling but the researchers testimony provided the scientific justification to approve SRP-9001. Top pediatric neurologists testified that they witnessed SRP-9001 causes changes in function that they had never seen in their prolific careers. These experts included: Jerry Mendell, Kan Hor, Anne Connolly and Linda Lowes o Nationwide Children's Hospital; as well as pediatric neurologists like John Brandesma, of Children's Hospital in Philadelphia, Aravindhan Veerapandiyan of Arkansas Children's Hospital, as well as retired NIH DMD researcher, John Porter, MD, et al. Additionally, one parent commented that the FDA had not allowed all the trial's investigators to testify, thereby limiting the presentation of the totality of the evidence and expert opinions in support of SRP-9001's approval.

In Sarepta's presentation and briefing documents was evidence about 4 boys who were treated in the early open-label trial without placebos. These boys are still alive today, beating the disease's natural history. Subsequent studies are corroborating those early findings.

If Promising Pathways were the law, many of these boys could have been helped before they lost critical function. If our regulatory laws can't exercise the broadest o regulatory flexibility for little boys with a terminal illness, we need to change the laws.

IV. Why Current Legal Standards are Insufficient for Drug Approvals for Rare Diseases

As you know, the current FDA law provides two regulatory pathways for approval outside of the EUA pathway that was used for COVID therapies. The standard approval pathway requires a therapy to demonstrate "substantial evidence" of safety and efficacy. Typically, that requires two Phase 3 trials that meet the trial's pre-specified endpoints of clinical meaningfulness as well as statistical significance, with a p-value better than 0.05. To determine if a therapy has a clinically meaningful impact, the FDA is supposed to ask the question: does a therapy improve how a patient "feels functions or survives?"

Pursuant to FDASIA passed in 2012, the Accelerated Approval pathway is intended for serious or life-threatening diseases with unmet needs. The approval is based on surrogate endpoints like biomarkers that are "reasonably likely to predict a clinically meaningful benefit."

Pursuant to 21st Century Cures and its own Guidance Documents, the DA is supposed to consider Real World Data, Real World Evidence and Patient Reported Outcomes as supporting evidence of efficacy. They are now ailing to do so unless that data is pre-specified by the drug sponsor. This is an unconscionable disregard for the human experience. This is the type of evidence that should also support the early evidence o efficacy standard under the Promising Pathways Act.

Additionally, given the "critical unmet need" in ALS, Amyloidosis, DMD and many other rare diseases, the FDA is supposed to exercise the broadest of regulatory flexibility. However, they have failed to do so consistently. Then making that situation even worse, people who are dying have no statutory recourse to challenge that failure.

We hope you will consider the above evidence in support of the need for the Promising Pathways Act.

With hope,

Michelle Lorenz
VOICES FOR ALS

cc: Katie Campbell, Legislative Director
Gilbert Ruiz, Legislative Director

Jeff O. | Arizona



Age: 50
Year of Diagnosis: 2019
Type: Sporadic

With very few treatments available currently I would welcome any new medications. I believe any medication it is still worth a try. I would be willing to try it before approved

ALS is a horrendous disease that has been known about for over 100 years. It is pathetic that there are not better treatments available or even a cure. I am no longer able to hug my family and friends, move any part of my body on my own, or even use the restroom without assistance. It is humiliating and 100% deadly.

There are not words to explain how this impacts my family and my children and friends. It is horrible for them to know that they can't save me and that I have a limited time to be with them. It is heart breaking
You become solely dependent on everyone else for everything and that it is always fatal.

Please find a cure as soon as possible!

Judith M. | Arizona

Age: 65
Year of Diagnosis:
Type: Limb Onset

We Can't Wait

When my husband, Alex, suffered with the disease of ALS, he was willing to try anything that would possibly help with the progression of the disease until he got to the point of requiring a trach tube for breathing. **He wanted to live even in a wheel chair, but when he lost his ability to move his hands and breathing was so strained he decided it was time to end his battle**. He had 18 months prior to advancing so quickly that he would have tried anything. He took the one drug, Rilusol, I believe that possibly extended life for 3 months.

It would have depended on his side effects.

If the clinical trial is complete with good results then try it. **These patients only have a short time to live - what can possibly be worse that the effects of ALS.** The covid vaccine happened quickly without FDA approval. Just don't make the cure so expensive that no one can afford to take it!

My husband died at the age of 61! 2 years with ALS. His personality was bigger than life itself and he continued that spirit thru the disease. He was a hard working family man and was missed by the huge number of people he impacted. Take the time to view the YouTube video - "Alex Massey Farewell" and you will understand what a loss he was to his family, church family and employer.

What a good spirit these patients have during the battle.

Get going on a cure.

Amanda C. | Arizona



Age: 36
Year of Diagnosis: 2016
Type: Genetic

My Mother could have enjoyed a longer time on earth, with more capabilities. Instead, she lasted three months from being diagnosis.

I think having that chance is so important, not only to the individual but the family. Me personally, I had tried anything to stay on this planet with my family.

If I know I'm going to pass, the FDA approval is not important to me. I would rather have access, knowing that I could help improve others' chances.

The only word I know to describe is heartbreaking. I watched my mother deteriorate in front of my eyes. Everything she once was independent at, turned into having to rely on everyone around her. I had to take family leave with no check to help my father with my mother because we could not afford to higher anyone to come help.

Not only did I watch my mother die before my eyes, I watched my father fall into pieces over the love of his life. It is a cruel disease.

Its not pretty. There is no cure. And it is a death sentence. Its not like cancer, where there can be hope. There is no hope with ALS. You just have to learn how to live with that fact, both individually and as a family.

We are suffering. It's not about the money, it's about lives.

[redacted]

My name is Jamie Dubuque, formerly a long time resident of New Jersey and residing in Northern Arizona since July 2020.

My son Declan was born on January 31st, 2022 with Barth Syndrome. For the first eleven months of his life, this ultra rare syndrome was undetected in his body. Hindsight is 20/20 but we now know that his petite figure, lack of weight gain, energy and strength were linked directly to this serious disease. Our world was flipped upside down on December 30th, 2022 when Declan went into cardiac arrest. He endured 20 minutes of resuscitation efforts and was put on life support within 24 hours from his arrest. Our family suffered through two weeks of unknowns, uncertainty and no suggested recovery. This long, terrifying roller-coaster lead to his Barth Syndrome diagnosis while we simultaneously and fortunately weened him off of life support. At diagnosis we were offered an opportunity to receive a trial drug called Elamipratide. Coming from a mother who intended to raise her son holistically, I can assure you a decision to accept would be a major leap off of a cliff of even more scary unknowns. As a family we considered the reality that there is no known cure for Barth Syndrome or alternative drug for our boy. At the time, putting him on Elamipratide truly felt like a half of a step in the right direction. Our hope was to see slight improvement in Declan's very sick heart within twelve to sixteen weeks on drug.

On January 27th, 2023 he was put on a second form of life support. When the support device was implanted the doctors told us it was more likely to be a bridge to heart transplant rather than recovery.
While we watched Declan go through therapies, exceed expectations and meet goals in place, he was also thriving. Everyday we waited for our miracle to happen and something to drastically change in his heart. Within fifteen weeks of being on drug, Declan's doctors saw his heart return to normal function and size. Fast forward to late July 2023, recovery was confirmed and after the life support was safely and successfully explanted on August 2nd, 2023. We credit Elamipratide for Declan's recovery and believe that without it our son's hospitalization would have been more challenging and quite frankly twice as long. It is true for most if not all other Barth Syndrome children, if they survive beyond heart failure, transplant is typically their path forward.

Our son is home as of August 31st, 2023 and even today it seems surreal that he is with his native heart. Without knowing his medical history or taking notice of his temporary feeding tube, you'd think there is nothing holding him back, especially rejecting the idea that he is living with a debilitating disease. Not only can we not keep up with him as he races around like a toddler should, we can't even keep up with the good news. His heart doctors tell us his latest echo on October 10th, 2023 shows a

heart that seems to have never been sick or had a surgical device implanted within it's walls. As Declan grows, something he struggled with prior to drug, he will outgrow his heart medications.

The importance of having this therapy or others comes from necessity. If we were to lose access to this drug, our greatest advantage to moving forward with a healthy child would be taken from us. To have to think about the possibility that a day will come that I can't help my son, having sacrificed so much of his young life already with his hospitalization. As a mother, I can't imagine again having to watch Declan struggle the way he did in his early infancy. How could I possibly prepare my only child and his adoring family for such a huge disappointment?

Thank you for your time and attention.

Sincerely,
Jamie Dubuque
Arizona



Alfred A. | Bullhead City

Age: 77
Year of Diagnosis: 2009
Type:

It is important to have access to medicine. ALS is devastating.

I am filled with sadness that they couldn't do more to improve my quality of life.

The ability to do the normal things of life leave you. Like walking, swallowing, picking up a spoon, bathing yourself, etc.

[redacted]

Esteemed members of Congress:

My name is Phillip Farris. I live in Turrell, Arkansas. My son, Luke, suffers with the rare disease, Barth Syndrome. Only about 300 people worldwide have been diagnosed with this disease. His Barth Syndrome has caused him crippling cardiomyopathy, causing him to experience extreme fatigue, leaving him without the energy to perform many of the normal tasks that the normal 17 year old would do. His fatigue causes him exhaustion during the school day to the point that he must take a nap after school just to function in the afternoon hours. Of course, his extreme tiredness affects his education in that he has trouble learning and paying attention while exhausted. Access to experimental therapies could be potentially life-changing for Luke and may even extend his life-expectancy, which is currently about 40 years old. Luke and I would appreciate your consideration as you advocate for better access to experimental therapies for rare diseases.

Thank you.
Phillip Farris

[redacted]

My name is Kellye Farris and my son, Luke has an ultra rare disease named Barth Syndrome. We live at 160 Pollard Road in Turrell, Arkansas 72384. Barth Syndrome causes Luke to have a rare heart condition called left ventricular non-compaction cardiomyopathy, which is where the left ventricle is thick and sponge-like, and as a result, it doesn't pump blood throughout your body as effectively as it should. (Some boys with Barth Syndrome have had heart transplants.) This disease also causes Neutropenia which is a compromised immune system. If Luke gets an infection or a fever he must go to St Jude within the hour for testing because any infection could be life-threatening for him. Barth Syndrome also causes Luke to have extreme muscle fatigue to the point that he usually takes a nap after school every day. Any physical exertion causes him to become extremely tired. He gets winded if we go on any kind of long walk or hike. His life expectancy is shortened because of this disease. He also has learning disabilities because of the effects of Barth Syndrome. He has a difficult time with math, which is common among Barth patients. He has an IEP at school because he needs a lot of accommodations with his work because of the extreme fatigue and disabilities he suffers from due to this illness.

On November 28, 2020 we were at St Jude when we were told by Luke's doctor and his geneticist that he had #BarthSyndrome . They were nervous to tell us. We had been going to St Jude since July 2018, and up until that point they had no cause for his neutropenia that had been discovered in June 2018. They had become like family in that time. They gave us advice, suggestions, good wishes, and kindness through all those months and years. They were nervous to tell us that Luke had Barth Syndrome. They explained it as best they could, but having never cared for a person with this ultra rare disease they could only tell us what they had recently learned about this rare disease themselves. The geneticist (a knowledgeable, kind woman) had lots of papers and diagrams and information for us to go over. The doctor (a wonderful man) had contacted the authority on Barth Syndrome (Dr. Vernon) and had us set up to talk with her. He gave us the contact information for a lady (Shelley Bowen) from the Barth Syndrome Foundation to talk with about this disease our then 14 year old had just been diagnosed with. Our doctor at St Jude did so much footwork for us. He had to prepare himself to tell us Luke had this rare disease that he had just learned about himself. He had cardiologists added to Luke's care team at St Jude. Many of whom know Dr. Vernon personally. Some have even worked with her at Kennedy Krieger.

Nearly two years ago Luke was diagnosed with Barth Syndrome, an ultra rare genetic disease that causes cardiomyopathy, neutropenia, muscle fatigue, learning disabilities, and early death in some. Many boys with this condition don't make it past 5 years old. But. BUT because of the Barth Syndrome Foundation and the families and volunteers and doctors and researchers who donate their time, knowledge, and money to this wonderful foundation, people with this ultra rare disease are living longer and happier and healthier lives. Historically death from heart failure or infection occurred by three years of age, but with improved diagnosis, medical therapy and monitoring, survival has been extended, with many survivors now into their adult years. Survivors of BTHS, however, almost always live with extremely compromised physical health, and those few who enjoy relatively good health live every day with medical conditions that can

become life-threatening with little or no warning. Someone with BTHS will likely suffer with varying degrees of BTHS symptoms. It is critical always to remember that BTHS is a complex inborn error of metabolism. Because the disorder affects many systems of the body, treating a patient with BTHS often requires involvement of experts from a wide range of medical specialties.

The FDA is not giving these patients a fair shake by not allowing them access to drug therapies that have been proven to improve the lives of patients with Barth Syndrome. There are not many patients with this disease, but why should that mean that they should not have a chance to live a healthier life? Elampretide has shown to improve the heart and muscles in patients with Barth Syndrome. Please give these patients, my son, others' sons the opportunity to have a treatment for this life-threatening disease.

Thanks so much,
Kellye Farris
901-857-3645

[redacted]

Living with Barth syndrome is an everyday chore because as a person living with Barth syndrome I have very little energy throughout the day. most days after school I come home and take a nap. last year at school we had a carnival day. By the end of that day I was so weak I could bareiy walk. It was like I was walking on jello.
Having Neutropenia coincides with having Barth syndrome. Neutropenia is the scientific term for having a compromised immune system, meaning if I get an infection or a fever I have to go to the hospital. getting an infection or a fever is a pretty regular thing for me.
Birth syndrome also causes Left ventricular non compaction cardiomyopathy that means the left ventricle is thick and sponge-like, and as a result it doesn't pump blood through my body as effectively as it should. I also have to visit a cardiologist every 6 months to make sure it's not getting worse.
elampretide Which is a drug therapy, would make my life so much better because it has shown to improve the heart and muscles in patients with Barth syndrome
- Luke Farris 160 pollard road turrell arkansas



SARAH MICHELLE NELSON

La Crescenta, CA

Sarah was our oldest child. She was born in 2004 and was never ill. On a Girl Scout camping outing I noted she was having difficulty seeing and her eye was turning out. Upon returning home I took Sarah to the doctor who reported everything was fine. I pushed for more tests. An ophthalmologist discovered she had double vision and ordered an MRI. That's when we were told that Sarah had a tumor in her brain stem. The doctor told me it was less than a 1% survival at one year. There were no promising drugs in the pipeline, not many studies going on in this area of brain cancer research as it was hard to treat and hard to get drugs to. While Sarah passed away in 2013, we have never given up hope of helping other families not have this same experience. We want other families to have choices and options. We want them to have a fighting chance.

Why the Promising Pathway Act is Important to our Family: The Promising Pathway Act is important to me because we can't wait for drug trials to be done in adults first when there aren't comparable adults. This is a disease of childhood. While there are adults with the condition their tumors are very different from those of the children and we don't know how hormones play a role. We don't want to miss out on a drug that will help our kids because we don't have the adults to do a trial with first, or that the trial in adults is unsuccessful because their tumor is different and we miss out on a drug that could help our children.

Our children are our future. It's too late for Sarah, but it's not too late for the other warriors currently in the fight, or those that we don't yet know about. We have to do better for our kids.

Shannen Nelson

Mother of Sarah

10/20/2023

Dear Chairman Casey, Ranking Member Braun, and Honorable Members of the U.S. Senate Special Committee on Aging:

My name is Amy Bekier, and I live with a lifelong continually progressive disease called Facioscapulohumeral Muscular Dystrophy, or FSHD.

I often refer to living with a rare disease and its progressive disability which is compounded on top of aging as 'peeling the layers of an onion'. Each layer reveals additional interacting difficulties, sometimes making aging indistinguishable, only accelerated, and worse, from the added burden of the disease's progression. As we age the weight of the two, age and disease, becomes untenable and unbearable. The medical community does not know how to deal very well with aging let alone aging with a progressive disease. We are often left to our own clever devices without viable funding for treatments or medication to even mitigate the disease symptoms. Today I might be able to scratch an itch on the top of my head but tomorrow I may forever lose the ability to raise my arms to feed myself or roll over in bed. Prematurely losing independent control of your body, having to rely on others for the most very basic things in life such as toileting, bathing, transferring, preparing, and eating food, walking, dressing and the like take a huge toll not only on the physical aspects but on the mental outlook of the patient and their family and caregivers.

There are more and more seniors, like me, who have lost friends and family and have absolutely no relatives available to assist in our care. The new-found term is "Elder Orphan". There are tens of thousands attempting to age in place and not be a castoff burden to friends or society, many without the monetary wherewithal to subsist alone. This is a rising epidemic, a burden on society, a mental health crisis, and a monetary catastrophe. For healthy Elder Orphans, the senior years can be filled with contentment but for those with rare progressive diseases simply managing to live through the day becomes an all-consuming effort. Many of us still have enough mental acuity to contribute to society but the energy required to survive takes more than we can give.

In my opinion funding for treatments, assistance with qualified home carers, less onerous applications for durable medical equipment, more access to maintenance physical therapy, and better mental health management to facilitate independence would be a good starting point.

I believe that this country is far better than the way we are currently kicking this powder keg down the road. The greatest need is for qualified subsidized home care assistants and transportation for this growing community. Right now, almost all permanently disabled people must spend down assets and be forced into poverty before we can get assistance, and the lack of training and quality of those assistants is so poor as to merely supply a warm body. The stress of finding qualified care, the fear of them simply not showing up and the anxiety of constantly looking for qualified help only exacerbates the downward mental health and physical abilities of the patient.

It is relentless. It is accumulating. It is devastating.

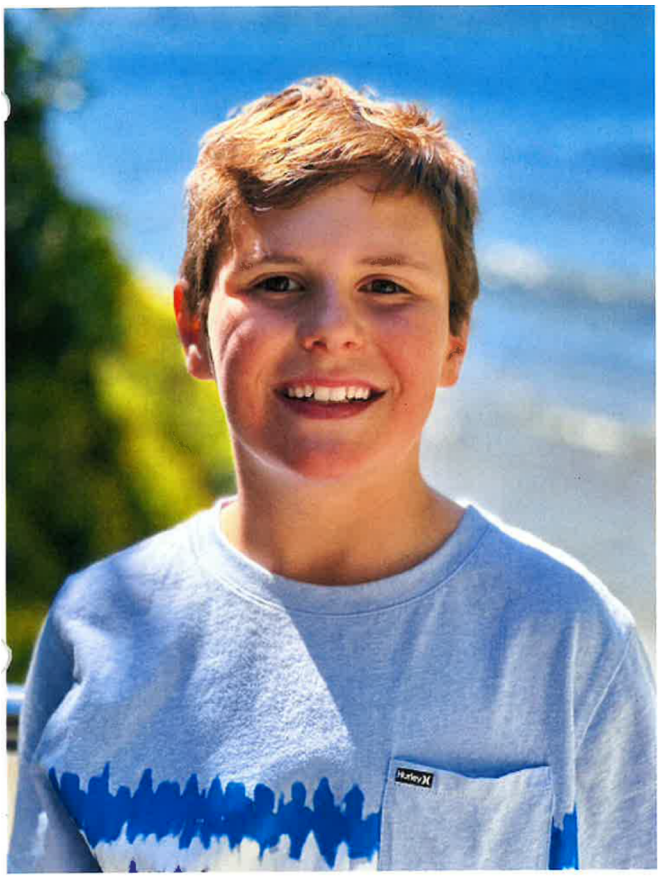
I have been afforded the opportunity to be featured in an international award winning 11-minute short film documentary called, "The Reinventor – one woman's experience living with Facioscapulohumeral muscular dystrophy". https://youtu.be/Ivd3wKe6S9Q
Please feel free to contact me if you would like to follow up on this.

Sincerely,



Amy Bekier
San Diego, California

CC: U.S. Sen Senate Special Committee on Aging
Sen. Bob Casey
Sen. Mike Braun
Sen. Kirsten Gillibrand
Sen. Richard Blumenthal
Sen. Elizabeth Warren
Sen. Mark Kelly
Sen. Raphael Warnock
Sen. John Fetterman
Sen. Tim Scott
Sen. Marco Rubio
Sen. Rick Scott
Sen. J. D. Vance
Sen. Pete Ricketts


HurleyX

Omar S. | California



Age: 39
Type: Bulbar Onset





I pray for a miracle everyday. It is the most important thing that could happen for us. If a medication doesn't have any benefit, at least we were able to try instead of being sentenced to an early death. **I don't care about side effects if I have the chance for my body to no longer be a shell with a brain.**

Clinical trial process isn't important to me, we can all be the trial. We can no longer wait on the FDA to let us continue to meet our demise waiting on trials. If we can do it for covid which people have a chance is sentenced to 100% fatal should be granted the same opportunity, we have done nothing to cause this illness.

I can no longer work or do anything for that matters that doesn't include minimal use of my left hand. I can't even get out of the house as we cannot afford transportation that my chair can get into. **I lost everything I worked for within months.**

It's a nightmare My wife isn't the same, it's affected her health I would do anything to see her smile again. My friends, coworkers and family are devastated, once not knowing about ALS to educating themselves to everything they can read about.

I would like the right to possibly delay my demise from this disease. I have 12,8,6m old children. We are willing to take side effects, we (I) want a chance. **I want to see my kids graduate and make more memories. I want to hold my daughter again. I haven't been able to hold her since she was 3m old. Please hear our voices please.**

Shaun K. | California



Age: 39
Year of Diagnosis: 2017
Type: Limb Onset



A few months of extra life is better than nothing. **I'd rather die trying than die waiting.**

It is not important to me to wait for FDA approval. I am diagnosed with a terminal illness. ALS has upended my entire family life.

My family all suffer as they watch me deteriorate before their eyes.

I wish the world truly knew the **devastation** it takes out on entire families.

Conditionally approve treatments so patients can at least try hope, you already know what we want.

Susana R. | California

Age: 62
Year of Diagnosis: 2019
Type: Limb Onset

We Can't Wait

I believe new therapies are very important so that life can be extended without the horrible symptoms and disabilities.

I would be willing to try a new therapy but would need to find out the side effects.

Clinical trials are good of course, however, just like the COVID 19 vaccine I would be willing to try a new drug.

I have the slow progressive ALS but my life has been impacted as I walk assisted with a walker. I have weakness in my hands and my energy level is 50% of what it was b4 ALS diagnosis.

The diagnosis has had an emotional impact on my husband and sons.

I wish people would realize this is a terminal disease as the patient slowly deteriorates.

Please collaborate with countries such as Israel and European countries where there have been good results from their clinical trials.

Sybil C. | California

Age: 72
Year of Diagnosis: 2020
Type: Limb Onset

We Can't Wait

Guardedly – I may try some medication.

Not sure if I would take on risks; would need more information. That would be highly reassuring if it was approved by FDA first.

Would it be an understatement to say it has ruined my life? Devastatingly cruel. **It is a cruel, horrible disease.**

I beg you to hurry with a cure. What about pouring money into NU9 and speeding that along?

Brenna N. | California (1 of 2 pages)

We Can't Wait

Age: 20
Year of Diagnosis: Dad: 2020
Type: Bulbar Onset

The ALS community is desperate to place their hope on a drug that can potentially offer modest benefits. As of right now the available ALS medication that my dad was given, Riluzole, is just a band aid. There have been zero significant findings that Riluzole helps an ALS patient in any way. There is no guarantee the medication will give you an additional three weeks or three months of life. When my dad was first diagnosed with ALS in December of 2020 the Bulbar onset ALS specialist with Kaiser Permanente said they did were not in favor of it because it is not an effective medication. Every ALS patient responds differently to medication and the medications that are available to ALS patients today are not promising. ALS patients need a variety of medications, treatments, and therapies available to them in order to prove the effectiveness of each one. What do ALS patients have to lose? Their disease is 100% fatal anyway.

I would weigh a new therapy that offers the change of a modest benefit in balance with the risk that the therapy ends up having no benefit at all to a therapy that also has significant side effects all on the same scale. To me there is no reason to be holding medications back from ALS patients that could be risky, could have no benefit at all, or could have significant side effects. ALS patients are diagnosed with a disease that has absolutely NO HOPE IN LIFE. ALS patients are diagnosed with a disease that is 100% fatal. 100 % fatal. I would rather my dad, whom I am a caregiver for, trail with medications. If he were to pass because the medication failed him and many other ALS patients who were trialing the same drug, then the FDA can rule out that the drug they were in trail for and not give it to future ALS patients. Our ALS patients need to be tested with the medications, treatments, and therapies so that the future of ALS can have hope. Our ALS patients have nothing to lose at this point.

It is not important the clinical trial process is complete, and the FDA has approved it. As I mentioned above. Current ALS patients need to be the ones testing the medications, therapies, and treatments that are being held up so that future ALS patients can have hope. There is no reason why ALS patients who are willing to be involved in a trial, even outside of being approved, should be denied the right to test the drug on themselves. This disease is 100% fatal and they have nothing to lose.

I am my father's caregiver and am being is advocate in my responses. My dad can no longer communicate and therefore I need to be his advocate. Many ALS patients can not communicate and that is why ALS awareness is not as big as it should be. Once ALS patients can no longer be "normal" in public they stay at home and hide because they are ashamed of what their bodies have become. The public eye does not see what ALS does to individuals and unless you have known someone with ALS or have an ALS patient in your family you have no idea what ALS is like. It is something only experience can show and those who experience someone with ALS need to speak up and show even the hardest parts. No one understands.

Brenna N. | California (2 of 2 pages)

We Can't Wait

Age: 20
Year of Diagnosis: Dad: 2020
Type: Bulbar Onset

My dad's diagnosis has impacted my life greatly. I now have no doubt in my mind that I will forever be an advocate for the horrible disease ALS. **ALS is a nightmare that I wish I could wake up from**. I am a 20-year-old full time college student who balances my father's needs with the needs of my own. I can no longer go out and have the college and fun experience with my friends because I am needed at home. **Every little moment with my dad is so precious even if I am just talking to him while I push water through his feeding tube.** My dad's ALS diagnosis has significantly changed the way I view life and forever impact me in all that I do. Life is precious and every moment matters.

I wish people understood ALS on a deeper level. I wish I new more about ALS before my dad was diagnosed. I knew a family whose dad passed from ALS and all I knew about the disease is that it affected his muscles enough to be put into a wheelchair and nothing more. No body, including myself before my dad was diagnosed, truly knows what ALS is. People need to be exposed to all the details of ALS and not just the surface facts. I have to use the suction machine multiple times a day in order to try and clear my dad's throat of mucous. No body knows the extent of ALS and how horrible of a disease it is. Surface facts are not enough.

Medications, therapies, and treatments of ALS should not be held back if an ALS patient has a ZERO PERCENT chance to live anyway. **I am here to fight for my dad and all ALS patients present and future.**

Mary Ann W. | California (1 of 2 pages)



Age: 66
Year of Diagnosis: 2018
Type: Limb Onset, Sporadic



I am speaking for my husband, Harry who passed away from ALS in October 2020. Harry was a man who lived his life with extreme optimism. He wanted to believe that a therapy would be developed in his lifetime that would significantly increase his life span or possibly cure ALS. As much as scientists know about ALS and other motor neuron disease, it is clear there is more that is unknown. Without trials that may move the dial even slightly in the right direction how can we even hope to find a therapy that could significantly impact progression or cure ALS. This is a disease without hope and without any good outcomes. We have no choice but to try and rejoice in the slightest progress.

The only way we will come close to learning more about ALS will be if we engage in aggressive trials. The risks are more than worth it if it will bring us closer to finding out why this disease occurs, how we can slow its progression and potentially find a cure. ALS victims have no other choice, and they have no other hopes.

It is of no importance to me

For Harry, it altered all his life plans and expectations. It took away his future. He went from independent to dependent, from one who prided himself as giving person to one who needed to accept from others, from one who loved to give hugs to one who had to request a hug. He could have easily lost his dignity, many do. However, he did have to fight hard to maintain that dignity. He lost so much control over his life and had to patiently accept what that meant. We were fortunate to have financial resources and strong community to help us through. Many ALS victims do not. **It can be a very lonely journey with devastating financial consequences for the family**

Mary Ann W. | California (2 of 2 pages)



Age: 66
Year of Diagnosis: 2018
Type: Limb Onset, Sporadic



Watching Harry's disease progress over three years was devastating. The stress involved in his care was overwhelming. There were so many things that needed to be attended to, medicines, medical equipment, caretakers, insurance, doctors. There was the stress of something going wrong and knowing if you didn't do it right, it could kill him. His disease made him a moving target. No sooner did you solve one problem, when suddenly that solution no longer worked. Everyday ended in exhaustion, only to know that in the morning you would have to do it all over again. The sadness could be all consuming. It changed us and it changed our relationships with Harry and each other. As I said, we had financial resources to help with Harry's care. But many do not. In these cases, it requires family members to assume the full burden of care, often resulting in loss of income. Our children are adults. I can not imagine what it must be like for a family with young children and a parent with ALS. What this disease takes away from them will impact them for the rest of their lives.

Harry's biggest challenge was teaching others that even though his body did not work, he was still Harry. He needed to put him self out there and help people become comfortable being with him.

I watched Harry be repeatedly disappointed when he was rejected from one trial after another. He was willing to do anything that may have helped him or helped others in the future. The availability of trials and being part of a one should not be so difficult. ALS is only one of many motor neuron diseases afflicting people all over the world. More needs to be done to learn about these diseases and help discover viable therapies. It should not be about the money. **Real people are being impacted and one day it may be one of your family members.**

Chris M. | California



Age: 58
Year of Diagnosis: 2013
Type: Bulbar Onset



My brother had bulbar onset ALS and died but he wanted desperately to find ANY new therapy to offer ANY chance of ANY benefit, however small.

My brother had bulbar onset ALS and died but he did not care AT ALL if the trial process was complete or if the FDA had approved a drug before he could start to give it a chance.
My brother had ALS and died but he would say it was devastating, very time consuming and very expensive. He pursued any type of therapy he could possibly find, however remote a chance it had of helping, including many sessions of stem cells which were very expensive and made him travel to remote places, including Mexico where therapies are further along than here in the US.

My brother had bulbar onset ALS and died but he would say that those around him were devastated and distraught. They tried to make life as comfortable and as fun as possible, but it meant they had to take off work a LOT and pay people to come help with his daily life.

My brother had bulbar onset ALS and died but he would say that he wished people understood that ALS is the most cruel, horrific disease that exists.

PLEASE, PLEASE, PLEASE find a cure - soon!!!!! Or, even better still - find a vaccine or some way to avoid ALS in the first place!!!

Peter S. | California

Age: 36
Year of Diagnosis: 2018
Type: Genetic

We Can't Wait

I feel the choice should be made available to anyone that has this mutation, and it is up to the patient advocate to make the patient fully aware of their decision before the treatment.

That sounds good, I have opted to try a new physical therapy routine I found online.

It is extremely important, as I received care and treatment prior to finding out my true diagnosis. I had a surgery on my cervical spine when I was complaining of lumbar pain that progressed.to more intense pain.

I have developed new treatments, that require minimal cost. But the relief of the treatments are temporary.

I don't know to be honest what to do anymore.

The ALS disease is a lifelong disease that progresses to involve your life, those close to you and it is a difficult task to deal with.

I would like to thank you and your colleagues for giving me this opportunity to make my opinion known. Please have a wonderful day.

Marsha M. | California



Age: 66
Year of Diagnosis: 2020
Type: Limb Onset

Access to new therapies is critical for individuals with ALS. Time is not on our side. Imagine if you had the opportunity to extend your life by additional months or improve your quality of life for the remaining months with your family, friends and community. I believe everyone with ALS, a terminal disease, should have access to the benefits of these therapies. **The potential rewards outweigh the potential risks.**

I would discuss the options with my doctor, research the therapy, review results of clinical trials, and weigh each potential therapy for possible rewards and potential risks. Regarding side effects - **each person responds differently and can stop the therapy if the reward/risk equation is not positive.**

I believe that the FDA process is important but very lengthy. For ALS patients facing a terminal disease diagnosis, the timeline for completing all the clinical trial phases is too long. If a therapy has met the safety requirements, has proven efficacy after Phase 1 & 2 trials, I believe ALS patients and their doctors should be able to have access to the therapies.

My life has been radically impacted. I am fortunate to have incredible family, friends and colleagues to support me, as well as access to an excellent ALS clinic. Over the course of a few months, I have had to greatly reduce my personal and professional activities due to limited mobility and energy.

My ALS diagnosis has had significant impact on my husband in our day-to-day activities and our business together. He is now managing the lion share of our home, family and work responsibilities. My diagnosis has also been very difficult for our children, our extended family and close friends.

I wish people understood the complexity and variations of ALS. I was stunned to learn when I was diagnosed that **only 8% of cases are genetic and that 92% are from unknown causes** (mine is not genetic). The general assumption is that Lou Gehrig's Disease is a genetic disease. The research on ALS could be a window into the diverse factors in our environment that impact our bodies in profound ways. **This research could provide greater understanding and possible solutions to many related neurological and neuromuscular diseases affecting the greater population.**

I fervently request the FDA to allow for expanded access and compassionate use of available drug therapies for ALS patients. We are battling this disease on limited time and request the opportunity to extend our time and quality of life with our loved ones.

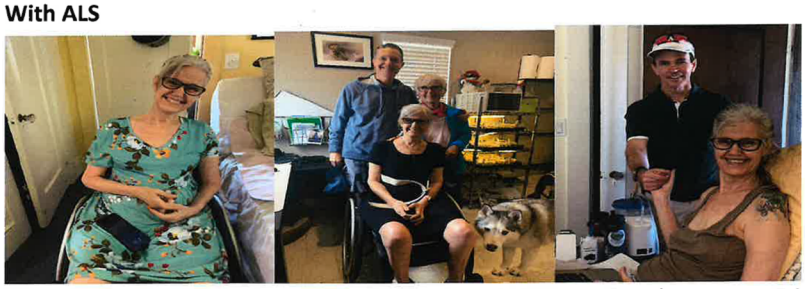


Before ALS

My daughter Laura Ann Marie Hanson
Warm, Friendly, Smart, Caring, Beautiful, Energetic, Sister, Daughter, Aunt, Friend, Animal Lover, Adventurer, Environmentalist. Business owner. Impishly Humorous, Smiling, Kind, Energetic, Thoughtful.
Loves to cook and eat. Loves to walk her dog, feeds her chickens, pet her cat, travel with her husband. Loves her work. Loves her friends. Loves life.

LAURA IS A SHINING LIGHT. HELP KEEP IT SHINING. ERADICATE ALS

With ALS



Warm, Friendly, Smart, Caring, Beautiful, Energetic, Sister, Daughter, Aunt, Friend, Animal Lover, ~~Adventurer~~, ~~Environmentalist~~. ~~Business owner~~. Impishly Humorous, Smiling, Kind, ~~Energetic,~~ Thoughtful.
~~Loves to cook and eat~~. ~~Loves to walk her dog,~~ ~~feeds her chickens,~~ ~~pet her cat,~~ travel ~~with her husband.~~ ~~Loves her work.~~ Loves her friends. Loves life.

Maggie Bedord

[redacted]

How my daughter Laura Hanson is affected by ALS

Maggie Bedord
102 Drake Mews
Sonoma, CA 95476

Maggie Bedord
E-mail: maggiebedord@gmail.com



Dear Senate Committee on Aging,

I will briefly give you my background. I was a newly married practicing anesthesiologist and pain management physician when I was diagnosed with ALS at 35 years old. I was quickly disabled by this hopeless disease and the heavy burden and inability to start a family caused my wife to file for divorce. **ALS has taken EVERYTHING from me**.

Changing ALS from 100% fatal to treatable requires urgency and flexibility by allowing a new time-limited approval pathway giving timely access to promising treatments for 100 percent fatal diseases like ALS. We can't wait a decade or longer for the FDA approval process when the average lifespan of an ALS patient is only 2-3 years. ALS has been uniformly progressive and fatal since the first reported case in 1869. ALS IS NOT RARE and is rapidly becoming more common. **We need the Promising Pathway Act to bring hope for effective treatments and cures in our / your lifetime**.

The **Promising Pathway Act** provides a pathway for provisional FDA drug APPROVAL for life threatening / terminal illnesses **(including future pandemics)** that have no meaningful treatment. **This approval needs renewal by the FDA every 2 years**.

ALS faces tremendous scientific hurdles to overcome in the currently available FDA approval pathways. These will further delay effective treatments if you don't pass the Promising Pathway Act. Most treatments approved by the FDA have thousands of trial participants and have very clear outcome measures which can easily detect efficacy. Our trials are small because people with ALS die so quickly leaving a small LIVING population at any given time. The outcome measure used for the trials is an extremely flawed questionnaire with 12 activity questions to measure disease progression. The disease is heterogeneous with significant clinical and biological variability. These reasons make it exceedingly difficult to show efficacy in a traditional ALS trial even for effective treatments.

The FDA does not have a Center of Excellence for neurodegenerative diseases like it has for oncology to allow agility and flexibility in trial design, evolving improved efficacy measures, and evaluating accelerated approvals of treatments that show safety and early signs of efficacy.

The unmet medical need for people living with ALS is critical. This community needs access to promising treatments. **Please cosponsor and pass the Promising Pathway Act.**

Please watch this video montage of just a few ALS patients: Https://clipchamp.com/watch/zSKoXUh26FL

Thanks for your time.

Shahriar Minokadeh, M.D.
Anesthesiologist -Johns Hopkins Hospital
Pain Management -UC San Diego Now dying of ALS & fighting for FDA regulatory flexibility for 100% fatal diseases



[redacted]

Dear Senator Braun,

You and your colleagues are only hope that people with ALS now have access to Nurown.
I can tell you on behalf of many sick people including my husband how awful ALS is and Nurown is our ONLY hope to live, breathe on our own, see our kids and grandkids grow.
The headline today should read:
FDA AdCom ignored MAYO Clinic neurologists who testified that NurOwn works on a "significant number" in this brutal, 100% fatal heterogeneous disease.

- FDA failed to allow many in the trial (and their neurologists) from testifying in violation of their Constitutional Due Process rights
- One of those prevented from testifying was Navy Pilot Matt Bellina, when he and many in his family served our country to protect our Due Process Rights and yet Matt was not given his own Due Process rights
- The Voting Questions & the questions for discussion by the FDA-CDER were drastically different than those for NUROWN by FDA-CBER
- FDA violated 21st Century Cures (law passed in 2016) as patients' clinical data is Real World Data and Real World Evidence and the AdCom was not instructed as such
- Janet Woodcock told patients in a recorded PFDD meeting in 2019 that the mechanism of action "doesn't matter" and was irrelevant to approval, yet the AdCom spent hours discussing it
- The Voting Question that should have been discussed regarding "Substantial Evidence" was how NurOwn made people "feel function & survive" and yet those words weren't uttered by a single AdCom member

It was obvious that FDA bias and then salt in wounds was panel fanning flames by one panelist saying they don't want to give false hope. How is it false hope when you hear reversals confirmed by Mayo Clinic Neurologists?

There are only 55 days until the **CRUEL**
FDACBER
regulatory RIGIDITY will ensure that ALS remains a **DEATH SENTENCE** *by denying* Nurown
Accelerated Approval with a Phase 4 confirmatory trial **PLEASE** don't allow this to happen ALS
's **100% FATAL since 1869.**
Senator Braun, SHAM Nurown AdComm hearing WASN'T set up to find the Truth.
MANY with UNPRECEDENTED RealWorldEvidence were even DENIED an opportunity to speak.

ALS community is about to lose the most effective treatment in its 154-year history FOREVER. Please shine a light on the FDA regulatory RIGIDITY for 100% FATAL ALS that has left generations to die WITHOUT HOPE. Please talk to FDA to grant Nurown Accelerated Approval with a Phase 4 confirmatory study.

What would you do if you or your loved one is denied a treatment that WORKS and is left only with the option of CERTAIN DEATH?

How is this CRUELTY allowed to go on for a disease WITH NO SURVIVORS since it was first identified in 1869?

PLEASE don't allow this BLATANT FDA CORRUPTION & longstanding prejudice for this small Israeli biotech company to result in a DEATH SENTENCE for generations. That AdCom was a complete crucifixion of Brainstorm, the manufacturer of Nurown. The company worked hard for over a decade to bring a tailored treatment and was destroyed just like that.
It was a premeditated murder of every single ALS family out there for decades to come. It was a set up, I hope people saw it.
The speaker clearly mixed up ALS with relapsing-remitting MS where the period of disease progression is followed by some remission. It is devastating to find out that FDA chose Adcomm voters with no thorough knowledge of ALS (cardiologists, surgeons) and opinions of the world renowned neurologists were ignored.
Please ask the FDA why is holding Nurown to a different set of standards than treatments from larger pharmaceutical companies that were approved for ALS recently (with mediocre benefits and lack of phase 3 trial) with bigger lobbying budgets. Money, antisemitism?

People who are against Nurown could be the next ones to be diagnosed with ALS and maybe only then they fully understand the cruelty of their decisions.

Thank you for your help!!!
Victoria Kalinsky,
Laguna Woods, California

October 22, 2023

Dear Chairman Casey, Ranking Member Braun, and Honorable Members of the U.S. Senate Special Committee on Aging:

My name is Heloise Hoffmann, and I'm a nineteen-year-old living with facioscapulohumeral muscular dystrophy, or FSHD.

As a child, I lived the life of my dreams. My passions revolved around athletics, and I spent all the time I could playing tennis and riding horses. The sensation of wind ripping through my loose hair while racing sprints at recess was one of my biggest joys, and I was excited by my prospects of joining the varsity tennis team as a freshman at a notoriously athletic school in Texas.

But at ten years old, things started to go seriously wrong. I would drop my tennis racquet on the court and wake up with sore and uneven shoulders after just an hour of riding. I went from doctor to doctor, trying to find out what was wrong with me. I had to drop my sports, which were my favorite things to do. After a few months of physical therapy, I was told I was getting weaker instead of stronger. I flew from Dallas to San Francisco a few times to run tests, which came back inconclusive. An esteemed pediatric neurologist at the local children's hospital told me my pain was due to my budding teenage imagination. But after three years of endless prodding and poking and examining, my answer came: FSHD.

My world flipped upside down the day I received my diagnosis. Words like "progressive weakness," "deteriorating muscles," "variable prognosis," and worst of all "no cure" were dropped casually in my lap while I watched the life I had imagined for myself literally shatter in front of my eyes. A million questions flooded me at once: will I need to stop playing sports? Will I be able to wash my own hair? Will I be able to do the dishes? Will I be in a wheelchair? Will I be able to hold my children? Will I be able to live independently as an adult? These are not questions that a thirteen-year-old should have to wonder about, yet they are the inescapable reality for FSHD patients.

The two years after my diagnosis are characterized by darker days than I imagined were possible. I retreated into a shell of my own creation, not even sharing my diagnosis with my best friend. I was convinced that, if I didn't talk or think about FSHD, it would just disappear. Despite the gratitude I feel for the strong support system that surrounded me during that time, neither I nor my parents knew whether I'd be able to make it out of this deep spiral. All these feelings that I turned inward brewed into serious mental health problems. I was diagnosed with severe anxiety and depression. I became severely suicidal. I underwent very strong medical and behavioral treatments, but it seemed like nothing anyone could do or say or put into my body helped me digest this diagnosis.

A family move to Florida helped me see my diagnosis from a new perspective. In this new environment, I realized I wouldn't immediately be recognized as "the girl with the disorder" or "the loser who doesn't play sports." Little by little, I allowed myself to shed my shell. Though I still kept my diagnosis to myself, I arrived at a point where I finally accepted it. I resolved that I couldn't just sit around and wallow in self-pity anymore while others were advocating and researching for a cure - I had to be part of the solution myself. I resolved that it was time for me to control FSHD, not the other way around.

I launched myself headfirst into advocacy for FSHD when I founded the Southwest Florida Chapter of the FSHD Society, the world's preeminent patient-focused research organization for FSHD. Our first fundraising campaign was a tremendous success, raising $65,000 to support research. I'm still in awe at that number. Because there is hope, people want to help – people want to contribute to the cure for FSHD.

opposite. Instead, I want you to see the reality that the FSHD community faces daily and feel that the hope of a treatment is what keeps us going.

Yes, FSHD is devastating, and yes, our muscles are deteriorating before our very eyes, stripping us of the activities we love and the most basic abilities. But hope is stronger than this fear. There is so much happening in research labs, clinics, and the patient community itself as we speak. Across the country, patients are mobilizing to sign up for clinical trials. Therapeutic companies are working hard to design those trials. Researchers are developing cutting-edge technologies so that, even once we have a treatment, we can continue to explore more effective paths until we arrive to an absolute cure, whether it be through gene therapy, muscle regeneration, biologic therapeutics, or a combination of these. The time is now to act on these initiatives to accelerate the pipeline for a cure.

I imagine a very near future in which DUX4 is no longer attacking my muscles. A future in which I can run on the tennis courts, feel the wind blowing through my hair on a horse, dance in musicals, and ski black diamonds with my family again. I imagine a future in which children are not told that their pain is due to teenage imagination. A future in which those who have been wheelchair-bound since they were ten can run again. A future in which grandfathers can lift their grandchildren to the sky, a future in which mothers can carry their babies without worrying about letting them fall. I imagine a future in which no child must fear losing their independence.

I hope that, by sharing my story with you, we can work toward making this future a reality.

Sincerely,

Heloise Hoffmann
Stanford, CA

CC: U.S. Sen Senate Special Committee on Aging
Sen. Bob Casey
Sen. Mike Braun
Sen. Kirsten Gillibrand
Sen. Richard Blumenthal
Sen. Elizabeth Warren
Sen. Mark Kelly
Sen. Raphael Warnock
Sen. John Fetterman
Sen. Tim Scott
Sen. Marco Rubio
Sen. Rick Scott
Sen. J. D. Vance
Sen. Pete Ricketts

Dear Senator Braun, October 23, 2023

I am reaching out to you in response to your request for stories on the unmet medical needs faced by people with rare, progressive, and serious diseases for a hearing by the Special Committee on Aging to be held on October 26, 2023.

I am a participant in programs offered by the Huntington's Disease Society of America (HDSA), a leading national organization dedicated to the care and cure of Huntington's disease (HD), a rare and fatal hereditary disorder that manifests as a neurological disease with both physical and psychiatric components. The mission of HDSA is to promote and support research to find a cure for HD; help people and families affected by the disease; and educate the public and healthcare professionals about HD. Currently, there is no clinically available pharmacological, biological, or surgical agent or method that slows or stops the progression of HD.

The father of my children carried the gene for Huntington's disease. I had never heard of Huntington's disease, and although my husband's mother died from Huntington's disease just one year before we got married, I don't think he really understood just how much at risk he was to inherit the fatal gene, since the time was 1968, and not much was known about the disease, even by doctors! He was drafted and received orders to go to Vietnam, and he wanted us to get married before he left. We planned our wedding in three weeks, and the rest is history. I had three children within the seven years that followed. As fate would have it, my husband soon started demonstrating symptoms soon after my third child was born. The worst was yet to come. All three of my children developed juvenile Huntington's disease, and all three of them passed within a seven-year period as vey young adults.



Becoming a patient advocate has been the most important thing in my life in the last 30 years. Ironically, it has been 30 years since the gene for HD was identified. We thought at that time that we would soon have a treatment or cure for HD, but 30 years have passed, and so have my children and their father, and we still don't have the treatment or a cure. It is baffling to me that although Huntington's disease is like having MS, ALS, Parkinson's all at once, and fatal, not much effort has been made by our government to pass the Huntington's disease Parity Act to at least waive the two-year waiting period to approve Medicare benefits for our loved ones who are totally disabled. Without a support system, an HD patient will end up homeless or found dead in the streets. Many HD individuals may commit a crime in order to be arrested and have a roof over their head or a meal to keep from starving.

HD individuals who do have a family but are too sick to be taken care of at home may end up in a carehome, and there is a crisis taking place in carehomes that the public seems to be oblivious to. Carehomes are more often than not a facility where they will be violated, sexually assaulted, (as was my daughter was), or beaten up and so badly that the carehome will wind up sending them to the hospital, (as was the case with my son), and then refusing to re-admit them, stating that they require too much care. The problem is that the carehomes are understaffed. Carehomes get away with this even though they have signed a contract with Medicare and Medicaid that would prohibit them turning patients away due to the nature of their illness or the amount of work required to care for them. Those patients who don't have a movement disorder will simply be warehoused. The carehome industry is powerful in D. C. as they have many lobbyists working for them. The problems arising from lack of care in carehome facilities had been seriously overlooked by the government and the public. Residents are often kept in horrific conditions, often being kept locked into basements in filthy conditions, with little or no access to food or toileting facilities. Sometimes a carehome owner will sell his facility to an new owner who will use the seller's license without a license of their own. Carehomes operate under the radar with powerful lobbyist to cover for them should they get caught.

Patients often suffer from extreme weight loss, dehydration, untreated bedsores, inadequate hygiene, mental and physical decline, and inappropriate use of psychotropics. It was not until our country went through the Covid Pandemic that government officials got a good look at how patients are neglected at carehomes. What they saw was shocking, but now that the pandemic is somewhat behind us, it seems that the horror that the public witnessed is starting to fade from their memory. What we cannot forget are the many lives that were lost in carehomes that could have been avoided if people and government officials had been mindful of the living conditions that the most vulnerable and helpless individuals are thrown into to suffer through end of life.

It seems unconscionable to me that an orphan disease such as Huntington's disease should get less attention or simply ignored because they are less in numbers. The suffering that HD patients endure is the same and even greater than what patients of other diseases suffer. HD affects the entire family, as it is genetic and generational. With no treatment or cure, the patient will die, and juvenile onset patients, such as my children will die at a very young age. The suffering does not end when one generation passes, as the offspring will face the same fate as their family members. In my case, I have two grandchildren who are now in their early 20's, and I pray every day that they will not be carrying the same fatal gene as their mother, my beautiful Margie.

Most HD families become financial devastating from the sacrifices that need to be made, sometimes having to leave a job to take care of two or three members of the family affected by HD. There is not sufficient support for the family caregivers, as well. I have known several such caregivers who become so drained that they may pass before the HD patient, either from heart problems, cancer, or plain heartbreak.

Most health care insurance companies will not cover In-Vitro Fertilization to help young couples wishing to have a family to go through IVF and ensuring that their child will be free of the mutant gene for HD.

There are so many unmet needs for our HD community, and our government could really serve our underserved HD community by:

- Passing the HD Parity Act, which has not even made it to the House floor in 12 years to be voted on and waive the 2-year period that makes them wait before receiving Medicare benefits and badly needed specialized care for HD.
- Support ongoing Huntington's disease research and patient care.
- Vigilant oversight of carehomes and calling out facilities who understaff in order to get a bigger profit. Fine care homes guilty of patient neglect and abuse currently taking place in carehome all over the country. Penalizing carehomes is not enough. Revoke their license and if necessary, shut down the facility.
- Ensure that government agencies support HD families rather than look for reasons **not to support them.**

Thank you, Senator Braun, for taking the time to listen to my concerns and for your effort to alleviate the suffering that our Huntington's disease families are forced to endure.

Sincerely,

Frances D. Saldaña

Frances D. Saldaña, HD Patient Advocate
41805 Corte Montia
Temecula, CA 92592
franceshdcare@gmail.com

October 25, 2023

Dear Senator Braun,

I am reaching out to you in response to your request for stories on the unmet medical needs faced by people with rare, progressive, and serious diseases for a hearing by the Special Committee on Aging to be held on October 26, 2023.

I am a participant in programs offered by the Huntington's Disease Society of America (HDSA), a leading national organization dedicated to the care and cure of Huntington's disease (HD), a rare and fatal hereditary disorder that manifests as a neurological disease with both physical and psychiatric components. The mission of HDSA is to promote and support research to find a cure for HD; help people and families affected by the disease; and educate the public and healthcare professionals about HD. Currently, there is no clinically available pharmacological, biological, or surgical agent or method that slows or stops the progression of HD.

This is about our daughter Kellie who was adopted at birth and was diagnosed with Huntington's disease. We were made aware of Huntington's disease after we received the family's history and the fact that the great-grandmother and grandmother on the maternal side of the family had passed away from Huntington's disease. This was after we had made the adoption final.

We are faced with many obstacles for her care and financial assistance. Kellie did not qualify for SSDI due to the fact that she was unable to hold down a job & does not have 40 quarters for SSDI. Huntington's Disease is considered a "Compassionate Allowance Disease "per Social Security rules. It is in line with Cancer, Parkinson's, Leukemia and even Rheumatoid Arthritis. Because of Kellie's age, 48 years old, she does not qualify for any of the programs from Meal Service to being able to join a Senior Center for activities. This is totally unacceptable. We were told that if we have evidence of her having symptoms of Huntington's before the age of 22 years old that we may have a chance for her to receive SSDI. Kellie is currently receiving SSI, which will not be enough with the current cost of living. Kellie was born with the HD gene and was diagnosed in September 0f 2020. Huntington's does not have a timeline – it just happens.

She did have behavioral issues during her teenage years, but we didn't realize it was from Huntington's disease. Forty-eight years ago, Huntington's wasn't even talked about, nor was there any research being done. Behavioral issues are one of the symptoms. There is no cure or treatment for Huntington's disease. Our concern is for her future, where will she end up and who is going to care for her to make sure she lives a comfortable life? This is a terminal disease – NO CURE!

More needs to be done for people with these sorts of diseases regardless of their age. Where will the help come from? Very sad! This is a never-ending problem.

Sincerely,

Charles & Carol Gregan
10770 Black Mountain Rd #286
San Diego, CA 92126

[redacted]

Hello my name is Marc and I live in California. I was diagnosed with Mucous Membrane Pemphigoid in 2007 while living in Colorado. Pemphigoid is a rare, serious, and potentially life threatening autoimmune disorder characterized by painful blistering of the skin and mucous membranes. The blistering occurs because of an immune response that results in autoantibodies attacking the proteins that bind the cells of the skin and mucous membranes together. Open sores left by the blisters increase the risk of infection, which can be fatal if it spreads through the bloodstream.

I first had symptoms in my eye and just thought that I had an eye infection. After seeing several eye specialists who did not know what I had, I began to also have symptoms in my mouth, in my nasal cavity, in my throat, and on my skin. After 2 months, cornea surgery, and seeing several other doctors, I was referred to a dermatologist. After 2 biopsies, it was determined that I had Mucous Membrane Pemphigoid.

Because I have a rare disease, medical and dental professionals are unaccustomed to seeing it in practice. As a result, people like me are often misdiagnosed with having a more common illness that is seen more frequently by healthcare providers. Clinically, many rare diseases can mimic other conditions and are therefore misdiagnosed or go undiagnosed. Laboratory studies, including a biopsy and immunofluorescent studies, are needed to distinguish my rare disease from other blistering and erosive diseases and to achieve a correct diagnosis. These tests are invasive, expensive and not readily available to patients in the U.S.

I then began the long journey of treatment known as step-therapy. I was prescribed high-dose corticosteroids, and an anti-malarial drug. These drugs were ineffective, expensive and just made my quality of life worse with more side effects. They caused uncertainty, fear and anxiety for me and my family as I lost my eyesight and became partially blind, lost my career and professional life, and wondered if I would ever be a productive part of society again. After being hospitalized twice, and undergoing expensive treatments, the financial burden of the disease was immense. My doctors even told my wife to get my affairs in order because they didn't think that I would make it. I wondered if I would ever have the chance to watch my daughters walk down the aisle when they got married or share the joy of being a grandparent with my wife.

Having a rare disease affects people well beyond just their healthcare. Like all people that are diagnosed with a rare disease, I was not prepared for the challenges that came with my disease like; the loss of employment and accessing stable work, the financial hardship, difficulty accessing appropriate healthcare, and the stigma of being a person living with a rare disease.

Although the United States is increasing public awareness of the public health crisis of rare disease, the burden of rare diseases is still overwhelming. The estimated economic cost of rare diseases reached nearly $1 trillion in the U.S. in 2019. These costs are driven by direct medical costs like; Inpatient and outpatient care, Physician visits, prescription medications and their administration, and medical devices and equipment. Indirect costs include; forced retirement, job absenteeism, and the reduction in community participation and volunteer service. Then non-medical and uncovered medical costs, which also carry significant emotional and psychological burdens come into play. These out-of-pocket costs are associated with; modifications to one's home or automobile, transportation and education costs, and items not covered by insurance like experimental treatments, medical foods, and specialized therapies.

Gratefully,

Marc Yale
IPPF Advocacy & Research Coordinator

PLEASE SUPPORT THE WORK WE DO!
Donating today helps someone tomorrow.

Donating today helps someone tomorrow!
www.pemphigus.org or at #healourskin

International Pemphigus and Pemphigoid Foundation (IPPF)
915 Highland Pointe Drive, Suite 250 | Roseville, CA 95678
(855) 4PEMPHIGUS (855-473-6744) |
Direct: 916-922-1298 x106 | Cell: (916) 529-2048

To receive information on upcoming educational opportunities, regional support groups and the latest information for pemphigus/pemphigoid, please sign up to receive emails from the IPPF.

website | awareness | map | email | living with p/p | facebook | twitter | linkedin

A COMMON HOPE | AN UNCOMMON BOND
Serving those affected by pemphigus and pemphigoid since 1994.

[redacted]

To the Senate Special Committee on Aging,

Thank you for taking the time to hear my voice. I strongly believe that change needs to happen for millions of Americans that are suffering from rare diseases, and I am hopeful that with your support, it can.

I'm Megan Branagh, and I live in the San Francisco Bay Area with my husband, John, and our 4 boys. I'm reaching out as a mother of a child with an ultra-rare, life-threatening disease called Barth syndrome.

My 2nd son, Henry, is now 11 years old. He was deathly ill throughout infancy and as a young child due to severe heart failure from cardiomyopathy. Thankfully, he is stable now, but continues to take maximum therapeutic doses of serious heart medications, and will continue to his entire life. While these medications help his weakened and damaged heart to function, they do not address the underlying issue of why his heart is not healthy in the first place. Nor do these medications address the many other symptoms of Barth syndrome that strip life away from Henry every single day like the overwhelming fatigue, muscle weakness, and low white blood cells that make him susceptible to infection.

There is currently NO approved treatment for this multi-symptom, deadly disease. However, a drug does exist, elamipretide, but is on the verge of never being accessible. A clinical trial was started over 5 years ago on this drug in treating Barth syndrome. The treatment showed positive results in the initial trial period and multiple **statistically significant improvements** during the extension period of the study. Follow-on analysis also showed very positive cardiac improvements that **defied the disease's natural history**. And yet, the **FDA has refused to fully review a new drug application**. The FDA's actions are demonstrating that Henry (along with millions of others suffering from ultra-rare diseases) is too rare to matter.

And that is why I am writing—I believe that no one is too rare. I am **asking for a fair, equitable and appropriate review of elamipretide in Barth syndrome by the FDA** before we lose access to this drug, the only medicine currently in development for this ultra-rare disease.

Even though Henry's heart is stable at this moment (this could change at any time, for no explained reason, especially as we enter into his adolescent years), Barth syndrome affects every aspect of our family's life, every day – all of our daily decisions factor in Henry and his ability to access a full life, in more ways than we have to think about this with our other boys. And the worry about his well-being and future are tenfold.

Barth syndrome makes life for Henry extra difficult. For example, he just started middle school. He wishes he could ride his bike to school, like most of the other kids in our neighborhood, including his older brother. But this is physically not possible for him. He wishes he had a fun elective like most of his peers. But he must use his elective period as a study class to keep up with his schoolwork, as a full day at school is exhausting not only physically, but mentally, making keeping up with his work extra challenging. He actually loves sports, and mentally has a desire and the coordination to play, but physically cannot keep up with his peers. This is all in addition to the emotional anxiety that he endures as he navigates living with an incurable and deadly disease.

It is quite difficult to put into words what is at stake for Henry, my family, and many others in a similar situation, whether it be Barth syndrome or another ultra-rare disease. It is both sickening and devastating to know that a drug exists (elamipretide in our case), but that it may not ever be available to Henry or others with Barth syndrome. Not because it was deemed unsafe or ineffective; but because the FDA has not reviewed it fairly, consistently, and completely.

Thank you for not standing aside as this continues to happen in the rare disease world and people continue to die. I am very grateful for your time and effort, and will remain hopeful that a treatment for Barth syndrome will be available in our Henry's lifetime.

Hopeful for change,

Megan Branagh
(on behalf of my family in Walnut Creek, CA — John, Grady (13 yrs), Henry (11 yrs), Wesley (8 yrs), and George (2 yrs))

*** Our family hosts an annual Barth syndrome awareness and fundraising campaign in honor of Henry and benefiting the Barth Syndrome Foundation ~ Happy Heart Week. The 11th annual event was this past May 2023. We currently send our newsletter to over 500 households, have raised over $875,000, and have sold 945 HAPPY t-shirts. We have plans to host another in-person party in May 2024, and it would be overwhelmingly joyful to announce that along with the help of Congress, we were able to bring about change for the rare and ultra-rare disease communities at large.



PIPER WANEKA

Glenwood Springs, CO

Piper was smart, creative, and carried an innate confidence beyond her years. She dreamed of turning 5, going to kindergarten, inventing a way to make her hair stay pink forever - and eventually - flying to the Moon as the first princess astronaut. Her whole world changed on June 12, 2017, when subtle symptoms quickly became concerning and she was rushed to Children's Hospital Colorado where she would be diagnosed with Diffuse Intrinsic Pontine Glioma, or DIPG. There is no standard protocol to treat DIPG, but there is a standard counsel given at diagnosis: make memories. DIPG is inoperable, terminal, and carries an average prognosis of 9 just months. With radiation, clinical trials, experimental treatments, and tenacious hope, Piper fought for 16 months but passed away 60 days shy of her 5th birthday. She would never see her kindergarten classroom or fly to the Moon, but she did embody love, strength, and possibility. Her brave fight inspired a whole community known as Warriors for Princess Piper and together we have raised our voices and nearly $150,00 in research dollars to aid the long-overdue search for a cure. Piper's family, including two younger sisters, started a Colorado Chapter of The Cure Starts Now to honor Piper by saying her name, remembering her joy, and continuing her legacy. Together, we will change this unacceptable prognosis for future children.

Why the Promising Pathway Act is Important to our Family: This innovative act is important to us because we know how devastating a terminal cancer diagnosis can be and we know how it feels to have no options. Even though Piper's fight is over, more children are facing this horror every day and we want their outcome to be more hopeful than ours. PPA goes beyond granting expedited access to drugs it also uses the data collected to inform research – and that will have a life-changing impact on children and families who need it most.

Carrina Waneka

Mother of Piper

[redacted]

My name is Claudia Salmeron. My mom, María Elena Cuellar, was diagnosed with ALS in March of 2022. She passed away just one year later on March 22, 2023.

Simply put, ALS destroyed my family. My parents immigrated to the U.S. in their early twenties. My mom came from El Salvador and my dad from Ecuador. They both arrived and spent some years in New York City; however, they didn't meet until they were both in Chicago. After a few years together, they had me and when I was four years old, we moved to Aspen, CO because my aunt, my mom's sister, was living and working there. She sold my mom on visiting for a summer because it was a good community with available work and a good school for me. My mom fell in love with the town, and we planted roots. My parents worked hard in physically demanding jobs. My dad as a sous chef at a restaurant and my mom as a housekeeper in hotels and private homes. We weren't part of the wealthy elite in this winter wonderland, but the three of us were together and we were happy. I grew up and graduated from Aspen high school. I moved to Los Angeles for college and then started working in the city after I graduated but would always go home to my parents in Aspen any time I could visit. In 2020, I was going back and forth as much as possible once it was safe enough to travel after Covid, because I was so worried that my parents would get sick, and I wanted to protect them. ALS wasn't even a thought. The mom of a close childhood friend in Aspen was suffering from ALS. She had been diagnosed about three years prior, but I (regrettably) didn't know much about it. My parents knew even less.

'n May of 2021, my mom noticed fasciculations in both arms. Her doctor shrugged it off. A few months later, my mom mentioned to me that she was having trouble turning the car key in the ignition and was struggling to lift and put away dishes in the kitchen cabinets. This is how the weakness in her right arm began. That Fall, she began to have terrible lower back pain and started complaining that she felt out of breath. My parents had been in the mountains, living at nearly 8,000 feet for over thirty years at this point. Their lungs were accustomed to the altitude. My mom had always loved to walk, hike, bike, dance and be active. I thought maybe she was just a bit out of shape since Covid kept us cooped up for so long and thought we just needed to get moving again. In late October of 2021, she had her first laryngospasm. She felt like she was choking, except she hadn't been eating or drinking anything. She felt her airway close, and she couldn't breathe. I took her to the ER. They ran several tests and did x-rays. The doctor told us her left lung was partially collapsed. Although frightening, at least, I thought, this was something that could heal. They prescribed oxygen because her oxygen saturation level was a bit low. I was worried but at worst, we could move my parents to sea level, and all would be fixed. Unfortunately, that wouldn't be a viable solution. In fact, there would be no way to save my mom's life. After the first ER visit, my mom continued to feel unwell and that started the unending array of doctors' appointments. As they do, doctors were looking into anything and everything that it could be and going through the process of elimination. This took months; from October 2021 through February 2022. Life had already changed by this point as my mom didn't feel well and I continued to stay in CO month after month to help her with all the appointments. My boyfriend of eight years was holding down the fort in CA and taking care of my dog. I was still able to work remotely. ALS had already changed our lives and we hadn't even gotten the diagnosis yet.

The neurologist first said the letters A-L-S on February 14, 2022. I've hated Valentine's Day ever since. The doctor also had a horrible bedside manner. Very cold and didn't take that Spanish was my mom's preferred language into account at all. I had to translate everything for my mom. It's not that I minded translating, as I was accustomed to this role, but it became overwhelming and too much to process, and I couldn't just be a supportive daughter and reassure my mom ,hile translating the shocking information the doctor was giving us. When the doctor said this was looking like ALS it felt like I was outside myself; just watching the scene instead of living it. I wish that had been the case. Everything was a blur, yet intensely in focus. I burst into tears and my poor mom was sitting beside me, holding my hand, clueless about

care, so he became a wonderful guide for us in El Salvador. I was still able to work remotely and my boyfriend (now of nine years) would come down every other month to bring us supplies and medications from the U.S. We had a system. And while still incredibly difficult, it felt sustainable (at least for me). I selfishly thought that if we had a perfectly crafted system that my mom could live like this forever. My love for her was blinding me from seeing how much her ALS had progressed and how much she was suffering. She fought valiantly for an entire year. My beautiful and amazing mom, Mami, passed away on Wednesday, March 22, 2023, at 1:30pm. It is the greatest pain I have ever known. She was my best friend, my everything and I miss her immensely every single day. There's not a moment that goes by that I don't think about her. Sometimes I forget and I think of calling her to tell her about what's happened that day. And then I remember and my heart breaks all over again. Again, and again. I have immense guilt that I couldn't do more for my mom. I did everything I could, but I couldn't save her. First you deal with the anticipatory grief and then the immense grief of your loss once your loved one is gone. My mom should be here. She was, by all accounts, a healthy and young 71-year-old when she was diagnosed. It's not fair that this happened to her; she was robbed of her life.

It's been six months since my mom passed. Life is completely different. We had to give up my parents' place in Colorado. My dad couldn't stay there all by himself and so he's moved to Ecuador to be with his family. This has been extremely difficult for him. He's been in this country for over fifty years and is now starting over without the love of his life. He's grieving his wife and the loss of life as he knew it. There is no longer a home I can go to in Colorado; my parent's house no longer exists. So far, I've had to endure my first Mother's Day, her birthday and my birthday without my mom. I don't even want to think about the upcoming holidays. There is nothing to celebrate. She should be here. Perhaps she could've been saved. If possible treatments had gone through the lengthy regulatory process faster. If we had had access to other treatments that could've slowed down the progression of my mom's disease. I would give anything to have had more time; one more day, hour, minute, second. There just isn't any time to waste with a diagnosis of ALS. My mom was gone within a year; that's not very long at all. To have to wait a year for a second AdComm for Relyvrio cost so many their lives. ALS is urgent. We all need to better understand the burdens and challenges families face when they get an ALS diagnosis, for patients, their families, and caregivers. It is not as rare as we're made to believe and that is certainly no excuse once someone is diagnosed. We must do better. Thank you for taking the time to read our story. Everything I do is in loving memory of and to honor my sweet Mami.

Claudia S.
818.442.7559

Nancy K. | Colorado

Age:
Year of Diagnosis: 2018
Type: Limb Onset

We Can't Wait

I am a primary care giver for my husband. It is extremely important that ALS patients have access to any new therapies that show promise. **People impacted by ALS do not have the luxury of waiting for the usual process that the FDA requires for clinical trials.**

If a therapy offers a chance of modest benefits, I think it would be acceptable as long as the side effects did not worsen the condition of the patient.

In the case of ALS, FDA approval is not important. It is much more important to make any therapy that shows promise available as soon as possible.

Our lives have been totally upended by ALS. We spend almost every waking moment trying to produce solutions for the newest symptoms that appear. Trying to plan any kind of outing is a major undertaking. Where once we spent our retirement hiking, exploring the outdoors and planning visits with our children, we now spend most of our time inside a small condo surrounded by accessibility items.

Everyone in our family has been impacted by the diagnosis.

How devastating this illness is, and how little time there is to wait for clinical trials to offer any help.

There need to be exceptions to your very stringent rules for approval. Trials need to be open to more patients and in more locations. I tried to get my husband into at least 4 trials, and he was not accepted for one reason or another.

Cathy S. | Colorado

Age: 64
Year of Diagnosis: 1954, 1990, 2017 (Family)
Type: Genetic



We Can't Wait

Life changing, any help for slowing progression until a cure is found.

The risk is worth the outcome, family members are already dying.

Not important- acceleration needs to happen and **risk is worth it all.**

LOSS! A FUNERAL everyday of a LOSS of physical function- grieving each and every physical loss daily- a daily funeral of loss.

FEAR, SCARED, TRAGEDY, LOSS, We are in a club we do not want to be in.. ALS

That outcome is HOPELESS and has been HOPELESS for 150 years with NO CHANGE is treatment or cure.

That we are ALONE! Only help for us is talking with other patients. Neurologists say- get your affairs in order, you have 2-5 years to live. That is the only treatment.

Christine Ann H. | Colorado

We Can't Wait

Age: 55
Year of Diagnosis: 2019
Type: Limb Onset; Sporadic

I would be grateful to have medication that would slow progression, but **I want more than a few months.**

I think it's important to be allowed to try any medication that might have even a modest benefit.

It is not important at all.

ALS has taken so much away. **I was a nurse for 26 years.** I worked in Oncology and Hospice. **I administered life saving treatments to cancer patients, now I have a disease without a cure.** I am now unable to work. I moved to Colorado 15 years ago because I love the mountains and thoroughly enjoyed hiking. That has been stripped away. Independence was always very important to me. **Now everything is a struggle.** Shower days wipe me out. Getting dressed takes a long time and sometimes I need help. The fatigue that goes along with ALS is maddening. I am often too tired to socialize. If I have plans, I have to ensure that I get 9-10 hours the night before, then do very little leading up to the activity. An example: I can't clean the kitchen and go shopping the same day. It's just too much. **I think the shorter answer would be to tell you how has ALS NOT affected my life.**

My fiancé lost his hiking partner. That was one activity that brought us together. **We had planned on hiking together for the rest of our lives.** He now has to do much more. He does all of the cooking. He has to do a lot of the cleaning. He has to help me, at times, with getting dressed. Eventually I will be completely dependent on him for all of my care. ALS has had an emotional toll on him. He worries about me if I don't answer the phone, thinking I may have fallen again. He worries about how we will pay for all of the expenses coming up. **He worries about how much time we have left together.**

I wish people understood that it is terminal. I wish they could see a day in the life of someone, through every stage of the disease. I want people to know how cruel this disease is.

I would like them to know that we are going to die and we will try anything. Most people with ALS are trying every supplement that has been rumored to have a benefit.

Melanie B. | Colorado

Age: 70
Year of Diagnosis: My father was diagnosed in 1958.
Type: Genetic

We Can't Wait

Critically important like water in the desert.

I would want to know the significant side effects but would most assuredly go forward with the new therapy. **Just as Chemotherapy has significant risks to Cancer patients it saves lives.**

It's a devastating disease that takes and takes until you have nothing left to give. The toll on caregivers is exhausting and emotionally devastating too.

Please hurry!

Teri D. | Colorado

Age: 40
Year of Diagnosis: 2016
Type: Limb Onset, Sporadic

We Can't Wait

Important to have access to all medicine.

No side effect is worse than ALS.

Not important.

You're kidding, right? Is this a serious question?

It could happen to you, too.

Restricting access to therapeutic agents for ALS is unconscionable.

Carl M. | Colorado

Age: 57
Year of Diagnosis: 2019
Type: Limb Onset, Sporadic

We Can't Wait

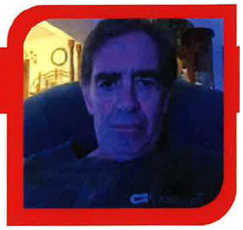
Extremely important to have a chance to ty something that will help. Especially if it is very good. But it depends on the side effects. It is not important to me if it is approved yet.

I want:
Significant reduction in mobility and quality of life

Significant reduction in freedom

We need more medications and therapies

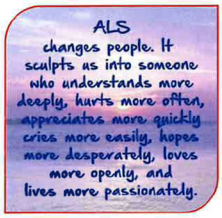
Don B. | Colorado



Age: 66
Year of Diagnosis: 2017
Type: Bulbar Onset



People is a very broad group. Many do have a basic understanding. The medical community should respectfully understand that the rate of "progress" to a cure has been tortoise-like. **ALS was identified 153 years ago. Lou Gehrig was diagnosed 83 years ago. Where are real tangible results for patients?**



Most importantly, the current processes should not continue indefinitely. **Years matter.** The risks of expediting trial treatments is acceptable when you don't have the luxury of time to wait. We put a man on the moon 53 years ago because it became a priority for the scientific community. **Curing ALS could be an easier accomplishment with a high enough priority. I realize that other diseases generate higher profits in the world of medicine.**

October 25, 2023

Dear Senator Braun,

I am reaching out to you in response to your request for stories on the unmet medical needs faced by people with rare, progressive, and serious diseases for a hearing by the Special Committee on Aging to be held on October 26, 2023. I am a participant in programs offered by the Huntington's Disease Society of America (HDSA), a leading national organization dedicated to the care and cure of Huntington's disease (HD), a rare and fatal hereditary disorder that manifests as a neurological disease with both physical and psychiatric components. The mission of HDSA is to promote and support research to find a cure for HD; help people and families affected by the disease; and educate the public and healthcare professionals about HD. Currently, there is no clinically available pharmacological, biological, or surgical agent or method that slows or stops the progression of HD.

I am writing this from the perspective of caregiver. My father was diagnosed with Huntington's disease back in 2000. It was a devastating blow to myself, family, and friends. This is when I learned that Huntington's was very rampant in my family. Since his news of diagnosis we lost his brother, sister, and my cousin, before he passed away on March 16, 2019. What a horrific thing to experience, watching and living with the changes it brought upon our father.

My sister and I moved him out to Colorado so we could give him the care that my step-mother could no longer provide on her own. He lived with my sister for quite some time, a decision we made due to me raising three young daughters in my home. As the disease progressed, so did his temper and outbursts. For the safety of my sister, we had to make the difficult decision to move him into a full time care facility. The members of this facility were great. We explained his condition and gave them info and resources to help them better understand Huntington's disease and how to evolve their care as the progression continued. All was well in the beginning. My sister and I visited twice a week and brought treats and thank you notes to the nursing staff on the floor. We always let them know how grateful we were for the care that they were giving and if there was ever a problem to call us, no matter what time of day.

Huntingon's disease started aggressively taking over. Dad could no longer speak on his own and we noticed he was sleeping more and more. On many of our visits he would gesture for us to leave. We knew it was because he did not want us to see him that way. We were at a new juncture at this point and after several meetings decided to let a team of hospice workers come in and give extra care and provide more comfort for him. Sadly, one of the hospice workers came in for her visit and witnessed two of the care facility nurses physically and verbally abusing my father. If she had not been there, we would never have known it was going on. She immediately reported this to her supervisor, who instructed her to let the head of the care facility know. The two care workers were stripped of their keys and ID badges and escorted off the premise. The nursing facility called and us and we went in for a meeting with the board and staff. There is nothing so gut wrenching as finding out your father is being abused by the very

people who are supposed to be providing care and comfort as he lives out what is left of his life. We don't even know how long he endured this abuse.

Most people do not understand Hungtington's disease, including most care facilities. My wish is for more education and training and compassion in any given care facility. We could not afford to put him in a specialized facility, and even if we could, he would have been too far away from us. The cost of keeping him in the facility was through the roof and my sister put a lot of time and research into figuring out what aid we could use and how to go about it. It was a frustrating ordeal because his retirement, social security, and disability income were hurting our chances of what we could even use. How is that even possible? How is the average person supposed to get decent care when those three, small incomes, were saying he had too much money? I find it disgusting and disrespectful. My father was a retired Master Sergeant First Class for the US Military. Before Hungtinton's disease tore his life, brain, and body apart, he was a happy man. He enjoyed life, retirement, fishing, boating, and doing all of these with his family and all of his grandchildren. I choose to remember those amazing times rather than the difficulties we had to endure with his care.

Thank you for the opportunity to share my story.

Sincerely,

Brandy Ledgerwood
PO Box 1455
Wellington, CO 80549



AVERY LAFFERTY

Milford, CT

We are a family of an 11- year -old girl battling a Diffuse Midline Glioma (DMG), which is a high- grade brain cancer and a terminal illness with only ~ 10% living beyond 2 years. When Avery was diagnosed right before Christmas in 2021, we were "lucky" to be able to understand her tumor genetics through a biopsy, and "beyond lucky" to have a surgical procedure which was able to remove the majority of her tumor. Still, following the surgery, the typical standard of care radiation treatment and limited clinical trials were our only option. We were told quite frequently – none of this is considered a cure but it may by time. Avery continues to fight today as she was fortunate enough to be enrolled in a clinical trial that has bought her more time. Time that we're thankful for every second of every day.

Why the Promising Pathway Act is Important to our Family: The Promising Pathways Act hits close to home for us for this reason and gives us something hard to find – Hope. As we think of next steps for Avery, we have inquired about particular therapies which may have demonstrated promise for Avery's tumor type - only to be told we would not be eligible. Even under Compassionate Use protocols, we do not have the time to wait for something which would potentially give her an increased chance of survival. The PPA would allow us a quicker pathway to these therapies, allow for better access to data for our own decision making, and for those facing future battles. Please, we encourage you to put yourselves in our shoes, and advance this to a full vote by the Senate and the House.

Paul & Lisa Lafferty

Parents of Avery



KIERA GALIPEAU

Putnam, CT

Our daughter Kiera was diagnosed with DIPG 4 days before Christmas in 2020. She was 3 years old. She went through radiation therapy, which currently is considered the "best" treatment option for DIPG. Which has been the same course of treatment for decades with no better outcome. We then tried to find a trial for her to get on. Unfortunately while preparing her for the trial that was being done in Rhode Island we learned her tumor grew and there was no more we could do. She passed away May 2022, just 5 months post diagnosis.

Why the Promising Pathway Act is Important to our Family: This act is important to me because our children deserve more. No child should lose out on their future. No parent should have to watch their child suffer and die. No parent should have to feel hopeless in knowing there is nothing that can be done. More needs to be done, research needs to be done. Being allowed access to treatments that can in hopes save a child or even alleviate the symptoms of this disease is so important. Our daughter won her fight with DIPG because she is no longer in pain, however we lost her fight, we lost her. Now we just want to help find a way so no other child has to go through this, and so no other parent has to lose their child. Cancer is a horrible disease that takes so much from all of us.

Kayleigh Ann Galipeau

Mother of Kiera



ALISON PEARL VERHAALEN

Putnam, CT

Alison Verhaalen was a courageous and beautiful young lady who was diagnosed with DIPG, an inoperable and aggressive form of brain cancer, just a few weeks before her tenth birthday. Alison had the biggest heart and showed everyone exceptional kindness. Her sweet giggle was contagious, and her smile could light up a room. She loved animals, giving big hugs, and was extremely creative, strong, and brave. She had a sweet tooth for chocolate and loved the savory taste of barbeque chips. She enjoyed swimming, traveling, and visiting Disney World. Most importantly, she loved her family and had a strong relationship with God.

Why the Promising Pathway Act is Important to our Family: The PPA is important to me because my child should be here! She deserved a chance to grow up beyond 10 years of age. My life and my families lives have been shattered by an unknown (DIPG was unknown to us at the time of diagnosis on 4/10/2014) evil that lurked in her head. We did everything that was available at the time~ steroids, radiation, and a phase II chemotherapy trial. Nothing prolonged her life more than 8 months. We were desperate. Ali wanted to live! We wanted her to live! She did not understand why her "healthy" body was failing her, all while her mind was fully intact. She was a little innocent girl full of life and joy. Her smile was contagious and her humor was infectious. The Promising Pathways Act is a clear step in a new and positive direction. Since I can no longer save my child, you and I together with this Act CAN save lives and give children like Ali time to grow up!!!

Tricia A. Verhaalen

Mother of Alison

Karen K. | Connecticut

Age: 67
Year of Diagnosis: 2020
Type: Limb Onset



We Can't Wait

Extremely important. As there is no cure presently, time is precious to ALS patients. Having more time makes being alive for a cure a better possibility.

If the drug ends up having no benefit then nothing was lost for trying. As for side effects, each individual would need to determine the risks vs. the benefits for themselves. For me, it would depend on what the drug did to the quality of my life to determine if it was worth continuing.

Not terribly important as ALS patients don't have the luxury of sitting back and waiting for a future decision. Each individual should be able to make a personal decision with their doctor and as many facts that are available at the time.

I am in a wheelchair as I can no longer walk. I can no longer drive and we had to buy a wheelchair accessible van so that I wouldn't be housebound. I need help with dressing, food preparation, toileting and bathing. I miss simple things like baking, shopping and especially running around with my grandchildren or even preparing a meal for them. As I was diagnosed approximately 6 months after my retirement I feel like my retirement was taken away from me and I've become a burden to my husband. I've had to give up my independence. **And I know that I am only going to become more disabled and helpless until I am totally paralyzed.** It's both physically and emotionally exhausting.

Although my husband is wonderful, he is my primary caregiver **and very overwhelmed at times with both the physical and emotional aspect of my 24 hour care**. It has changed any plans for our retirement and each day has to be planned around my care. As I am dependent on him, his independence has also been curtailed. He has a hard time emotionally as he is unable to "fix" me.

How devastating it is physically and emotionally for both the patient and families to watch the decline and know that there is no cure. It's a horrible disease and a horrible death. Why is there no cure yet?

Please work on finding a cure but in the meantime allow patients to use their own discretion as to what treatments they are allowed to try. We're dying and time is something we don't have.

Michael L. | Connecticut



Age: 66
Year of Diagnosis: 2018
Type: Limb Onset

Any therapy that can produce positive effects to slow disease progression is welcome

I just completed a drug trial which I was on for 18 months and open label for 8 months and the drug manufacturer did not meet their end goals and has now cancelled the open label so yes, I would take the risk again.

I am a firm believer that all drugs should go through all phases of the clinical trial's before being fast tracked by the FDA. The trial process is on place for a reason.

To date, had to sell our house, change positions at work, lost the primary use of my legs, had to buy a handicap van, had to stop running and much more.

My wife is my primary caregiver so her daily life has been impacted although I am still self sufficient there are things I cannot do on my own. My relationship with my children and especially my grandchildren has changed although they do like riding on my power chair!

ALS affects everyone differently and that it is a very complex disease with no true path. My progression has thankfully been slow, but I know others who have not been so lucky

Nothing specific as I think the drug companies are doing more today then anytime in the past and hopefully there will be some breakthrough in the near future.

Richard E. | Connecticut

Age: 62
Year of Diagnosis: 2020
Type: Limb Onset, Sporadic

We Can't Wait

It's important because "slowing" is better than nothing

Define "modest benefit". No one likes bad side effects. However, ALS is a death sentence with a life expectancy of 2 to 5 years. And a quality of life significantly less than that. So the risk is minimal

NOT important at all.

Again, ALS is a death sentence with a life expectancy of 2 to 5 years. And a quality of life significantly less than that. The FDA moves way too slowly for pALS. Again, ALS is a death sentence with a life expectancy of 2 to 5 years. And a quality-of-life significantly less than that. **Quit my job, started making final arrangements**

Wife is distressed and depressed.

Mention ALS and only two names are ever mentioned; Lou Gehrig (who died 80 years ago) and Steven Hawking (a longevity anomaly). This tells me there is a publicity problem. 1. No cure. 2. No effective treatment. 3. Life expectancy 2 to 5 years. 4. Quality of life much less than 2 to 5 years. 5. Under funded research. 6. only two approved treatments both having very little positive results

Forget about Steven Hawking living 50 years with the disease, he was an anomaly. Quality of life much less than 2 to 5 years. **Pharmaceutical companies need to think out-of-the-box for new effective treatments and lobby US Congress for increased funding.** Two quotes come to mind; **Albert Einstein, "The definition of insanity is doing the same thing over and over again and expecting a different result."** Also, James Ling, "Don't tell me how hard you work. Tell me how much you get done."

Lou Gehrig died 80 years ago and since that time only two drugs have been approved which only extend life for about 3 months, not a very impressive track record of accomplishment. I'm suggesting a different, perhaps more radical approach be brainstormed and implemented in accomplishing ALS objectives. Unfortunately, I don't have the answers. Hopefully people smarter than I can come up with more efficient, out-of-the-box ways to achieve the goals needed by ALS patients, because with the average lifespan of an ALS individual to be just between 2 to 5 years and their quality-of-life years considerably less than that, **four years to achieve an accomplishment is a lifetime for an ALS patient.**"

[redacted]

Dear Senator Braun and Senator Gillibrand,

First, thank you for introducing the Promising Pathways Act.

Here is a secure link from which you can download one of the videos which our charity has created for our supporters to show the devasting effects of Niemann-Pick type C disease.
https://f.io/sMx1tLaQ

Our family-founded charity, Dana's Angels Research Trust, or DART, funds research into an ultra-rare disease, Niemann-Pick type C (NPC), a fatal cholesterol storage disease afflicting children. Our second oldest child, Dana, was diagnosed with NPC at the age of 8 after our three-year search for a diagnosis. Tragically, three years later, our youngest child of four, Andrew, was also diagnosed with NPC at the age of 5. At the time, most children suffering from NPC died in their early teens, so you can imagine the devastating impact this diagnosis has on a family.

Sadly, Dana passed away in the Summer of 2013 at the age of 19. When Dana died, she was confined to a wheelchair, no longer talked, suffered from frequent pneumonia and required constant care, but she always had a smile on her face and was an inspiration to many, both here and around the world. Amazingly, Andrew is now 24 years old and relatively stable, although with the passing of his sister, Andrew started having seizures. Andrew has benefited from two experimental medications which our community of families, charities, researchers and clinicians have been able to bring forward. Unfortunately, none of our potential treatments has yet to be approved, though one, Miglustat, is approved by the European Medicines Agency and in other areas of the world.

Again, we thank you for your efforts on behalf of the many patients with rare diseases.

Sincerely,

Phil and Andrea Marella
Greenwich, CT

[redacted]

My name is Barbara Lazarus and my husband Gary and I have two adult sons who were diagnosed with Niemann-Pick Type C, an ultra-rare neurodegenerative disease, six years ago at the ages of 28 and 30. Though NPC has historically been considered a childhood disease and referred to as 'childhood Alzheimers", in recent years, it has become apparent that this devastating, fatal diagnosis can occur at any age, from infants to adults.
Our sons, David and Daniel, led normal typical lives through their teens and both attended 4-year colleges with David earning an Associate and Bachelor's degree. Their symptoms began in their early twenties and included psychosis, ataxia, tremor, and memory difficulties. After an eight-year journey to get a diagnosis that devastated us, we immediately investigated treatments that might be available and learned that there were no approved drugs. They began a trial being offered for adults and Daniel continues to receive this drug through a bimonthly infusion. David takes a different experimental drug through an expanded access program. They have continued to show progression but their decline has been slowed, we believe, by these drugs. We fully understand that this is a fatal disease but have at least some hope that their quality of life is better because of these drugs and that, through advocacy and persistence, others with this diagnosis in the future may find it to be a manageable disease as opposed to fatal. These drugs have become a lifeline for our family in an otherwise dismal and depressing situation and have allowed them to remain somewhat functional beyond typical expectations for this disease.

Our sons now require full-time caregiving and supervision which is provided by my husband and me since we have been unable to find Personal Care Assistants at the rate our state programs offer. Because they fall in a degenerative category, they also do not qualify for developmental services or TBI services and there are no day programs available to them. Their world has narrowed and is in no way typical of a young adult life. This disease has robbed them of the futures they planned for and robbed us of the retirement we worked so hard for. They have limited access to state services because of the restricted allotment of funds for their age group (18-64) with disabilities beyond TBI. So, no, our family and our sons have not been well served by the current systems in place and continue to live restricted and unfulfilled lives.
We as a family and as an NPC community need the backing and support of our government to get access to research, drugs, and programs that will improve the lives of those who live with this ultra-rare disease and ultimately lead to a cure.
Should you have any questions or require further information, we are always available.
Thank you for your time and attention,
Barbara and Gary Lazarus
Oxford CT
203-509-1124

[redacted]

Dear Senator Braun,

I am reaching out to you in response to your request for stories on the unmet medical needs faced by people with rare, progressive, and serious diseases for a hearing by the Special Committee on Aging to be held on October 26, 2023.

I am a participant in programs offered by the Huntington's Disease Society of America (HDSA), a leading national organization dedicated to the care and cure of Huntington's disease (HD), a rare and fatal hereditary disorder that manifests as a neurological disease with both physical and psychiatric components. The mission of HDSA is to promote and support research to find a cure for HD; help people and families affected by the disease; and educate the public and healthcare professionals about HD. Currently, there is no clinically available pharmacological, biological, or surgical agent or method that slows or stops the progression of HD.

I am a volunteer Huntington's disease advocate, and I am writing regarding the unmet needs of my friends. The genetic nature of this horrendous disease and its onset during prime working years has a tremendous financial impact on families living with HD. The destructive impact cognitively and physically robs the person of their ability to live independently. They are also your constituents, and they need your support now. Our friends in the ALS community received much-needed relief in 2020 with the passage of the ALS Disability Insurance Access Act. However, our HD community has been begging for the same waiver (The HD Parity Act; also known as Huntington's Disease Disability Insurance Access Act) for thirteen years. With that bill in congressional limbo, we are looking to other ways we can help those living with HD RIGHT NOW.

My best friend, Jodie lost her battle with Huntington's disease on October 16, 2020. I watched her struggle with the simplest of tasks, drain her well-being, and whittle away to sixty-seven pounds before dying a slow and painful death three weeks after turning fifty-years-old. Jodie had a warm and energetic spirit, loved ALL music, had a savvy fashion sense, and absolutely loved being surrounded by her friends. I just adored her. We all did. Jodie was forced to leave her beloved New York City in 2010 to move to Florida to be closer to her sister — who would go on to become Jodie's fulltime caregiver. There is not a single day that goes by that I don't miss Jodie's boisterous laugh, her gorgeous smile, and the way she fiercely protected and loved me.

Unlike other letters you may be receiving about Huntington's disease, my case is a little different. I do not have HD in my family. I will not die of this horrible disease. I am fighting against injustice in our healthcare system. I'm fighting for my friends. We all have them. Sometimes, we even thrive because of them. They enrich our lives and they become our chosen family. And I miss my friend, terribly. Since getting involved in the HD community, I now have many friends with this devastating disease. I have dedicated the past thirteen years to helping those who are struggling with this horrible disease.

Many people with HD struggle to find the proper medical care, cut corners on medications, and put their health and safety at risk. This disease is unfair and gut-wrenching to witness. Why do we have to make it harder for members of our community — your constituents, who are already struggling with basic tasks we all take for granted?

I am pleading with you, Senator to step up for the HD community. We may have a small voice, but I assure you, it is persistent and very **LOUD**.

Thank you for taking the time to read my letter and allowing me to share my story.

Warmest regards,

Tracy Toscano
407 Burton Avenue
Lewes, Delaware
19958

[redacted]

Honorable senators,
Less than 2 years ago I was working full time as a pediatrician in private practice, and as an associate professor of pediatrics at the University of Virginia. I ran every day, and was happy that my times were keeping Pace with aging. Today, I am dictating this email because I no longer have functional use of my fingers. Being able to dictate is coming to an end as well because my voice is disappearing quickly. I have ALS. I am in a wheelchair, and dependent for all my daily needs including eating or drinking. There is no cure. The functional decline is unrelenting. It is truly a miserable disease with few options for treatment that aims to Limit The decline at best.

Many new medications are in the scientific pipeline for ALS. We need a functional regulatory pathway to get those new treatments into bodies urgently.

Current accelerated approval processes are not available to new ALS treatments because they require a proven biomarker. There is no clinical biomarker for ALS, such as is used for measuring efficacy of cancer chemotherapy (tumor size) or HIV treatments (viral load). Accelerated approval is available for cancer and HIV treatments. In ALS we have a functional rating scale, a questionnaire that measures functional decline. It is scientifically validated but it is not a biomarker. As an aside, there is no biomarker for depression or anxiety.

The promising pathway Act would provide a way for treatments with proven safety and promising efficacy to be available to ALS patients who have no other options.

I urge you strongly to support the promising pathway Act because it provides Equity to patients and hope to their families.

Sincerely,
Jim Plews-Ogan

[redacted]

My name is Darlene Freeman and I have ALS. I was diagnosed 2 1/2 years ago with a disease that is 100% fatal and that has an average life expectancy of 2 to 5 years. The diagnosis has upended my life and has taken many things from me in ways that I could have never imagined. It is a cruel, relentless, progressive disease that little by little takes away your ability to move, to speak, and to breathe.

I am a retired attorney, and when I got my diagnosis, I was living the life that many retirees dream of. I had a four-story townhouse in old town, Alexandria, Virginia, my daughter had recently married and was living. Five minutes away, I was on the board of directors for my townhouse community, and I was walking 4 miles every other day for exercise. I was always healthy, never smoked, kept a healthy diet, and was convinced that my regular exercise would keep me living long enough to spend time with my daughter and hopefully someday enjoy grandchildren. I first noticed my problems one day when I was walking. Something felt off with my left foot. Five months later I had been diagnosed with ALS. I started using a leg brace, and I put my townhouse on the market because I knew I would eventually not be able to walk up and down the stairs. I moved into a single level condominium and started using a walker. I am now using a motorized wheelchair, because I can no longer walk. I have experienced so many losses and that is one of the things that people who have not had ALS or not familiar with the disease cannot comprehend. Every day you wake up and wonder what you're going to lose that day. In addition to being unable to walk, I have lost functional use of my right hand, and I've had to learn to type and feed myself, with my left hand, which is not my dominant hand. I can no longer write. I have always followed the news, and I've always been a big reader. I can no longer turn the pages of a book or the pages of a newspaper. I have begun experiencing breathing issues and have to sleep with a noninvasive ventilator. All of that sounds like some thing you would read in a medical book but what it doesn't cover is the loss of so many of the things that I loved doing. My dog will not jump on my lap anymore because she is afraid of the motorized wheelchair . I can no longer attend my favorite performances at the Kennedy Center, I can no longer travel, and it's very difficult for me to go out. As for the future, I will probably not live long enough to meet any grandchildren. My daughter and I are very close and she had always said to me that she wanted me to be with her when she gave birth. That is a loss for me and a loss for her. I live alone and have 24 hour care. I cannot visit my daughter at her townhouse because it is not wheelchair accessible. My joy is in having her and other family members come to visit me. The things we don't talk about are the things that we used to do during those visits, like play cards. My hands can no longer hold playing cards.

Those of us with ALS try to stay positive, and hope that we can live as long as possible to enjoy our families. There is no cure for ALS. But there are a lot of efforts to find drugs that can slow the progression. It takes a long time to develop these drugs, and have them go through clinical trials and obtain results that can then be given to FDA in the hopes that a drug can be approved. Since there is no cure for ALS, and since it is a fatal disease, I am floor Congress to do the right thing and enact a law that will allow us access to drugs that are investigational, and that have promise to prolong our lives, even if they have not yet reached a point where they would be approved by FDA. Our lives depend on it and maybe, just maybe,one of these drugs will give us that additional time that we all pray for.

Darlene Freeman

[redacted]

Karin Gander was my best friend. Karin was born in November, 1961 and she loved her life. Karin and I used to run half and full marathons together and we had a blast doing those races. We met a lot of great people and loved traveling to races all over the US. In 2019, we traveled to Portugal to see one of our favorite artist, Bob Dylan; and later that year we went to London to see Neil Young and Bob Dylan. We were living life to the fullest.

In February, 2020, Covid hit and we were stuck at home but we continued "racing" virtually. In the summer of 2020, Karin started complaining about pain in her calfs when we ran so we started walking. She said it was like she couldn't bend her ankle and felt like she was walking like "Frankenstein". This was the beginning of the diagnosis for ALS. She went to the doctor and they told her she had "foot drop" (or drop foot) which is a neurological issue. She went to a neurologist who did test on her and assured her that she did not have ALS. Soon, speaking clearly became difficult for her and it wasn't long after that she went to a neurologist at George Washington University hospital who confirmed on October 26, 2020 that she indeed had ALS.

We lived in Fairfax, VA and Karin had inherited a house in South Bethany, Delaware. She could no longer work and decided that she wanted to spend the rest of her life at the house in Delaware. I was retired so I agreed to go with her and take care of her. We moved in April, 2021 and took full advantage of living at the beach while Karin still could. We went kayaking, riding bikes, going swimming etc.

Karin did not want to die and was willing to try anything to halt the progress of ALS. We went to ALS clinics at Johns Hopkins where they monitored the progress of the disease. It was evident that she was losing muscle mass and had already lost the ability to speak. She entered a trial at Johns Hopkins because she was willing to try anything she could to live. She tried every new drug that came out and was approved by the FDA. It was very frustrating waiting for the FDA to approve such drugs like Riluzole, Relyvrio and Radicava. There are other drugs waiting for FDA approval and are floundering in the system. Please understand that when a person has a terminal disease they will try ANYTHING. What have they got to lose??? They are already dying.

Day after day, I watched Karin slip away and there was nothing I could do. Please let ALS patients try any of these drugs that would give them hope. Hope is all they have.

On December 7, 2022, Karin texted me to please take her to the ER as she was having trouble breathing. They admitted her into the hospital and immediately started treating her for pneumonia. She didn't have the strength to fight it. Karin died on December 18, 2022 and I lost my best friend.

Please help so that others don't have to go through life without hope and knowing they are going to die a slow and painful death. Thank you.

Joseph Harris

Sent from the all new AOL app for iOS

Justin P. | Delaware



Age: 38
Year of Diagnosis: 2019
Type: Sporadic

I think it's very important to have access to new therapy and **should be my right to decide if I want to try them**

I think it's worth it to me

I think it's important that clinical trials show that they work but I don't care if FDA approves it first

ALS has made my life very difficult I can't do stuff I enjoy doing. I loved working and providing for my family and now I can't **I struggle every day and the little bit of money disabled gives me don't let me provide for my family**

It's put a lot of stress on my wife. **It really hurts my kids because their father can't do anything with them anymore**

This disease is no joke it turns your life upside down quickly and we need better treatment or cure

I would like for them to know that **sometimes you need to think about the people living with this disease and not your pockets**

Suzanne G. | Delaware

Age: 59
Year of Diagnosis: 2021
Type: Limb Onset

Click Here to Play Video

A new therapy is extremely important. It is extremely important to me that the clinical trial process is complete, and the FDA has approved it before you take a new drug.

I would like to choose for myself

It has completely changed my life. I can not walk. I have no strength. I fall a lot. I am dependent on others. **I was set to retire. Now I'm set to die.**

It has caused extreme anguish and grief

That it is terminal. There is no cure. You become completely dependent on your family- when you were looking forward to your golden years.

My dad died from ALS on April 29, 2015. My husband was diagnosed with ALS on January 11, 2021. **ALS is NOT a rare disease**



ABIGAIL ADEWUNMI

Tampa, FL

Abigail "Abby" Adewunmi was a passionate and opinionated yet measured and relaxed young woman. She cared about faith and family first and foremost; however she had a sizeable passion for justice and service.

Abby had a variety of interests, she liked math, science, art, music, history, and keeping up with current events. She was deeply passionate about her interests and would learn all she could about a topic. She sought out knowledge and used this as a tool to better herself and the people around her because she cared so deeply about the people in her life and people she had never met. She was quietly competitive both inside and outside of the classroom as a phenomenal student who found time to pursue other major interests including Bible Quiz, Tennis, Photography, and Travel.

Abby's nickname was "Miss No Stress," her calm demeanor and laid-back personality drew people to her like a magnet. She had an ability to effortlessly let the difficult moments of life fade away in the spirit of always celebrating the good moments of life. Abby loved her family deeply and will always be her family's greatest inspiration. She set an incredible example of how to walk with faith and keep pushing, even in difficult moments.

Beginning in April 2021, Abby began to experience major headaches that would not subside with medication. She also reported double vision as she saw "two tennis balls" coming towards her during her weekly practice, and she started to have a noticeable facial droop.

After struggling through her brother's college graduation, the intensity of her headaches prompted an MRI leading to her diagnosis with DIPG on May 4, 2021.

At this point in time, life seemed to whirlwind. She immediately experienced a hospital stay as her family learned the severity of the diagnosis. She was soon enrolled in a clinical trial headquartered in Gainesville, FL and began radiation and chemotherapy in June 2021

Although this illness took a physical toll on Abby, she never lost her sweet, determined spirit. She continued to maintain her quiet strength, her smile, and her thoughtfulness for others. She remained the beautiful, intelligent, and passionate 16-year-old that she was until the day of her passing January 12, 2022.

In her honor, her family founded Abby's Corner, an homage to her loyalty to her family. They will always be in Abby's Corner, fighting for her with all they have. Their hope is that there will be options available to kids and to families that prevent experiences like Abby's, options that provide hope to families and advance our efforts for a cure. The Promising Pathway Act will aid in that effort.

The Adewunmi Family

Family of Abigail

[redacted]

My name is Troy Fields and I was diagnosed with ALS in June 2018. I am a husband, father of four, grandfather to three grandsons. I am a son, a brother and a friend. I say this because when I talk about the impact of ALS in my life I'm really speaking of the impact to all of the relationships in my life.

I was in the 35th year of my professional career, doing a job that I thoroughly enjoyed and with eyes towards the next phase of my life when I heard my neurologist tell me that I had ALS. In many ways while my heart was still beating I felt a big part of my life came to an end with the diagnosis. Rather than thinking of the next milestones in my life and the life of my family, such as birthdays, weddings and graduations, I was forced to redirect my focus on what was the next piece of equipment, what was the next function or movement that I would lose or how much time I had left to live my life. The regressive clock was front and center.

At different times since my diagnosis I have been asked to explain how I felt the day I received my diagnosis. I have tried several analogies such as a punch in the stomach or the feeling of the floor disappearing below you, but none of those phrases come close to capturing that despair of the moment. However I can say, after 5 years I am hopeful that with the help of Congress we will significantly increase the research investments needed to find disease altering treatments or even a cure and make the necessary regulatory changes that provide faster approval and access to treatments that show early therapeutic benefit. I am prepared to accept that such changes might not impact my disease journey, as long as it benefits the next generation of people diagnosed with this horrific disease and stops the cycle.

I have come a long way since my humble beginnings. At the age of 14, I moved to Tampa, Florida from San Juan, Puerto Rico with my mother and my brother to start a new life. We came to Tampa with little in our pockets. My mother worked three jobs to provide a roof over our heads. I started my studies at University of South Florida at age 16 carrying a full-time load while working over 30 hours a week to help pay for my studies. When I graduated college at the age of 20 I approached my professional career with the determination and a strong work ethic that I had learned from my mother. That effort allowed me to provide for my family and to offer them a better life than the one I had when I first moved to Florida. It is that same determination and work ethic that has made me a strong advocate following my diagnosis. I've been proud to be part of the board of directors of the ALS Association Florida Chapter where I served in multiple capacities as well as receiving recognition at the State and National level for my efforts advocating on behalf of the ALS community. I'm also a volunteer of the I AM ALS organization where I serve as co-chair of the Legislative Affairs Team. I am so proud to be part of this community of people affected by ALS even though I never asked to be part of it or even envision that I would one day be affected by this disease.

It is my sincere hope that in sharing my story, Congress is able to develop a better understanding of what life with ALS is about, what we have lost, as well as supporting our drive towards eradicating the disease once and for all.

Sincerely,
Troy Fields

Marc L. | Florida

Age: 64
Year of Diagnosis: 2019
Type: Limb Onset, Sporadic

Click Here to Play Video

Since there is no cure, this is the only way to treat the disease. **I find it heartbreaking that physicians can really offer no help. But if some drug therapies can slow The disease this would be extremely beneficial for those affected by ALS.**

The effects of ALS are worse than any potential risk from a drug that could have modest benefits. I would accept Significant side effects over continued disease progression given the choice of no therapy at all.

As a physician I feel it's important for the clinical trial process to take place. The FDA approval process has always been a part of getting drugs to patient safely. However, with certain diseases such as ALS the balance of how much benefit and potential risks have to come in to play. I do not feel that phase 3 trials are needed for every ALS drug.

I was an interventional cardiologist implanting life-saving therapies daily for patient care. Now I am relegated just sitting in a wheelchair, unable to use my hands with any purpose. Obviously, my career is over, and all my years of experience are lost.

This has affected my family, friends and patients. **Patients whose lives I have saved in the past now will outlive me and are trying to help me keep going on. There are no treatments available with any significant benefits.**

We need a paradigm shift in how we handle this disease for FDA approval of drug therapies. We should not have to wait for large phase 3 trials.

David F. | Florida

Age: 73
Year of Diagnosis: 2019
Type: Limb Onset

We Can't Wait

Slowing down the progression is a yes! Anything to provide us hope and relief!

Side effects, depends on whether I am willing to risk it. I would like to know more.

Takes too long to wait for FDA approval.

I am devastated, changed all my plans. Quit job, overwhelming

Everyday is worse with never a hope of improvement family doctor Kevorkian make sense Suddenly.

Suddenly I understand dr. Kevorkian

Deborah H. | Florida

Age: 70
Year of Diagnosis: Father
Type: Limb Onset



We Can't Wait

I believe this is of the utmost importance. My Father was dx in 1993 and died in 1995. I prayed we could have more time with him. I believe for him it was like having a ringside seat at his own demise.

I would have wanted to take the chance of making a modest benefit for my Dad but would not have wanted him to have significant side effects in addition to being trapped in his own body and choking to death.

I believe that the FDA should follow through with their clinical trial process. As we have seen with Covid vaccine side effects, it is extremely important that the FDA complete these trials.

I have not been diagnosed, but again, my father was diagnosed. Watching him slowly lose the ability to walk; breathe; feed himself; care for himself in any way was grueling and very sad. In the end, I prayed for God to take him due to the insurmountable suffering. I'll never forget seeing him on a ventilator, staring at the ceiling and a tear falling from his eye. He died the next day.

My entire family was devastated that my Dad died at age 68. He was a kind, loving, cheerful man with a heart of gold.

I wish people understood how important it is to find a cure for this horrendous disease. People are dying way to young!

Yes...I believe the pharmaceutical companies have billions of dollars and should take some of those billions to pour it into research. We must learn to give back. The greed in our Country is going to kill us.

Bobbie C. | Florida



Age: 49
Year of Diagnosis: 2020
Type: Limb Onset, Sporadic

I think anything we can get that helps, whether it's a few months or longer, we should have access to. I think we should have access and let it be our choice to deal with side affects. Considering that chemo has major side affects, why can't we have that chance too. It should go through some testing, of course, but we should still have access if it is showing improvement. We should have access to any compassionate care drugs.

I had to sell my business, give up my career, lost ability to do everything. This disease has affected every aspect of my life and my ability to make money or provide for my family. I am now completely reliant on someone else to do every single thing for me. Even something as scratching my nose, I cannot do that myself. **Every single thing, big or small, is affected and taken away from you.**

My two children have given up their careers and their lives to take care of me. Caring for an ALS patient takes so much time and energy. You have to give up every aspect of your life to be there and be an ALS caregiver.

I wish people understood that, as ALS patients, we still have our minds, and we can still make decisions. We can still hear you; you don't have to shout. What is inside is the same, but your body can't move. I wish people understood more about what this disease is because living with it is so grave, and people don't seem to understand how awful it is.

I want them to know that we need access to affordable treatment and caregivers. We are expected to quit our jobs, family members have to quit jobs, so no one can make money, but we have to pay for our own caretaking and pay out of pocket for so many medications because little is covered by insurance. **WE NEED HELP!! WE NEED HELP FROM EVERYONE!!** We need a way to be able to sustain some kind of livelihood and at the current state that this country is at with ALS, we are not able to sustain livelihood.



Richard C. | Florida



Age: 57
Year of Diagnosis: 2019
Type: Sporadic

From the time of my diagnosis it is always in my mind when will I pass. The longer time passes I wonder when I close my eyes at night will they open in the morning. My feelings are we have been given a death sentence so what do we have to lose. What we could possibly gain is life.

Any medication is worth the try no matter what.

It has taken everything from me. My job my house my motorcycle and most importantly my independence.

My daughters have altered the lives to be near. And it pains me to have to see them hurt because of me.

That it's a death sentence. Before my diagnosis I new very little about ALS.

It is torture knowing your time is very limited.

Johnny F. | Florida

Age: 62
Year of Diagnosis: 2019
Type: Limb Onset, Sporadic



We Can't Wait

Anything to let me live longer. Who would take that choice from me? It is my choice. Just like cancer, all you can do is hope for the best.

FDA is taking my choice away from me when it restricts access to new and potentially life saving drugs. **The key part of that is "my choice", not the government, and that should be an inalienable right for all people.**

Mobility, planning for the future, more hope and more let downs

They took more time than I did to come around to the idea that I may not be around for long.

How badly it is underfunded. Research needs to get more funding to speed up finding a cure.

I am lucky the VA helps pay for my treatment. **We need to elevate the importance of the little people who are dying from these diseases, who are in poverty because it costs so much to treat.** I must have resources generate 150k per year to pay for 1 of the 2 FDA authorized treatments. **People cannot afford this, price controls please.**

Rick M. | Florida



Age: 67
Year of Diagnosis: 2019
Type: Bulbar Onset

Any treatment that can give me more time with my family would be a godsend. However, if that treatment requires me to sit in a hospital for weeks every month, then I would not be interested. Traveling to hospitals or being confined to one isn't beneficial to me or my family, not for the "possibility" of only a few months.

That may be just what I need. Yes, even with the risk, that might be just the ticket. Look at the risks and rewards and side effects of the two "approved" drugs currently available to us. **The "risks" may well be worth it.**

Not important at all. **After all the dealing with COVID, and previous ALS trials, I have very little faith in the FDA even caring about ALS patients.**

My diagnosis was devastating, but nothing compared to actually having this dreaded disease. My wife and I had just retired and had extensive travel plans, most of which was canceled. **I have gone from walking and talking to mumbling and spending 16 hours in a power wheelchair.** It's been hardest on my wife, knowing that the man she married and planned on getting old with won't be there for her.

I would wish that everyone would know that ALS is always fatal and nothing can change that. That funding for AIDS and erectile disfunction took precedence over research for ALS. That not enough people die from ALS to make it worthwhile for Big Pharmacy to care about.

Just one question... when all the other diseases have a treatment, will you then decide to bother helping the 6000 people who get ALS every year? We all know why there is no cure...Money. It just isn't profitable.

Shawnee B. | Florida



Age: 58
Year of Diagnosis:
Type:

Even the slightest bit of hope is an improvement.

Anything would be better than nothing.

With the alternative being death, not important at all.

My Daddy was unmercifully attacked by the cruel unrelenting disease of ALS. After an otherwise relatively healthy 83 years, being an avid runner since the 70's, active in his community, this disease erased a lifelong of responsible choices in the matter of mere months.

No one in our family has ever had this disease, and even if we could have predicted it, there are ZERO options to defend against its ravages. Be warned, it can and does strike anyone as it pleases. It's awful for one to be told not only you face a deadly disease that will slowly lock you into your own body. But to add there are no choices or hope and to be forced to just take it, is devastating for the victim and their loved ones.

Please use your good will, position and influence to shine a light on the need for a cure before it rips and savages another family. **Dad gave his life, spine and brain in his fight.** I carry the torch in raising awareness and pass it to you.

Robert M. | Florida

Age: 76
Year of Diagnosis: 2016
Type: Limb Onset

We Can't Wait

Constantly looking for any breakthrough. With modest anxiety I am certain anything that provides hope is worth it.

Literal game changer, a total change in the quality of my life. I loved my job and had to give it up. I now and 95% wheelchair bound

Horrible stress on my spouse, I'm having to depend on her constantly for any movement. **Very discouraging when you can't pull up your own pants or put on your own socks.**

How debilitating and stressful it make you feel. Your helpless and all that can be done is monitor where you are with your physician

Losing muscle strength and the withering & deterioration of your body is Devastating

Vincent M . | Tampa

Age: 86
Year of Diagnosis: 0
Type: Limb Onset, Sporadic



We Can't Wait

We have developed a natural occurring metabolic treatment protocol, The Deanna protocol [DP], that makes patients more comfortable by suppressing incessant muscle symptoms and slows disease progression. Further in 2015 we have documented a borrelia infection as the etiological agent and treated the infection. My daughter's disease has not progressed since 2018. Other pALS have experienced similar results. Neuroscientists are reluctant to accept these results using the [DP] and have refused to fund clinical trials on the DP. Also, clinical trials should be funded at a specialty laboratory to document the presence of a bacterial infection in ALS. Then fund a trial on appropriate antibiotic Rx.

Not rewarding

The clinical trials are in the wrong direction

My daughter has overcome her disease but before we knew its cause was bacterial, she was treated only with the DP and lost muscle function until we eliminated the bacterial infection in 2018. We are now in the process in attempting to retrieve her muscle function.

Changes all our lives

It is curable and early Rx is important b/c once a nerve cell is dead it is not retrievable.

Open your minds and save millions worldwide from this devastating disease. See our results at the link below. Please help me help these patients. https://winningthefight.org/success-stories/

[redacted]

My name is Mike Vigliotti And I have been living with ALS for about 8 1/2 years now. Want to share a little bit about my story so you have a better understanding of what I'm about and how this disease affects myself and my family.

My first symptoms started early in 2015 at which point I noticed my grip strength was getting weaker and my right hand. Slowly I began to notice more things like a loss of fine motor skills and having trouble picking things up, using buttons and holding things like a utensil or a pen. I saw multiple doctors regarding this none of who could figure out what was going on. I even had one hand surgeon say that I had carpal tunnel disease so I even ended up having surgery for that but that was not it. After a couple of years I was finally able to get him to a neurologist at the University of Michigan who initially diagnosed me with the disease called Multi-vocal motor neuropathy. For nearly 2 1/2 years I had high VIG infusions done every other week. My progression still kept moving slowly which was not typical for ALS.Finally after several years I got a second opinion at the Mayo Clinic in Minnesota where I was finally diagnosed with ALS. Because it took so many years to finally get the correct diagnosis at that point I never qualified for any clinical trials because those trials normally involved people who were newly diagnosed for less than three years. We definitely need things to change with this because I know I'm not the only person in the situation and anybody with ALS should qualify for clinical trials no matter how many years they've been diagnosed.thankfully, more recently to the expanded access program I have been able to qualify for some clinical trials through my ALS clinic which is at Duke University. It is interesting that during the time that I saw several neurologist at University of Michigan, Mayo Clinic both in Minnesota and Jacksonville Florida nobody ever mentioned expanded access program for clinical trials to me. It just shows the desperate need that all of these neurologist need to be better informed on what options are out there for ALS patients.

Fast forward to today and here is how ALS has affected my function. I no longer have any use of my right hand or arm and have not for several years now. I used to be right-handed so I had to learn how to do everything not only left-handed but one-handed as well. If you ever want to challenge yourself try teaching yourself to write with your opposite hand! I am now also losing a lot of function with my left hand as well which is my complete lifeline. Without the use of that I will be relying on someone to care for me 100%.my legs are also getting weaker. I walk with a limp and unable to walk long distances without being completely exhausted. I do still exercise regularly, riding a bicycle and swimming and try to stay as active as possible. My breathing function is also now affected and I have to use what is called a trilogy machine which is a noninvasive ventilator at night when I sleep.Caring for myself is getting harder every day. Thankfully my wife works from home for the same company I work for so she is able to help me with daily tasks such as getting dressed, showering etc. I still can do some of these things on my own but it's getting harder every day.I am no longer able to do many daily chores around the house as I just don't have the strength in my left arm anymore. Can't cut grass, pull weeds, work out we are doing any landscaping or tinkering around in the garage.

I do still work full time in a sales position for a company that is been wonderful working with me. I do a lot of travel in the past but that has slowed down dramatically now. More recently I had to make the decision to stop flying on my own as it was just too stressful and hard. Luckily the company I work for has agreed to pay for my wife's airfare so she can accompany me when needed. They have also helped me with items to keep me working as long as possible. This email has all been done by talk to text software called Dragon.(please excuse grammatical errors as it is not perfect!) Because I have been losing function in my left hand now I have a hard time using the computer mouse so I now have an eye tracking device on my laptop that allows me to use my eyes as the computer mouse!

The financial burden of this disease is incredible. I'm not as advanced as many people but yet the cost are still ridiculously high. My insurance co-pay on the Trilogy machine alone is just under $400 a month! I also spent hundreds of

dollars a month on various supplements and medications. I have heard of many patients that are on Medicare that can get access even to some of the ALS drugs that have recently been approved because the co-pay costs or out-of-pocket expenses are so ridiculous no one can afford it. We definitely need changes made on this front so these drugs are affordable for everyone. It has been estimated that people in advanced stages of this disease have an annual cost of up to $250,000/year! This is one of the things that scares me the most is how could I afford to stop working. If I were to go on disability today my monthly check would be roughly $2700 a month. How could I even come close to surviving on that amount of money?

Prior to my diagnosis my wife and I were always very active. I was a very avid hunter, love to golf, bike and hike. Today the only one of those items I can do is ride my bicycle very gently. As the disease progressed I had to change my hunting style to learn how to shoot left-handed and always made sure I had help available in case I needed help dragging a deer out etc. Eventually got to the point where I could no longer do it at all. I loved to golf in the past and as the disease progressed I did find a brace that would strap my fingers from my right hand which no longer function around the shaft of the club. It wasn't perfect but it kept me in the game for a little bit longer. Today I can no longer do any of that and have very little recreational activities I can do anymore. As the disease progressed I found that living in Michigan with the colder weather greatly affected my function. About 2 1/2 years ago we made the decision to move to Florida so we could be in a warmer climate and try to remain as active as possible as long as possible. That has definitely been a blessing that has helped tremendously. Not everybody has the ability or opportunity to do that though.

Last month there was an FDA advisory committee meeting to vote on a trial drug called Nurown. This drug had been in clinical trials for many years. While not perfect there were many many stories of people that were actually able to regain function which is huge! You have no idea how much I would love to get some function back of my right hand so I can do more daily things on my own. I would love to be able to cut my own food up for an example or get myself a shower without any difficulties. I listened to that committee meeting all day long only to have the vote turned down and since then the company has pulled their license and are going back to see if they can find the funding to start another phase 3 trial. I learned a lot listening to that committee meeting and even though the committee is only supposed to be voting on the effectiveness of the drug the cost of manufacturing that drug came up often and I believe that is one of the reasons it did not get approved. Also, public testimony is allowed from outside people who have no skin in the game so to speak that did nothing but badmouth the drug. While people that were using the drug did not get much significant time to share their stories. Those are the people that should've had the most time as they have real world experience with the drug. Not some outsider looking in. I guarantee if one of those people had ALS themselves for a close family member with that their commentary certainly would've been much different I believe. As you know, these clinical trials take many many years. We need drastic changes made on this front as well. For starters, everyone should have access to the actual drug and not placebo. We need quicker time frames on the trials and for the approval process. A little over a year ago a new drug called Relvrio was approved but it took almost a year for the FDA to schedule a vote on it before it was finally approved. During that year thousands of people lost their lives waiting for drugs to be approved. As you may or may not be aware the average lifespan of someone newly diagnosed is 3 to 5 years. I'm very blessed that I have been over 8 years in and still function as well as I have but nonetheless I don't know when that progression may speed up further at any time. We don't have time to wait years and years for drug to get through the process before getting approved. We just all want a chance to live a little bit longer and enjoy times with our loved ones and friends.

thank you for your time.
Mike Vigliotti

[redacted]

Hello,

My name is Laura Manhardt and I am the primary caregiver for my mom, Patricia, who has been living with ALS since her July 2020 diagnosis. Two years before her diagnosis, in 2018, my mom was an active individual who ran her first half marathon. Today, three years into her journey, she does not have the use of her feet, legs, left arm, and left hand. Her right arm and hand have enough strength for her to operate her phone and in-home hospital bed remote, but they are quickly going. She needs complete assistance with personal care and some help with eating. She cannot lift her head up if it falls, and uses a portable ventilator almost constantly through the day and night to support her weakened breathing. She had to leave her job this summer when typing with one finger finally became too tiring.

As each part of my mom's body has fallen victim to ALS, I and her other caregivers replace that function with our abilities. Every day, I strain my own body to complete lifts and transfers, maneuver assistive equipment, and complete care tasks. Imagine your longest days - when you are moving from the moment you wake up to the moment your head hits the pillow, completely and thoroughly exhausted. That is every day for me. I am 27 years old and doing my very best to not let go of my own life despite of the horror that ALS has placed upon my family, and the challenges of caregiving. But the price of that is that my days are overflowing. I work a full-time job, which is luckily remote so that I can be around for my mom. I have friends, family, a dog, and a boyfriend that I love and spend time with during the all too few relief hours I have. I do my best to care for my body given how much stress it is under, which sometimes mean sleeping 7 hours instead of 6. I have passions and interests I spend time with daily, for the few minutes I have to spare. Keeping these good things consistent in my life, even just a little, is a challenge I have to endure, because the price of failing is that all I have left in my days is care and watching my mom die before my eyes, and I refuse to let ALS take any more from us than it already has. I say all this to try and convey how completely draining this illness is on the patient AND everyone around them, but in truth, you will never truly know this tragedy until you've been as close to it.

Roughly a century and a half after ALS was first identified, this is an insane position to be in. We've seen results for numerous other illnesses completely transform in that time, primarily cancer. And to be honest, I wish my mom had cancer instead of ALS. Because for the most part in cancer, you can still have the dignity of caring for yourself, or traveling to fulfill your bucket list (my mom can't fly with her breathing problems), or holding your first grandchild (my nephew was born in April and my mom's hands were too far gone to hold him). This illness is the same horror it was 150 years ago. We have a few treatments that extend life a few months and technology that helps immensely, but the disease progression is the same. The outcome is the same. My mom will die without intervention. After 150 years of this, the situation is more than dire. Patients need options and will do anything to get them. My mom spent $10k for two weeks at a functional medicine clinic in Miami. She's currently signing up to let Elon Musk plant a chip in her brain with Neuralink. We've seen others in this community fly across the world for stem cell treatments. The ALS community has suffered so greatly for so long, and the desperation grows with each new generation of patients that is diagnosed with and soon dead from this illness.

This is where you come in! Remember when you (hopefully) got into government with the idea of serving the people? This is that moment! ALS patients need access to new and emerging therapies ASAP. Us caregivers need it to, not just for the hope that our loved ones will get better, but also for the chance that we'll have more time to adjust between the functional losses that add more to our responsibilities. We are asking for you to help. ALS moves quickly and violently, and our current system is not set up to get patients access to treatments that they are willing to try. Our current system isn't even set up to listen to patients, which for ALS patients is especially devastating given how shrouded in uncertainty

so much of this disease still is. We need to operate on the ALS clock, which moves at a pace of killing an ALS patient and diagnosing another every 90 minutes.

If my mom had access to treatments, the difference in our lives would be, quite frankly, heavenly. I of course hope for access to treatments like NurOwn, which patients reported incredible results on. I doubt any emotion, even the birth of my child, could compare to the joy of seeing my mom regain function. My daily fantasy is that she'll suddenly walk into the room - and that's a possibility when patients can quickly access emerging treatments and start seeing what works for them. On a smaller note, I get my time back! I can actually think about getting married and planning a future, I can work on projects, I can spend an hour alone on a Saturday morning before I have to take care of anyone! That's the best case. At worst, I have more time to spend with my mom, my best friend, a person I hope I keep around in every lifetime. She gets to live a little more of the life she deserves to live. There are no downsides to changing up the status quo, and the consequences of not taking action is that we'll continue down this path and my mom will die and I'll fall into a few years of grieving depression and lose even more of my time to ALS. And that's not a joke.

So here I am, writing to you in the middle of the night (I told you my days were overflowing), begging you to please URGENTLY help these patients access new and emerging therapies, and provide plenty of flexibility to developers so that we can start fighting this illness at the same rate it moves. Help me and my mom, in our little corner of the world, so we can get back to the goals and dreams and richness of life that at this point we have earned the opportunity to live. So much of your days are the chaos of politics and witnessing the worst troubles in this nation and in our world. This is a moment to combat that horribleness with joy. Please seize it and run until patients have constant access to new therapies, until my mom can find something that improves her symptoms, until I can go to bed at night (as I am about to) and not wonder if today was my last day with my mom.

God bless,
Laura Manhardt



My name is Laura Nelson, and I live in Central Florida. My son Henry is 6 years old with an ultra-rare disease, Barth Syndrome. He was diagnosed with Barth Syndrome at 6 month old. His heart was failing. There was no surgery to help his heart. He would be given general heart medications in hope that these would help, but most likely he would either need a heart transplant or die. If he received a transplant, doctors told me there was hope he could possibly live up to 30 years. That is nowhere near the age you hope your son will live to. On top of his heart problems, this disease affects his entire body. As a mitochondrial disorder, any function in his body that requires energy doesn't work properly. He's been in physical therapy, speech therapy, and has extreme difficulty eating. It's such a rare condition that there are NO medicines or treatments to help him. This was a huge shift in the hopes and dreams we had for our little guy. We have so many fears for the future: needing a heart transplant, declining energy, and declining health. This disease is usually fatal at a young age. We don't want to watch his health deteriorate when there is a possible treatment that has already been through a clinical trial. We are just lacking FDA review of the incredible results of this trial. Heart function and exercise tolerance had amazing improvement. We are desperate for this drug to be available for our son, who currently has no other option for treatment. Science and technology are advanced to find many treatments for many rare diseases. However, if the FDA will not review a small clinical trial for an ultra-rare disease, then rare diseases are without hope of ever having treatments approved. A lack of FDA review for this trial is a perfect example of what needs to change for rare diseases. Please help our son.
Thank you,
Laura

[redacted]

Hi,

My name is Elsa Burgos and my daughter was diagnosed in 2019 (at 27 years old) with an ultra rare neurodegenerative fatal disease called Niemann Pick Type C. Before diagnosis Nicole was working full time at the Burn Unit at Tampa General Hospital and was a full time nursing student, now Nicole is disabled, not capable of working and needs assistance from us 24/7. She has been denied help from the state of Florida because her diagnosis was after 18 years old, even though she was born with this genetic disease. There are no medications approved by the FDA, she is currently taking Arimoclomol which was denied approval in June 2021 and will be resubmitted for approval this quarter.This medication has help with her balance, and fine motor skills and choking. We need multiple therapies but will take whatever is available to try to slow the progression of this devastating disease. As a mom, seeing my daughter deteriorate is not easy. Please watch this video and contact me with any questions you might have.

Have a great day,

Elsa Burgos
12726 Tar Flower Drive
Tampa, Florida 33626

469-396-8687

https://youtu.be/ix9p56UCjWQ?si=AcYJ2-c4WMupHTMd

James C. | Miami



Age: 51
Year of Diagnosis: 2017
Type: Bulbar Onset

This is important to extend quality of life.

I would try any medicine; I have nothing to lose.

I need options to try and want every opportunity to improve my quality of life.

At first, I went into a deep depression. I miss having a normal marriage with my wife as she is one of my caretakers. I miss my career. **I miss exercising and having normal, fluid conversations. I miss eating.** That being said, I have a decent quality of life using eye gaze software , I'm able to communicate and take college courses.

It has put a huge burden on my wife and children and finances.

We are still the same intelligent people we were before ALS.

Accelerate drug approval and give us access to experimental drugs.

[redacted]

I will be 79 this year (11/14). I have been treated for RR MS and its associated comorbidities since the 80's. These include: Atrial Fibrillation;celiac disease;hypotonic bladder;stroke;chronic pain.
I have been treated with Avonex as a disease modifying MS med. since 1999. It has been very effective; but difficult to have my prescription renewed by my pharmacy insurance coverage for 2 reasons: first the pharmacy management team changes the in network drugs available and certain physicians believe that thre is no need for MS drugs after 70 years of age even though there is no scientific evidence for that belief because the FDA does not require older patients to be included in clinical effectiveness trial data. As a 79 year old married to an 83 y.o. spouse our choice of medications are limited by lack of good evidence.
Sincerely,

Philip Posner
2542 SW 14th Drive
Gainesville, Fl 32608
(703)675-8151

[redacted]

Dear Senators

Prader-Willi Syndrome is a rare genetic disorder affecting approximately 1 in 15,000 births. The Syndrome is characterized by failure to thrive at birth and progresses to hyperphagia (uncontrollable urge to eat), uncontrollable skin picking, and aggressive temper outbursts by age 2. My son, Ian, is now 28 years old living with Prader-Willi Syndrome.

Although Ian had a good experience through the school years, adulthood is an entire different world. Think about how our lives' revolve around food. Almost every social event, store, sporting event, and cultural event revolves around food. Ian needs to have controlled access to food or he will literally eat himself to death in possibly one instant. This means limited work and social environments. Additionally, Ian can have quite violent temper outbursts. Many times involving food. Temper outbursts can be misunderstood in public domains, thereby further limiting community involvement.

The needs of the Prader-Willi community are great. More investment in research to find pharmaceutical treatments to address the hyperphagia, skin picking and temper outbursts. Better FDA regulations for drugs addressing rare diseases that would make it less expensive for drug development. More money committed to housing and employment opportunities that will provide the necessary protection for this rare community. Without current drug treatments people with this syndrome require limited access to the community. This is a burden on both the individuals with the ,yndrome and their caregivers. As an adult my son can't have access to food or money. However, he sees how others live and he wants an independent life for himself.

My asks are simple. More money for research, faster FDA approvals, better alternatives for housing and employment.

Sincerely,
Andrea Glass
5404 SE Acadia Ter
Hobe Sound, FL 33455
617-835-1027

[redacted]

I saw the deadline was 5pm on 10/19, however I had heard the deadline was extended, so I hope that is the case. I am sending along my story for the Congressional record.

Thank you,
Maggie Senese

My name is Maggie Senese and my youngest daughter Bridget was born with Prader Will syndrome. We live in Winter Garden, Florida.

Bridget is a smart, funny, compassionate, and full of dreams for her future. When she grows up she wants to be a police officer. She was inspired by all the Capitol police she saw on one of her trips to the Hill. I love that my daughter has hopes and dreams for her future, but I also know without and approved treatment for the most debilitating aspect of PWS, she I'll never have the opportunity or potential to fulfill her dreams.

The hallmark characteristic of PWS is hyperphagia, an inability to feel full, no matter how much one has eaten. No matter what we do to help Bridget keep up with her peers, eventually hyperphagia will take over and consume her life. Individuals with hyperphagia essentially become prisoners in their own home, with all access to food under lock and key. Their caregivers become the warden.

Our community needs treatments for hyperphagia. We don't currently have any FDA approved treatments for hyperphagia, but we do have one on the horizon. Access for non trial participants is non existent. It is devastating as a parent to know that a treatment that is safe and effective exists and can't be available to the PWS hyperphagic population.

I have seen the current treatment, that we are clinging on to with hope, face barrier after barrier, on the road to trying to be approved by the FDA. Each challenge it faces delays the ability for that treatment to be in the hands of the patients who so desperately need it.

Bridget is nearing the average age of when hyperphagia begins and my greatest fear is that her hyperphagia will start and won't have a treatment ready and waiting for her. With a treatment for hyperphagia, she could be part of a new generation of PWS patients who can have the potential to live an independent life. She could be part of changing the natural history of PWS!

We need access to treatments and treatment options. We need to continue and support therapeutic companies to develop innovative treatments for our children. Once those treatments are developed and proven to be safe and effective, we need to give access to these treatments to patients as quickly as possible. We don't have time to spare. Every day that is delayed is another day a patient lives with a debilitating challenge of their disease.

My hope is that by the time hyperphagia hits for Bridget, we will have an approved treatment. We were afforded that luxury of time as Bridget has grown up, but there are so many patients who don't have that. They need treatments and they need access to them now. It's vital to get them that access as quickly as possible.

On a regular basis, Bridget's teachers and principal at school tell me that her future is bright and that she is going to go so far in life. They say her strength, tenacity, and stubbornness will lead her to great things. It's so bittersweet to hear that. On one hand, it's what every parent would love to hear about their child, but I also know that unless we find a treatment for hyperphagia, that won't be possible for Bridget. Her dreams of becoming a police officer won't become a reality. Like all the others in our community, we need an approved treatment for hyperphagia to give kids like Bridget the potential to live independent lives.



CARTER WOODALL

Canton, GA

In September of 2022, our family's life changed forever. Our 5 year old son woke up from a nap with concerning symptoms. We rushed him to CHOA here in Atlanta hoping it was something treatable. The CHOA team initially diagnosed Carter with post viral encephalitis and treated him with high dose steroids and IVIG. Well, a month later at our follow up MRI they determined it was in fact a brain tumor. An emergency biopsy initially determined it was a LGG. We immediately started chemotherapy and prayed for healing. Precision medicine would return 7 weeks later and we received the devastating news that he in fact had a HGG, more specifically DMG. Terminal. Our beautiful, funny, previously healthy 5 year old has a terminal brain tumor. Devastated doesn't even describe how we felt. DMG/DIPG tumors have NO course of treatment. In the last 60 years or so, pediatric brain tumor research has been so underfunded that there are no medicines or treatment plans that offer much hope. So we signed papers and started emergency full brain radiation. Our 5 year old slowly lost his ability to walk. He endured radiation for 5 days a week for 6 weeks. He slowly lost his hair. Based on his tumor's mutation, he began taking a daily inhibitor medicine that was developed for and is taken by adults with lung cancer. With little information on how it will affect him, we march forward. We hope and pray that this medicine will keep his tumor stable. Carter is currently 13 months post diagnosis and we are thankful he is here, that we are still fighting. But we NEED to do better. We need to fund research and develop medicines that will STOP these types of tumors from growing, and ultimately stealing our children. Carter should be running around our yard with his older brother. Carter should be dreaming about being a firefighter or a daddy when he gets older. Carter should have better options and access to better medicine that will give him a chance to grow older, medicine that was developed and tested for kids like him. But for now, we continue to fight.

Why the Promising Pathway Act is Important to our Family: The PPA is important to us because children have very limited access to life saving drugs that are specifically made for them. Children that

have been diagnosed with DPIG/DMG are immediately given a window of time in which they are expected to die. It's 3-9 months. Our children have no extra time lying around waiting for the FDA to provide approval for potentially life saving medicine. I think if you were to ask parents of DIPG/DMG kids if we would volunteer our kids for trials meant for them, with drugs developed for them, we would whole heartedly say yes. We don't have the luxury of waiting for things to be tested and trialed on adults. And don't forget, pediatric brain tumors grow and mutate differently than adult tumors. Essentially we are already testing drugs on our kids when we are finally able to try an adult trial drug on them. As personalized medicine continues to grow and becomes more readily available, we will need the option to test combinations of medicines. We must be able to target multiple mutations and alterations, because not every tumor works the same. All we are asking for with this bill is options. Give our children options so we can have a fighting chance to save their lives.

Becky Woodall

Mother of Carter

[redacted]

Good morning,
It is my understanding that there will be a hearing on the unmet medical need experienced by people with rare, progressive, and serious diseases. It is my sincere hope that you will take my family into consideration, understanding that your decision affects real people, not just numbers.

My husband and I live with our three children in Roswell, Georgia. Our son, Jackson, and my brother, Walker, both suffer from Barth syndrome, an ultra-rare mitochondrial condition. Currently, there are no approved therapies to treat this debilitating disease. There is currently a promising drug trial that my brother has participated in for the past four years. However, the FDA refuses to look at the data because our sample size is too small. Barth Syndrome is ultra-rare, so we will never have hundreds of participants to study. We are not the only rare condition that they refuse to look at. It is a systemic problem, and we need your help.

The Barth community is NOT large, but we do matter, Jackson matters, Walker matters. If it was your child or your brother, they would matter too.

I would like to share our journey with you, in hopes that you will remember that your decision will greatly affect the lives of people I love.

Jackson was born in 2009 after a healthy pregnancy. But he was blue, and quickly swept away to the NICU . That afternoon he stopped breathing, we watched the nurse bag and start CPR our newborn.

That evening the flight team from CHOA brought him to Atlanta. He coded on the airplane. Thankfully, the skilled nurses were again able to bring him back to life.

He was six days old when we got a diagnosis of Barth syndrome, and he would need a heart transplant to survive. We waited 101 days in the hospital. We are incredibly thankful that the Temm family gave Madison's heart to save Jackson's life.

Getting a new heart is not a fix-all though. There are many children with Barth who die each year waiting on a heart. Jackson tried to die on us a few more times, but God was working hard inside his little body, and after 6 months he got to come home.

Jackson has grown into an empathic, kind, faithful, Braves-obsessed teenager. We are so very thankful that he survived and we get to be his parents.

He does still have significant struggles. He doesn't have adequate energy or muscle tone to keep up with his peers on the playground. He can no longer play in his baseball league. This summer he wanted to go to an overnight camp. There is no way he could walk around the large campus, so I had to go to drive him around. It is not "cool" to need your mom to go with you to summer camp. He has lost several friendships because he can't play the way they can.

Jackson does not have a normal life expectancy. We do not take him for granted. Many people diagnosed with Barth Syndrome die before the age of 5. The possibility of not outliving your own child is something I do not wish on anyone. Any therapy that could improve the quality or longevity of Jackson's life must be pursued.

As I said before, there is a potential treatment for Barth syndrome. My own brother, Walker, has participated in the study. He gives himself a daily injection, and describes the treatment as life changing. Plainly stated, Walker does not want to go on living without the drug.

Thank you for taking the time to understand our story. I know that your job is not easy, and full of hard decisions. I hope that you will choose to give my family a chance of living the best lives possible, by compelling the FDA to fulfill their obligation to look at data for rare-disease drug trials.

Most sincerely,
Sara Greene

[redacted]

Hello my name is Cecilia Crow and I live in Rome, GA. I was diagnosed with ALS at the age of 46, I will be 53 by the grace of God in December. Being diagnosed with a terminal progressive neurodegenerative disease is a feeling I don't wish upon anyone, since the feeling of hopelessness has just begun.

My husband and I were empty nesters, preparing for retirement and working hard to get all our ducks in a row. I was able to remain independent until March 2020. Thanks to Covid my husband was able to work from home and care for me as I could not do anything for myself anymore. We could afford 20 hours of help starting August 2021, and in October we were given 12 hrs of respite care from GA ALS Association.
Out of 168 hours in a week, 32 I had care. The remaining 136 hours my husband had to work and take care of me on his own. We are California transplants with no family around And this Wednesday I lose my 12hrs of respite.

Not only do we need to worry about keeping me healthy, but be able to pay out of pocket medical, out of pocket care and try to leave a home and some retirement for my husband. I tried to apply for Medicaid but my SSDI was $400 more than allowed. It does not take into account that my out of pocket medical insurance is $550 alone.

How is it that we have worked so hard our entire life and we cannot get help as I prepare to die? How long can my husband handle the stress of work, the stress of money and the stress of taking care of his dying wife before he falls ill? How is it that the FDA has no flexibility for neuro degenerative diseases that has no hope of survival? How can the USA not have different rules for support based on the severity of someone's illness? I am preparing to die and as I do, I have to worry about what will be left after I am gone instead of just enjoying the time I have left.

There has got to be a way to be able to die with dignity and peace, and not with guilt and worry.

L. Cecilia Crow
17 Bentley Ln SW
Rome, GA 30165

[redacted]

Dear Sir/Madam,

I have ALS. Before that I was a practicing, active pediatric oncologist, taking care of kids with cancer over a 45 year period. I am a former President of the American Society of Pediatric Hematology/Oncology, and hence very involved in my field.

I was diagnosed with ALS about 4 years ago, and have by chance had slowly progressive disease. I have participated in 2 clinical trials of innovative therapy, and there is no evidence to date that they have helped. BUT...clinical trials are the ONLY WAY we will advance the field [witness what we have accomplished in peds-oncology, with federally sponsored clinical trials]. I urge you to expand access to innovative medicines with ALS and other life threatening disease, with rigorous studying of the meds to determine efficacy.

Thank you in advance, sincerely William G Woods, MD

William G Woods, MD
Sent from my iPad

Shelby T. | Georgia



Age: 29
Year of Diagnosis: 2021
Type: Limb Onset





My mom is hopeful, ready, and willing to receive experimental therapy. This time last year, she was in the best shape of her life. She was competing in races, excelling in workout classes, etc. Just one year later, all of that has been taken from her.

It is a risk that she is willing to take. Considering that this a terminal illness, why not experiment with something that even has the slightest potential of increasing her life here on Earth?

If the trials have proven to be safe and effective, FDA approval is not as important. Take the Covid-19 vaccine for example. It is not fully approved, yet it is used for emergency use. Is ALS not an emergency? ALS is terminal, in all cases.

I can only speak for myself and not my mother.

My mother's diagnosis has affected our entire family, friends, etc. It makes the future almost unimaginable. **The progression of the disease comes with absolutely heartbreaking situations.** Anything that could possibly slow the progression is absolutely necessary.

I wish people were more informed about the disease. I wish the masses were fighting for a cure, and not just those that are affected by it.
We need this now. ALS patients cannot wait! They simply cannot wait. Each day can come with new obstacles. My mom can talk today, but she could begin to slur her speech tomorrow. My mom can walk today, but her legs could become weak tomorrow. There is no waiting period. The time is now. **Please help this community of people that are begging for your approval and begging for added life.**

Kerry P. | Georgia



Age: 69
Year of Diagnosis: 2017
Type: Bulbar Onset, Sporadic

I was willing to receive the Moderna vaccination although it was only "an emergency" vaccination. I would like to be given the opportunity to decide whether or not I take a drug for ALS.

Besides losing the ability to walk and talk? The loss of independence has been the hardest thing for me to deal with. In spite of it all, I have been able to keep a positive attitude.

My husband who is my caregiver has had to do a lot of things I used to do. In addition, he's concerned about leaving me for any length of time, so he rarely gets time for himself.

There is no cure. **The very few drugs there are available to treat ALS really don't help much.**

Percy M. | Georgia

Age: 72
Year of Diagnosis: 2010
Type: Limb Onset

We Can't Wait

It would be very valuable and important to have access to medicine. **If you don't try you fail.** Important to try everything.

Lifestyle change, new habits from eating to getting dressed. They have become adjustable to my needs.

ALS is helplessness beyond your control. Research is important to our society.

Bill W. | Georgia

Age: 74
Year of Diagnosis: 2019
Type: Limb Onset



We Can't Wait

I am a pediatric oncologist and clinical trialist. I have been heavily involved in clinical trials my entire professional career, including at the national level as a leader, and appreciate both the advantages and potential challenges of using innovative drugs, like serious side effects. BUT childhood cancer is mostly LIFE THREATENING and deserves every chance for cure. **This is not dissimilar to ALS!** Through NCI sponsored clinical trials, started in the 1960s, we have been able to take the overall cure rate of all childhood cancers from 25% at that time to 80% today. For most of the trials we did not wait for confirmatory trials to move forward, with arms of trials shown to be superior to the past 'standard' now becoming the NEW 'standard' [and I should note that for the vast majority of the drugs used, there was NO pediatric indication for most important agents, many of which are still used today without a peds indication!]. Since Richard Pazdur's leadership in ODAC, in charge of oncological new agents in the cancer world, many new molecular inhibitors have been introduced, with some **VERY SMALL** trials then showing efficacy in adult cancers. Many have then received 'Accelerated Approval', with the FDA following further use carefully through the drug companies, with subsequent analysis. Some drugs have been stopped for certain indications because of lack of efficacy in subsequent analysis, with more patients and longer follow up.

I HAVE ALS, DIAGNOSED IN 2019. WHY CANNOT THE FDA HAVE A SIMILAR APPROACH WITH DRUGS AIMED AT ALS? A great example: the two-drug combination called AMX0035, with a very convincing report in the NEJM of early efficacy. **Why not give the drug(s) Accelerated Approval?!** Then conduct a Phase III trial, single agent, or just collect data on ALS patients and see how they do? Most of us would want to go on such a drug, even if potential side effects ultimately are found. **Our disease is LIFE THREATENING, big time!** Those who don't want the drug do not have to get it, of course . But the rest of us will line up for it, with excitement. Similar other drugs should be evaluated like cancer meds, studied quickly, approved by the accelerated process if they show any efficacy, with careful follow up by the drug company and the FDA. **In my humble opinion it is time for the FDA to increase access to novel agents for patients with a disease like ALS, using a approach similar to the ODAC Accelerated Approval process. Clinical trial yes; full FDA approval NO, see above.**

ALS has 1] Led to retirement; 2] Now physically limited, cannot swim or bike, 2 passions. 3] Pain, not fun 4]sedentary lifestyle: I used to be very athletic and physically fit

My wife now does the vast majority of daily chores, very 'unfair' to her.

First, I bet the half the folks in the country don't even know what ALS stands for, and what it means.

I feel very passionate about this!

Kerry G. | Georgia



Age: 55
Year of Diagnosis: 2015
Type: Limb Onset, Sporadic

One more day! **When your life is put on a time clock every second matters.** Any treatment or therapy that extends your life makes it well worth the risk. It's been over 75 years since Lou Gehrig farewell speak to baseball and we're still no closer to a cure. Riuzole is still the same medication we had for the last 50 years, which is unacceptable. **We need your help to find a cure.** We have a terminal disease and are willing to participate in finding a cure but we're being handcuffed from even trying.

Nothing from nothing leaves nothing. At the present time we on a course with death. All I want is an opportunity to fight for my life.

The entire world has accepted vaccinations for Covid 19 in record timing. I have received the vaccine myself, yet it feels like a punch in the gut to see everyone rushing to find the Corona vaccine. While we restricted from taking our lives in our hands and trying new drugs. I'd rather die trying than wait for death to knock on my door.

My family and I have gone from an upper middle family to living below the poverty line. **ALS has financially destroyed my family.** With me being paralyzed and completely dependent on others for everything, my wife has also had to leave her job to care for me.

My children have missed out on a lot of things that kids normally experience. Either we can't afford it or do to me being unable to do things that a healthy father does. The level of care needed for each patient is incredibly expensive and critical.

Get us a fighting chance. Allow us to be involved in the decision to choose. Take a chance on the use of drugs. **I assumed the risk of playing football for 20 years. Now I'm being benched by not allowing me to fight for my life. Let me go down trying every reasonable opportunity available.**

[redacted]

Hello my name is Deahl Wilson, from Fayette, Ga my son Matthew is 14 years old was born with Prader-Willi syndrome, we were told Matthew would be a monster- Prader-Willi syndrome has many characteristics one being hyperphagia the inability to fill full.. the NICU doctor at time of his diagnosis gave us pamphlets to institutions to send him too.
My son Matthew 4 years ago started a trial drug DCCR (dioxide chloride control release) pills he takes in the morning, helps him function and fill full.. we were able to prove highly statically significance difference then baseline" without this drug my sons life will end in institution - he has hopes and dreams, please help us!! Any questions please call me 404-9347220
Deahl Wilson -Matthews mom.

October 22, 2023

Dear Chairman Casey, Ranking Member Braun, and Honorable Members of the U.S. Senate Special Committee on Aging:

My name is Jack Gerblick and I live with a disease called Facioscapulohumeral Muscular Dystrophy, or FSHD.

Thirty three years ago I was diagnosed with fascioscapulohumeral muscular dystrophy (FSHD). It's a genetic disease. I was born with it. My body over-produces a protein called DUX4 and this protein eats, destroys and kills muscles. And like all forms of muscular dystrophy, it's a progressive disease that keeps killing muscle and the muscles that the disease kills will never be healthy. In some cases, entire muscle groups can be destroyed in a matter of months. The uncertainty of not knowing what's coming next is very disconcerting and feeds my anxiety. There is no cure for FSHD.

It's a slow disease that gradually robs people of muscle in their face, shoulders and upper body. It takes things away like being able to get dishes down from the top shelf, wash your hair, the ability to smile, lifting up grandchildren in order to give them a big hug and other activities most people take for granted. For many of us, it progresses to legs and feet (which mine has) and begins to weaken and kill those muscles. This is a rare disease affecting an estimated 60,000 people in the U.S. and 870,000 people worldwide. Around 30 percent will need a wheelchair by age 50. Over 70 percent experience debilitating pain and fatigue.

The severity of this disease and the rate of progression is unique to each FSHD patient. The rate of progression for me over the past two years has been downright frightening. My mobility and balance has declined quickly over the past 2 years. I now utilize an AFO brace to help with the foot drop in my left leg along with a cane in order to walk.

One of my daughters has tested positive for this disease. She has two children ages 2 and 4 and they each have a 50/50 chance of also having the disease. Not only do I not have the ability to pick up my grandchildren to give them a big hug from Papa Jack but I constantly worry that they will also be affected by this horrible disease. In fact, my 2 year old grandson named Marshall is a mini me at that age. I pray that he only inherits my dry sense of humor and intellect! (smiley face)

This has not been fun. The last two years have been very difficult for me and my family.

Sincerely,

Jack W. Gerblick

Atlanta, GA

CC: U.S. Senate Special Committee on Aging

Sen. Bob Casey

Sen. Mike Braun

Sen. Kirsten Gillibrand

Sen. Richard Blumenthal

Sen. Elizabeth Warren

Sen. Mark Kelly

Sen. Raphael Warnock

Sen. John Fetterman

Sen. Tim Scott

Sen. Marco Rubio

Sen. Rick Scott

Sen. J.D. Vance

Sen. Pete Ricketts

[redacted]

Goodness. Where to begin?

My son, who just turned 25 earlier this month, was our first child. When he was born, we were not expecting anything but "normal." We had no idea what we were about to face. The day he was born was devastating. As a non-medical person, I was suddenly faced with specialist and medical terms, tests and labs. My tube fed baby was not allowed to go to the daycare facility I had carefully picked as a woman hoping to continue working at the archives at Emory University with plans to get my PhD there. My world crashed down around me.

With my career on hold, I tried to improve my son's health quickly. I signed up for as many therapies he qualified for through Children's Healthcare of Atlanta. I took him to every specialist I could. He did finally start taking a bottle with a special nibble but still had to be force-fed on an alarm-clock scheduled every three hours. I never got more than 2 hours of sleep at a time for those first months. I couldn't think. I couldn't do much but feed him and take him to appointments. I officially resigned from my job when he turned 7 months old, realizing that there was no where to leave him. No one to take care of him so I could work. Hell, no one to watch him so I could shower most days!

Just after resigning, a lost test for Prader-Willi Syndrome was found by his neurologist's office. One of five rare diseases the neonatologist had run when he was a patient in the NICU. He finally had a diagnosis. He has PWS.

I poured my heart into it. Met the president of the Georgia chapter. Took him to 6 therapies a week. Bought all the educational toys, sensory things, and therapy related toys like he used in speech, OT and PT. I was going to make him the best version of himself I could.

The days turned into years. Much of the in between was a blur of parent/teacher conferences, of sleep studies and blood draws. This has been our life for 25 years now.

He aged out of the school system when he turned 22. We had given education an honest effort. But there wasn't much more than can be said for it. My son has an IQ of 74. Too low to go to college, which is all his school years taught him to work toward. Too high for the special educational experiences so many of the colleges have these days. He is stuck between the two worlds.

He knows he is different. He hates it. He is angry with us, his parents. This is all our fault he says.

We now have the internet which we did not have when he was born. And through that, we see other people with PWS and we know that he is just like them. We hear tells of how they sneak around and get food or get into other forms of trouble which seems to be so common. As a teen, he ordered a truck from Mall of Georgia Toyota. Red tundra with extended cab and towing package. I didn't know until they called for him to come pick it up from the dealership! There were stolen credit card numbers used to purchase video games and him hacking into my Amazon account to make purchased. Most recently, he learned how to use Door Dash and he ordered a $5 milk shake from Chic-fil-A, paying $13.13 for it, all while my husband was working in the garage.

Our pantry and fridge have been locked since he was 12. He said it lower his anxiety. Just the thought that he could get something out at anytime was driving him crazy. But now, he has new sources for food. He has a couple people who we hire to take him out into the community and they don't want to tell him no because they don't want to be in public with

him when he has a meltdown over being told no. And this isn't just food but it can be no about anything and everything. His behavior is over the top. We have a behavioralist who works with him twice a month and has for 6 years now. But he is still acting out. He is on 7 prescription meds and 4 over-the-counter meds, most are for mood liability and anxiety.

He has gained some 15 pounds in the last 6 months. With the weight gain, his anger is worse. And as we try to help, he just gets worse. He recently asked to go back on human growth hormone which is the only treatment for people with PWS approved by the FDA. That doctor ran a full blood panel and now see that he is diabetic. And several of his other levels are out of wack. Not sure what they all mean yet. But it is like he has aged several years in the last 6 months. His health is deteriorating quickly.

Because of his ability to get food, we have had to cut his day program days to just twice a week, cutting out the possibility of extra food. I had to quit my little part time job at Talbots because no one was able to watch him and to monitor his food intake. Still after 25 years, I'm being punished for having given birth to him.

I want him to live his best life. He wants to move out. I'd love that. But last year he lived in a group home for 10 years and was forced to go to their day program. It ended with him receiving carpet burns from being drug by his ankles by tow staff members to a solitary confinement room. (Yes, those are illegal. Yes, his behavioralist had seen it. Yes, it was invested by the state and was confirmed to having happened and existing. No, the staff were not charged. The sheriff said there was not enough evidence that he was drug inspite of the investigation by the state and witnesses in the day program. One staff member was working under a false name and had not been through a background check. They are both still employed there. Nothing happened except my son ended up in the ER and now has no interest in going into a group home again.)

Life is hard. Life with a special needs adult who outweights you by 125 pounds and wants to harm you is impossible.

Tammy Galloway, mother of Kyle Galloway, age 25 primary dx Prader-Willi Syndrome



To whom it may concern:

My husband, Lewis Burger, and I live in Cherokee County, Georgia represented by Congressman Barry Loudermilk, Senator Raphael Warnock and Senator Jon Ossoff.

Our son, Walker, 34, and grandson, Jackson, 14, have Barth syndrome. Fatigue, weak and painful muscles, the inability to fight certain illnesses and the mental frustration seeing others do what they long to do but their fragile bodies will not allow are symptoms they endure.

Jackson endured a heart transplant due to extremely weak muscles caused by Barth syndrome.

Devastating to hear at diagnosis we were told there are no medicines, no therapies, nothing on the horizon to treat Barth Syndrome. No hope. This is something no parent or grandparent ever wants to hear.

Five years ago Walker volunteered to participate in the TAZ Power clinical trial. The study has changed his life. Mere days after beginning Elamipretide his energy level began increasing. He gained weight, muscle mass and energy. His heart output increased 40%. After three months, Walker was a new person. His energy level increased tremendously. Incredible! I would not have believed it had I not witnessed it.

Walker feels better and is happier. New found confidence and self worth are evident. I had not realized how badly he felt before Elamipretide. He had shouldered so much pain throughout his life both physically and mentally. It was incredible to witness this young man come alive with a new level of energy! Walker is enjoying so much more of life now and able to thrive!

Without FDA approval, Walker will not be eligible to use Elamipretide. His quality of life, productivity and general well being will greatly decrease. It is inhumane and unthinkable for Walker to be without Elamipretide. Without FDA approval, the unthinkable is possible.

I want Jackson to enjoy the benefits of Elamipretide. To see him with increased energy and a better quality of life would be as life changing for Jackson as it is for his Uncle Walker. It is unmerciful that Jackson and others with Barth syndrome cannot benefit from the life changing drug that I know first hand works!

I appeal to your humanity in asking for your support in encouraging the FDA to give Elamipretide a fair and just chance of approval.

Sincerely,

Sara "Sally" Walker Burger



BENNY WATTERS

Lake Forest, IL

Benny Watters was only 5 years old when he passed away from a Diffuse Intrinsic Pontine Glioma (DIPG) in 2010. The only approved treatment option available at the time was radiation which only postpones the inevitable and Phase I & II Clinical Trials. Sadly, although we know so much more about the biology of these tumors more than a decade later, the options for families has not changed much, that is unacceptable. For life-threatening diagnoses like DIPG, families need hope, and we need to rapidly advance potential drug treatments to find a cure. We are not only losing our beautiful children, but the impact on the whole family and community is devastating.

Why the Promising Pathway Act is Important to our Family: The Promising Pathway Act (PPA) is a commonsense approach to providing access for patients with diagnoses like DIPG to new and innovative drugs. The PPA will motivate pharmaceutical companies to not ignore these rare life-threatening diseases and the FDA will be empowered to collect critical data that could lead to life-saving treatments beyond even these rare diseases.

Lisa Watters

Mother of Benny

[redacted]

Hello Senators,

My name is Jenna Weets and my husband, Brad and I have two children - Claire, 13 and Jeg, 10. Our son Jeg was diagnosed with Niemann Pick Type C or NPC, an ultra-rare genetic storage disorder at the age of 4. NPC will take his ability to walk, talk, swallow, cause eye-gaze palsy, seizures, and then eventually death. He also has severe perianal Crohn's disease.

Jeg is a typical 10 year old boy who loves anything with a motor. He drag races and plays baseball. He loves movies and UNO. He has never met a stranger and loves to give hugs to anyone who will take them. He needs your help to change the path of future research and medications.

Jeg first started seeing doctors at our local rural hospitals at the age of 2 for skin tags on his bottom. They discovered his enlarged spleen during an exam during one of his GI visits and with some further testing over the next few months, they discovered his NPC. His genetic doctor had one patient with NPC and had nothing to say to us but good luck essentially.

Only because of a small miracle with a family connection to someone who wrote their thesis on NPC and happened to work in the lab of a well renowned NPC doctor was I able to get Jeg into a doctor in Chicago that was conducting a trial for a drug to stall his disease. We were able to start in February (5 months after diagnosis) through compassionate use. He has been receiving this drug now for 6 years this February and has progressed in his disease very little.

What I can tell you after 6 years of having a child diagnosed with an ultra rare disease is how absolutely horrifying this medical journey has been and is.
I have seen the FDA deny approval for my son's drug siting that the risk of his spinal taps for his medication are too big of a danger to approve it. I can tell you over the 145 spinal taps Jeg has gotten, he has never had a side effect or problem from them. He does not cry or worry about the procedure and has been doing this awake since COVID. The only side effect is hearing loss which occurs anyway with NPC and is correctable with a hearing aide. In the grand scope of his disease...we will take hearing loss.
I have seen the FDA recommend that we sacrifice our children a blind placebo trial for more data because they refuse to think outside of the box and use the many years of NIH natural history data.
We have been told that because my son is on one experimental medication, we can not participate in compassionate use for another when the experts in his disease know that one drug will not be saving him.
What I wish the FDA and anyone else involved in the drug making process for especially a rare disease is that we will do whatever it takes to save our children. If a drug is safe with mild side effect, we will give it a shot. But I will not take my son off a drug that has been stalling his disease for six years and put him in a placebo trial. We do not have enough of a population for that.
The process of approval for a progressive disease like my son's needs to change. These kids are dying because of red tape. Our NPC community has had more than a handful of drugs go through the approval pipeline only to be denied for some insignificant issue. Drug companies and researchers will not invest their time and money trying to put a drug through the approval process with the FDA if this continues. Which is very very disappointing as a parent of a child with an ultra rare disease. They are letting my child die because they are not getting the studies they want even though the data is there in other ways. They want the data in ways that work when you have a large population group to study from

that is just not possible in diseases like this. New ways have to be sought. Time is not on our side and the process of approval takes way too long.

Having a child with a ultra rare genetic disease is incredibly hard not just on the patient but on the whole family. We drive 6 hours round trip for Jeg to receive his medication in Chicago every 2 weeks. It means missing work, missing things with our daughter, missing school etc. His medical needs mean alot of appointments and because we live in a rural area, alot of travel to them. We are underserved when it comes to his need in our area because no one at local hospitals or even the bigger areas know what NPC is or how to help him. We live in an area that does not offer many types of schooling for him as he progresses so he will be bused to other towns. Every day is a fight for him and us. We fight for fundraising for research due to the small NPC population. We should not have to fight for him to keep his drug or to fight to get more drugs approved for him as well.

We have watched my son change over the last few years and we had such hope for new drugs to come along when we began our journey 6 years ago. Nothing has come to his and other's aid. Nothing. But I have seen how fast our country can approve things like a COVID vaccination when the funding is there. And the list of side effects for that vaccine or any vaccine is much longer than the drug my son receives but it is not approved. I hope for all rare disease patients that change is coming.

Jenna, Brad, Jeg and Claire Weets





Linda R. | Illinois

Age: 62
Year of Diagnosis: Mother - 1994
Type: Genetic

We Can't Wait

Every day I would go to work wishing time would just stand still so I could have more time with her. Everyone else was "waiting for the weekend" but I never was.

There is no risk when someone only has a short time to live anyway.

As stated before, how can there be any risk when taking the drug before it is approved.

My mother's ALS diagnose brought great sadness for everyone that was close to her.

It is a death sentence.

Any kind of hope is all you have.

Theresa J. | Illinois

Age: 80
Year of Diagnosis: 2007
Type: Limb Onset



We Can't Wait

My Loved One is deceased as of 3 years ago. **We would have welcomed any new therapy, any opportunity to have hope and time.**

I could not accept adverse side effects added to the already existing torture of ALS but if therapy had no benefit or modest benefit, we could not have been worse off.

FDA approval is ideal but traveling foe clinical trials is next to impossible and the disease does not allow the luxury of time. Apply "Warp Speed" money please and end this disease!

100% horrible

The worst experience of our lives, the worst pain and suffering. I can't even respond to this without sobbing. **We are shattered, broken, irreparably.**

I ask God to send wisdom and insight to the researchers and scientists for a treatment. I wish people understood this disease has chosen some of the most gallant of our families, the healthy athletes, the community and religious leaders, the parents and our beloveds, it is merciless and offers no hope for remediation.

Don't look at the incidence, look at the impact and the torture

[redacted]

Hello,

My name is Deb Paust and my husband Tim died 9 years ago from ALS at the age of 51. Tim lived 2 years and 2 month after being diagnosed. I stopped working as a manager and clinician of a Physical Therapy office to be his primary caregiver with help from our 3 children who were in college at the time.

We were doing well financially when the diagnosis came but eventually had to sell some of our assets to keep our youngest son in college. Our daughter was a big 10 cheerleader who quit her senior year to get a job so she could finish school. Our oldest son lost his job as he was helping me take care of Tim at the end of his life and Tims anxiety from being trapped in his body unable to move was a full time job to comfort and medicate. My son was torn and unable to leave his dad in such distress and was either late or unable to show up for. work.

Although Tim has been gone for over 9 years, my kids and I still suffer from depression,grief, PTSD and anxiety despite our best efforts, optimistic attitudes and zest for life. We are forever changed having to watch the brutal and rapid loss of function that was devastating for Tim as well as all of us.

Although they do not speak of it often, I know my kids live in fear that they will get this horrible disease. It's important to know that once the person with ALS dies, the suffering continues for the children, spouses, parents and friends. My youngest son has endured 2 painful Electromyography (EMG) tests to measure muscle response or electrical activity in response to a nerve's stimulation of the muscle. The test is used to help detect neuromuscular abnormalities like ALS. He suffers from severe PTSD and struggles to function with everyday activities of work and homelife. He just turned 30 and moved back home as he tries yet again to heal and get stronger to live a normal and productive life.

Many other children of ALS are putting off college due to the financial and emotional strain altering the course of their lives. My children and I continue with individual and have done family counseling to help us move forward but as I say, we want and strive to live life to the fullest for ourselves and to honor Tim, but the scars from ALS hold us back more frequently than we wish.

My husband had a good outlook despite his fatal diagnosis and did his best to show our children how to live and die with dignity and respect. I thank you so much for the opportunity to share just one small aspect of our family's continued struggle from the devastating results of ALS.

We are in desperate need of early access to promising therapies with the constant turnstyle of death. Please help people living with ALS today by supporting the Promising Pathway Act.

Sincerely,
Deb Paust (ALS Widow)

Deb Paust
Community Organizing Associate
Pronouns: She/Her

October 25, 2023

Dear Senator Braun,

I am reaching out to you in response to your request for stories on the unmet medical needs faced by people with rare, progressive, and serious diseases for a hearing by the Special Committee on Aging to be held on October 26, 2023.

I am a participant in programs offered by the Huntington's Disease Society of America (HDSA), a leading national organization dedicated to the care and cure of Huntington's disease (HD), a rare and fatal hereditary disorder that manifests as a neurological disease with both physical and psychiatric components. The mission of HDSA is to promote and support research to find a cure for HD; help people and families affected by the disease; and educate the public and healthcare professionals about HD. Currently, there is no clinically available pharmacological, biological, or surgical agent or method that slows or stops the progression of HD.

I also serve on HDSA Illinois Chapter Board.

This story is about my wife, Judy, who inherited HD from her father/grandfather/etc. He passed away at the age of 70 when, living alone, fell in his bathroom hitting his head on the toilet and died in a pool of his own blood. We didn't find him for 3 days.

Judy started showing symptoms about 15 years ago and had to quit her teaching and singing career because of the effect of HD on her body. Judy was a world class musician who taught music at Columbia University and was a singer with the Chicago Symphony Orchestra for almost 30 years, during which she was on over 6 Grammy Records! We first noticed a decline in cognitive and executive decision-making when she had a serious car accident. After that, her memory started to decline along with balance, coordination and occasional psychological outbursts. She was diagnosed around 2005 with a CAG count of 42.

We have two daughters and now 5 grandchildren, all of whom are at risk of inheriting the HD gene. I am now Judy's full-time caregiver and she no longer performs, teaches or even plays the piano, not to mention uses a walker and is unable to drive. She spends most days in front of the tv, unless we go to visit family or friends. I am in the tourism business and can no longer leave her alone for more than several hours – needless to say, our financial situation has taken a major dive and our lives have been permanently impacted. Nursing home costs are beyond our ability and finding quality at home care is a huge challenge.

At this point, all efforts go to the research community with fervent prayers for a cure.

Thank you for giving us an opportunity to share our story.

Sincerely,

Wayne and Judy Galasek
1031 S. Kenilworth Ave
Oak Park, IL 60304
wgalasek@aol.com

October 25, 2023

Dear Senator Braun,

I am reaching out to you in response to your request for stories on the unmet medical needs faced by people with rare, progressive, and serious diseases for a hearing by the Special Committee on Aging to be held on October 26, 2023.

I am a participant in programs offered by the Huntington's Disease Society of America (HDSA), a leading national organization dedicated to the care and cure of Huntington's disease (HD), a rare and fatal hereditary disorder that manifests as a neurological disease with both physical and psychiatric components. The mission of HDSA is to promote and support research to find a cure for HD; help people and families affected by the disease; and educate the public and healthcare professionals about HD. Currently, there is no clinically available pharmacological, biological, or surgical agent or method that slows or stops the progression of HD.

My name is Cody Coile. My mother passed away from Huntington's disease in January of 2021. She was diagnosed with HD in 2013. My mother was 51 years of age when she lost her battle with HD. One may be unfamiliar with HD, but many know MS, ALS, and Parkinson. HD is all of them in one disease. My mother, before her diagnosis, was a bank branch manager, substitute teacher, student pursuing her bachelor's degree, and a mother of two sons. She was in all the senses of the word "normal". She worked, drove, went to church, was the life of our family, and loved life. She loved my brother and I more than anything in the world. I am sharing our story because families like mine and all those impacted by HD have unmet needs. While my mother was a functional member of society for 35+ years our medical system, government and others failed to meet her and our family's' needs.

Laura's medical needs were unmet and so were the family's. Throughout our journey Laura began being able to walk, talk, drive, but by the end she had lost the ability to do everything. This process did not happen overnight but instead over 9+ years. Every HD patient is different. My mother's father died in his 40's in a car crash, and they had no idea he carried the deadly HD gene. One that he would pass on to my mother. My mother was tested for HD in 2013 after having an incident that caused us as a family to meet and try to see what was wrong. It was the internet that led us to an idea that maybe she had HD, and the specialists at Rush Hospital in Chicago that confirmed it with a blood test. When my mother was tested she was required to wait 30 days before knowing the results, and the results had to be read in person. These are fair choices to make for a person learning their fate of a horrible tortuous disease but for a family needing to know an answer to a question they more than likely already know the answer to was torture. We live three or so hours from the only doctors and facility that understood HD and could test for it.

Medical needs for Huntinton's disease patients are challenging. More often than not we were told that my mother was not disabled enough or that she was not old enough. Many of the programs that would have helped us, we simply did not meet the means tests for. Laura was denied social security disability twice. She submitted her application with a diagnosis and a letter from her doctor. Wait times are a large issue for people with HD and government programs or

assistance. Oftentimes these systems have a default six month or up to two year wait time to get an answer. Time is of the essence for an HD patient and having to wait six months to years led to our family having to reach out for help, money, food and more while waiting for a determination. Without the assistance of our local congressman, John Shimkus, we may have been denied again.

Laura required a caretaker 24/7. Caretakers do not get any support from social security or the medical systems for being a caretaker. Caretaking for a HD patient is comprehensive. Caretakers are not paid for their work unless a disability recipient can find it in their $1200 income to pay for one out of pocket. A family caretaker is the best person to care for their loved one with HD, especially if they have a home to care for them. There was little to no support from the medical system to allow us to keep Laura at home for as long as possible with our own ability to care or even a part-time person or nurse coming to assist. Later in Laura's battle with HD she was living with her mother, 75-year-old one armed retired state of Illinois worker, and because they lived together the means test for medical and financial assistance would take her caretaker's income and assets into consideration and deny Laura help because of who she was living with despite the person able to provide full and proper care for her.

Trials and studies were never offered to Laura. We wanted to do everything we could to help the HD community. We asked to be involved in as many studies and trials as possible to help fight for a cure. We participated in zero. There are little to no trials or studies being done for HD patients despite its overlap with deadly diseases like MS, ALS, Alzheimer's, and Parkinson's.

In conclusion, Laura's medical needs were unmet. With rare progressive degenerative diseases, there should be no wait time. They should automatically qualify for every program and system that the government has to offer. A family watching their loved one be tortured to death over many years is a traumatic and devastating tragedy. With the government supporting not only an HD patient with all their medical and financial needs, but a caretaker also we would have been blessed to have more time to spend with Laura and more time for her to be at home. There may not be a cure, but there's hope.

I want to thank you for the opportunity to share our story.

Sincerely,

Cody Coile
501 ½ N Ohio
Tuscola, IL 61953

[redacted]

Dear Senators...

Our family is honored to submit this written testimony for the Senate Special Committee on Aging hearing about the Promising Pathways Act.

On Thanksgiving Day 2010, our wonderful wife, mother, and grandmother passed from conditions related to ALS. Ann Seitz was only 53 and had lived with the disease for 30 months following diagnosis. During this time there were few, if any, pharmaceutical treatments in the pipeline and access to any she would have met the criteria for would have required travel far beyond her capabilities given her inability to walk.

We invested - we prefer to use this term rather than spent – thousands of dollars out-of-pocket on mobility devices and equipment, chelation treatments, removal of all mercury fillings, as well as nutritional supplements in the hope of stemming the tide of this despicable, incurable disease. We believed there was nothing to lose.

While each person or family impacted by any rare or incurable disease state is different, Ann would have welcomed an opportunity for any available treatment option. The inability to access specialized treatments or medicines compounds the hopelessness the patient already is experiencing. Give people hope by passing the Promising Pathways Act.

With highest regards,

Terry

Terry Seitz
Indiana Outreach Director
Office of U.S. Senator Mike Braun
Braun.senate.gov
Mobile/Text: 202.878.0980
Indianapolis Office: 317.822.8240
Terry_Seitz@Braun.senate.gov

[redacted]

Dear Senators,

Thank you to the Special Committee on Aging for holding a hearing on the Promising Pathways Act. Jennifer and I also appreciate the opportunity to submit our family's experience as testimony for the record.

Our dad, Doug Ordway, was diagnosed with ALS at the Cleveland Clinic in 1998. He was just 39 years old.

We didn't fully understand the implications of this disease as I was 13 and Jennifer was just 9 years old. In addition, information wasn't readily available as widespread access and use of the internet was in its infancy at the time.

All we knew about the disease is that there was no cure and it would be a long and challenging road ahead. Assistive technology was still being developed and support groups only existed in major cities so our family was left to figure out things on our own.

While it was predicted that dad would live three years, he made it over five and passed away in the Fall of 2003.

During the time dad was alive, the only FDA approved drug to treat ALS was Riluzole, however, its success has been minimal. While other treatments have slowly come online in the past 20 years, regulations have stifled the small entrepreneurial organizations that show the most progress in finding a cure.

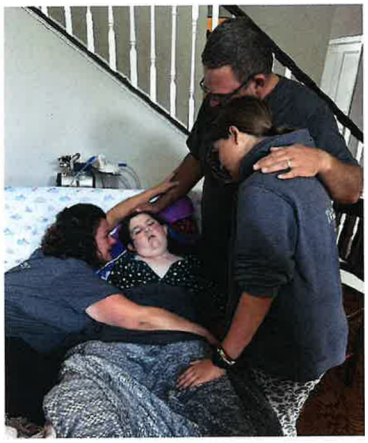
We do not know how much time is left for those with terminal diseases, therefore it is imperative that government and business work hand in hand to expedite opportunities for patients to access treatment options given the hopelessness they experience on a daily basis.

It also cannot be understated the amount of childhood trauma ALS left in its wake for our family. Finding a cure would minimize the emotional collateral damage survivors experience and further mental healthcare needed for remediation.

Jenn and I are optimistic that the Promising Pathways Act is the solution needed to help all people with rare and incurable disease. We hope that this hearing inspires another committee as well as the Senate at large to pass the Promising Pathways Act as soon as possible.

Thank you,
Robert Ordway and Jennifer (Ordway) Karagiannakis, Indiana





ADDISON VARNS

Bargersville, IN

On March 5th, 2019 our 6 year old daughter was diagnosed with DIPG. What started off as having a few headaches and fatigue, turned in to us finding out she had a "monster" growing in the most important part of the brain – the pons. That day we were told, "There is nothing we can do. Pull her from school and start making memories. She has about 9-18 months to live." We already know it is not "ok" to have a mass in your brain but it is most definitely not ok for a family to be told, "there is nothing we can do". After participating in 4 clinical trials in hopes that they would not be toxic and could possibly save her life or buy us more time, Addison passed away 53 months later on August 11th, 2023. Addison was beautiful, smart, energetic. She was kind hearted and brought a smile to everyone's face. She gave the best hugs. She was spunky, sweet and full of life. All of that taken away from her because we ran out of options. Now she is an angel.

Why the Promising Pathway Act is Important to our Family: The PPA is important because it will give our children a fighting chance, something that DIPG strips away from them instantly. DIPG is more commonly found in children. Children who do not have time to wait for a trial to be completed by a group of people that this disease is not as common with – adults. Families like mine would jump on the opportunity to try new treatments in a heartbeat. What has been tried in the past is not working. The PPA has the power to change that. The PPA gives us options. Options that our children are literally dying to have. What do we have to lose? Our children? We are already losing them, so why not try to fix that?

Heidi & Anthony Varns

Mother of Addison



LAUREN HILL

Lawrenceburg, IN

Lauren was diagnosed on November 20, 2013, and life as I knew it and imagined it would be, was forever changed that afternoon. Lauren was diagnosed with an inoperable terminal pediatric form of brain cancer located in the pons called DIPG. She battled for 16 1/2 months before her brain hemorrhaged and it took her life.

She was beautiful, smart, funny and gave the best hug. She was a scholar, an Honor Society Student with a love of sports, mostly basketball and soccer. She was a beacon of love and hope to her family, friends and other DIPG families. In 2014 the NCAA allowed her college basketball team in Ohio at Mount Saint Joseph University in Cincinnati, Ohio to be moved up in order for her to be able to live out her dream to play to play a collegiate level basketball game before her body gave out on her due to tumor progression and further complications from the tumor.

Her story caught a national platform and was covered by ESPN and a multitude of other media outlets. She believed her life's purpose was to serve as an ambassador for the DIPG community and to let everyone know the current treatments and research was absolutely unacceptable. As an intelligent young adult, she asked so many hard questions that as a parent and medical staff should not have had to answer. She had to know all the details, all the faults in the research system and understood the odds. Yet she gave every interview asked by news outlets and even went live on The View in 2015 to tell the story only DIPG Families knew. She was holding good on awareness and being a voice for all the little kids that had to go through and feel what she was feeling in her body. Lauren received numerous Courage awards from Indiana, Ohio, Kentucky, Pat Summitt personally delivered her courage award. President Obama even wrote her a note. Postmortem she won a 2015 ESPY, was entered into the Indiana Basketball Hall of Fame as well as the NCAA Women's Basketball Hall of Fame in Tennessee and countless other awards. Her awards now displayed at our local high school to remind students to Never Give Up on your dreams and to keep fighting for what you believe in.

She spoke not for herself, but for all the small kids that did not have the words or understanding of the severity of the situation. She raised $1.4 million in research funds in just 6 months before she passed.

If we had better treatments and medication that would have allowed her to live, who knows what platform she would be using now to make a difference in pediatric cancer. She may have even been working with all today, to give kids and families a chance at more life.

Why the Promising Pathway Act is Important to our Family: Imagine for a moment your child has DIPG or another terminal cancer with the odds of 99% that your child will pass away before 2 years and a median life span 9-12 months. You will watch them swell up on steroids, mentally and physically change as they lose body functions and their independence all unknown the hand you will be further delt, depending on what the tumor decided to turn off as it grows with nothing to stop it. These kids are knowing and trapped in their deteriorating bodies. As a parent we help fix things, our job to keep them alive and thriving to their fullest potential.

You will feel Hopeless, Helpless and that you are failing your child. There were hardly any new drugs to try. You would be desperate for anything with a chance. I was desperate..... Lauren was desperate to try anything new. She wanted to go down fighting and she wanted to win more life that DIPG was being robbing of.

In the weeks before her death at Cincinnati Childrens Hospital Medical Center. Nurses would come into the room and ask us multiple times a day if we needed anything else. One night, I dared to answer what was on my heart every time they asked. The only thing that I NEEDED or wanted was for anyone to go to the research building and use whatever they had on Lauren. I NEEDED to try anything and everything to save my child. I would have stollen it myself if I knew what I was doing.

I write this with tears in my eyes, feeling like I failed my daughter. WE FAIL OUR CHILDREN and that includes the government and the red tape that prevents families from having a chance. Why do they have to wait to get drugs that could possibly prolong or even save their life? Why do they have to wait for a chance to live just because they are smaller humans? This is totally unacceptable for our future productive citizens of our great nation. I don't want another family to feel the lifetime sentence of grief and pain of watching their child suffer, die, and bury them. You will never be the same again.

Promising Pathways Act absolutely needs to move forward, together we could make it possible to try the latest and greatest drugs and not the ones from years past that have proven to do nothing. Parents need choices! The end game is the same. At least we can go down fighting to our fullest potential. Please strongly consider helping these families that are in a desperate medical situation. In my ESPY speech, I pleaded for people to help change the outcome now. Do not sit on the sidelines and do nothing. You never know, one day, when it will touch someone, you love, and you wished you had opportunities of current and better treatments. To see video of Lauren herself visit: LaurensFightForCure.org/About

Lisa Hill-Fenstermaker

Mother of Lauren

[redacted]

My name is Donna Tennant. I am 59 and live in Jasper IN.
There are many drawbacks to having ALS.
I have worked since the age of 12. When a local company I worked at for many years had to make cuts, I survived several times to keep my job, but unfortunately it caught up with me. After having a very successful career, I had no job. My husband and I were in dire straits financially, and to find out I had to have a major surgery. Shortly after returning home, my mother in law passed away. We had to move our handicapped father to our home. I provided care for him and my husband with multiple seizure disorders. After my father in law's passing, I searched for work during COVID. I decided to change my career to become a pharmacy tech, and I did just that. After many falls and difficulties in speech, and every medical test known I was sent to the Cleveland Clinic. On day 2 January 6, 2023 I was told I have an aggressive form of A L S.
Yet again in a position of being with out a pay check. And to make matters worse in our Country you cannot draw Social Security disability/ for all the years I've paid in. Using the clause you didn't work outside of the home for 5 of the last 10 years and you don't qualify. I'll be dead by the time I can qualify.
This is wrong!!!!
We with terminal illnesses, should have access to funds if they paid in for years.
I've worked ever day of my life in this very town of jasper. It's my home. Please please send help quickly .
I also believe the passage of the " Promising pathways Act" is essential for individuals with ALS and other terminal illnesses so they have access to experimental treatments to increase their lifespan, and possibly even eradicate these horrible diseases.

Kind Regards,
Donna Tennant
812/630

[redacted]

Dear Senator Braun,
I have a rare disease story , for your consideration.

I'm from the Blue Ridge Mountains of Virginia. I graduated from Virginia Tech, and I would have stayed in Virginia, but the only job offer I got, was from Cummins. I thought I would stay for a couple of years, which turned into 20. They were very accommodating as my disease progressed, but eventually it got too hard to communicate, and I had to take disability.

I was diagnosed in November 2017, when I was only 37, so I have outlived the average of 5 years from diagnosis until death.

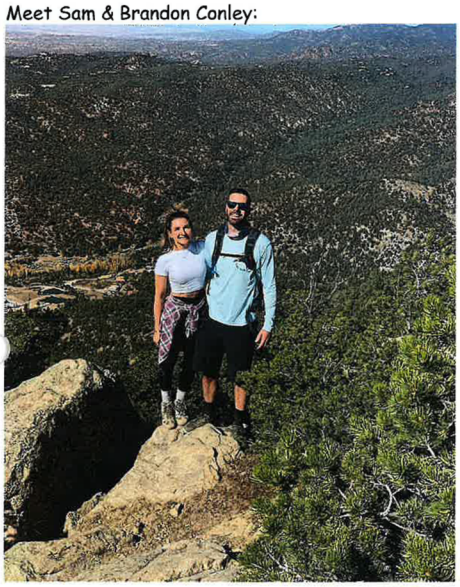
The progression of the disease has turned my life, and my family's life upside down. I have my wife, Erin, and two teenage boys, and the amount of time they spend caring for me is unbelievable. I have lost the ability to sing and speak. I have no use of my arms or legs. I type with my eyes, and that's the only way I can communicate. I have a feeding tube that goes directly into my stomach, so I don't aspirate food trying to swallow it. I breathe by way of a ventilator. Our house is a pig sty, because I can't help clean and the rest of the family is too exhausted from caring for me.

\nd then there's our little surprise, Joel, who is two and a half years old. I'm hoping that I live long enough for him to remember me. Or maybe it would be better if he didn't. These are the kind of horrible decisions that ALS causes me to have to make.

Thank you for listening to my story.
Mike Mattern, Columbus, Indiana

[redacted]

Meet Sam & Brandon Conley:



Hello, It's ironic that the Aging Committee is the entity that we were requested to write regarding ALS. Meet Sam & Brandon, ages 31 and 36. They are not the senior adult that comes to mind when speaking of ALS. My daughter, Sam, married the man of her dreams on October 27, 2021, with the knowledge that Brandon has ALS and that he was already two years into a disease that doctors say gives you 3-5 years to live. Though she knew he had the disease, neither of them could know how hard living with this disease would be and that no medical treatment is available.

Sam and Brandon met in 2019 and were a very active couple that enjoyed everything about the outdoors in Colorado. Brandon introduced Sam to climbing 14-ers. These are mountains that

soar 14,000 feet above sea level. Not easy to do and one must be in top physical condition. They skied, hiked, camped until they couldn't because of the disease. Brandon was a successful sales rep and Sam a social worker whose clients were homeless people in Denver.

ALS has progressed to the point where Sam and Brandon sold their Evergreen, Colorado, home and moved back to Indiana. They live across the street from Brandon's parents. They have engaged Hospice to help with the special equipment and services Hospice provides to the terminally ill. Sam had to resign her position in Denver to care for Brandon. Brandon had to resign from his successful career on disability.

The Promising Pathway Act is necessary NOW. ALS patients have no cure, treatment, or hope. When the FDA stands in the way of quickly approving treatments, people get beyond help and hope and they die a horrible death. Their family members suffer greatly watching them suffer. We should be able to do better for these patients and their families. **THE ALS COMMUNITY NEEDS HELP FOR INCREASED ACCESS TO PROMISING TREATMENTS AND NEW THERAPIES IN A TIMELY MANNER.**

Respectfully,

Sherry Felice Panetti

[redacted]

In March of 2014 I started slurring my words.my doctor sent for a brain mri but nothing showed up. So no stroke. I found a neurologist I liked. He ran several tests on me but he couldn't figure it
Out so he sent me to IU neurology in Indianapolis , Indiana. I have been going there ever since . After I had been there for two or three appointments I started having trouble walking and falling. I went from a cane to rollAtor walker and then a wheel chair. I now have a an electric wheel chair. I was diagnosed with a form of ALS in sept 2016. It is a less aggressive form of ALS called PLS. I live longer but the outcome is still the same. Any form of ALS is expensive . You need a lot of equipment for this disease. I am now in a nursing home. I am in here because I lost my home caregiver and I couldn't find a replacement . God has been with me the whole way and I know He will see me thru it.

Sent from Yahoo Mail for iPhone

[redacted]

Our home includes 2 people who suffer from rare diseases.

I'm a medically retired flight paramedic/RN who was diagnosed with Amyotrophic Lateral Sclerosis (ALS/Lou Gehrig's Disease) in 2005. My progression has been exceptionally slow, given that the typical survival from diagnosis to death with ALS is 2-5 years! I gave up a career that I loved and lost a middle class income when I was diagnosed (I continued to fly and work in the emergency department for a year after my diagnosis, until my condition deteriorated to the point where I could no longer meet the physical demands the job entailed). The cost of my disease in terms of just lost wages is staggering...not to mention the equipment and home and vehicle modifications that are needed for me to live a semi-normal life!

My three adult childrem have Fragile X Syndrome. Fragile X (FXS) is the most common inherited form of developmental/intellectual disability and is a leading genetic cause of autism. My daughter is able to live independently, although she is unable to drive. My sons need 24/7 care and supervision.

The common thread in our stories is that there is no real treatment and no cure for either ALS or FXS. Both Fragile X and ALS research is underfunded. There are promising therapies in the pipeline for both disorders, but without continued funding we will continue to languish.

Thank you for considering our story when considering support for the Promising Pathway Act.

Claudia Burrows
Muncie, IN

[redacted]

Thank you, Senator Braun, for your attention to the people who are struggling to live with serious, rare, progressive disease.

Diagnosed with ALS at 31 years old with two young daughters just 2 & 6 years old, I am one of the lucky few who, after 25 years, is still living with this incurable disease. Lou Gehrig was diagnosed in 1939, and there is still no cure and no effective treatment. I am lucky because even though I can't use my arms or legs, and need a machine to help me breathe, I'm still here to see my daughters live their lives. I can help spread awareness of the fact that many, many people are living with serious illness and it affects everyone, not just the person who is ill. We could use a little, or A LOT, of help!

Amie Thornburg
Spiceland, Indiana
diagnosed with ALS in 1998

Terry M. | Indiana

Age: 60
Year of Diagnosis: 2017
Type: Limb Onset

We Can't Wait

Totally agree. Just want the chance, **I'm going to die anyway, why can't I just have a chance to try?**

It's for me to decide. I decided I would try any and all therapies. Just give me the chance. Don't let me die waiting.

I'm am going to die anyway, I don't care if FDA had approved or not. Give me the chance to try.

It's monstrous for me and my family. No human being should have to suffer like this.

It had taken its toll on my immediate family. We are all exhausted, frustrated and just trying to get through each day. There is no time for enjoyment or tender moments.

It's ALS 24/7, no breaks for anyone involved. You and your family just endure suffering until you die. **There is absolutely NO HOPE.**

Give me a chance to try anything I want, it's my life. I have a disease that's 100 percent fatal. If ALS was contagious like COVID I know there would already be a cure.

Ron B. | Indiana



Age: 64
Year of Diagnosis: 2019
Type: Limb Onset

It is important to receive any medication possible to help provide us with better lives.

This is devastating and horrible.

I am devastated. My family is devastated.

Everyone is different but we need to find a cure.

Kent D. | Indiana

Age: 58
Year of Diagnosis: 2014
Type: Bulbar Onset

We Can't Wait

Anything that gives hope is worth it!

Anything is better then nothing

As long as it can't do more damage, I'm willing to try anything.

Still run a company but cannot communicate, tire easy, in a powerchair, can't play with grandchildren

Taken a toll on them, while I'm blessed to be able to do some things, always dependent on family and friends around me

Very little trials available and not enough money going into research. **One of few diseases since 1939 that really made no significant progress in slowing down**

People are praying for a breakthrough, in a cure, therapy or something to significantly slow this disease down. Don't you?

You will feel Hopeless, Helpless and that you are failing your child. There were hardly any new drugs to try. You would be desperate for anything with a chance. I was desperate..... Lauren was desperate to try anything new. She wanted to go down fighting and she wanted to win more life that DIPG was being robbing of.

In the weeks before her death at Cincinnati Childrens Hospital Medical Center. Nurses would come into the room and ask us multiple times a day if we needed anything else. One night, I dared to answer what was on my heart every time they asked. The only thing that I NEEDED or wanted was for anyone to go to the research building and use whatever they had on Lauren. I NEEDED to try anything and everything to save my child. I would have stollen it myself if I knew what I was doing.

I write this with tears in my eyes, feeling like I failed my daughter. WE FAIL OUR CHILDREN and that includes the government and the red tape that prevents families from having a chance. Why do they have to wait to get drugs that could possibly prolong or even save their life? Why do they have to wait for a chance to live just because they are smaller humans? This is totally unacceptable for our future productive citizens of our great nation. I don't want another family to feel the lifetime sentence of grief and pain of watching their child suffer, die, and bury them. You will never be the same again.

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Parents need choices! The end game is the same. At least we can go down fighting to our fullest potential.

Please strongly consider helping these families that are in a desperate medical situation.

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To see video of Lauren herself visit: LaurensFightForCure.org/About

Lisa Hill-Fenstermaker
Lauren's Mom
Co-founder of Lauren's Fight for Cure
1462 Fairway Drive, Lawrenceburg, IN 47025
(513) 652-1158
SE INDIANA Chapter of The Cure Starts Now

Promising Pathways Act and The Impact on Families

Your Full Name: Lisa Hill-Fenstermaker
Your City and State: Lawrenceburg, Indiana and Greater Cincinnati, Ohio Tri-State area
Your Child's Name: LAUREN E. HILL. Passed 4/10/2015, Forever 19 years old

Your Story:

Lauren was diagnosed on November 20, 2013, and life as I knew it and imagined it would be, was forever changed that afternoon. Lauren was diagnosed with an inoperable terminal pediatric form of brain cancer located in the pons called DIPG. She battled for 16 1/2 months before her brain hemorrhaged and it took her life.

She was beautiful, smart, funny and gave the best hug. She was a scholar, an Honor Society Student with a love of sports, mostly basketball and soccer. She was a beacon of love and hope to her family, friends and other DIPG families. In 2014 the NCAA allowed her college basketball team in Ohio at Mount Saint Joseph University in Cincinnati, Ohio to be moved up in order for her to be able to live out her dream to play to play a collegiate level basketball game before her body gave out on her due to tumor progression and further complications from the tumor.

Her story caught a national platform and was covered by ESPN and a multitude of other media outlets. She believed her life's purpose was to serve as an ambassador for the DIPG community and to let everyone know the current treatments and research was absolutely unacceptable. As an intelligent young adult, she asked so many hard questions that as a parent and medical staff should not have had to answer. She had to know all the details, all the faults in the research system and understood the odds. Yet she gave every interview asked by news outlets and even went live on The View in 2015 to tell the story only DIPG Families knew. She was holding good on awareness and being a voice for all the little kids that had to go through and feel what she was feeling in her body.

Lauren received numerous Courage awards from Indiana, Ohio, Kentucky, Pat Summitt personally delivered her courage award. President Obama even wrote her a note. Postmortem she won a 2015 ESPY, was entered into the Indiana Basketball Hall of Fame as well as the NCAA Women's Basketball Hall of Fame in Tennessee and countless other awards. Her awards now displayed at our local high school to remind students to Never Give Up on your dreams and to keep fighting for what you believe in.

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If we had better treatments and medication that would have allowed her to live, who knows what platform she would be using now to make a difference in pediatric cancer. She may have even been working with all today, to give kids and families a chance at more life.

Why the Promising Pathway Act is important to you:

Imagine for a moment your child has DIPG or another terminal cancer with the odds of 99% that your child will pass away before 2 years and a median life span 9-12 months. You will watch them swell up on steroids, mentally and physically change as they lose body functions and their independence all unknown the hand you will be further delt, depending on what the tumor decided to turn off as it grows with nothing to stop it. These kids are knowing and trapped in their deteriorating bodies.

As a parent we help fix things, our job to keep them alive and thriving to their fullest potential.

Larry P. | Indiana



Age: 62
Year of Diagnosis: 2020
Type: Limb Onset, Sporadic

I'm not interested in extending this living hell on earth. I need a treatment that leads to curing it or at least controlling it.

I'm only interested in a treatment that leads to curing it or at least controlling it.

Not important whatsoever, if the new drug puts me in a position to be cured.

ALS has and is destroying what used to be our happy little family in our happy little home on a big hill on 15 acres way out in the beautiful country. We are devastated. I feel more sorry for my wife and daughter than I do for myself. Not only do I suffer physically, but mentally too while I watch them. I feel like I'm stranded on the planet Mars, all alone and slowly dying by a thousand paper cuts while strapped in a chair in front of a mirror with my eyelids propped open with toothpicks.

My 19-year-old daughter can't hardly process it. It's like she pretends it's not happening. My wife is being destroyed, one day at a time. I'm quite sure all three of us need therapy.

That it can strike ANYONE at ANYTIME.

Please help us. Please...

[redacted]

Tiffini Allen
Indianapolis, IN
Barth syndrome

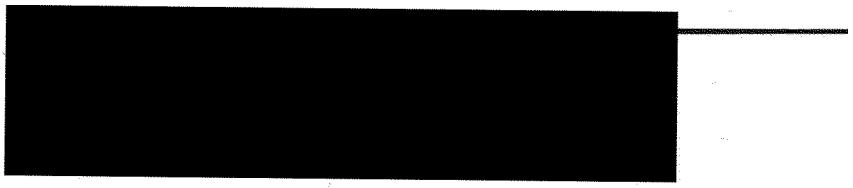
My son was 18 months old when he was diagnosed with Barth syndrome, a rare genetic disorder that greatly affects his day to day life. Since the day he was born he starts each day by taking many medications and supplements, and ends each day with even more medications and supplements. Due to a weakened heart and low muscle tone he struggles to keep up with his peers. He is now in high school, and is unable to walk long distances and must take frequent breaks to even walk a short distance. When he gets a fever we make a trip to the ER which usually leads to a couple of days in the hospital due to his compromised immune system.

Therapies for all kids with Barth syndrome and other ultra rare conditions are greatly needed. Access to these therapies is imperative and can dramatically change my son's life, as well as others... lives can be saved with these therapies.

Thanks,
Tiffini

Tiffini R. Allen
City Dweller Photography, LLC | pets & their humans
Stutz Business and Arts Center
212 W 10th St, Studio A-350
Indianapolis, IN 46202
317.345.7335 | tiffiniallen@gmail.com
www.citydwellerphotography.com

Thank you to our 2024 Dogs for Riley pack who raised over $16,000 for the kids at Riley!



"The Polen Family wholeheartedly support the Promising Pathway Act and commend Corey for his tireless efforts in shaping this vital legislation. The PPA is a significant step forward in empowering individuals providing opportunities to fight for their lives and to secure access to safe, promising therapies. We are proud to #StandForCorey in championing this important cause."

Corey Polen – Brownsburg, Indiana

Diagnosed with ALS at 40.

Battled ALS for 7 years.

Passed from ALS on February 11, 2023 at age 47.

Corey worked tirelessly as an advocate for the Promising Pathway Act. These are a few of his thoughts, written with his Eyegaze February 23, 2022

I have spoken to several offices over the past 3 years with regards to the Promising Pathway Act. I am very grateful for Senator Braun for championing this bill on behalf on myself and my dying friends

People impacted by ALS or the 7,000+ other rare diseases are not isolated to a political party. We are just Americans like you, but we suffer from the lack of meaningful treatments.

Almost all rare diseases and neurological diseases are not allowed to utilize the Accelerated Approval pathway because we simply don't have enough patients or science can't identify a biomarker for us. This excludes us from the very pathway the FDA has to expedite treatments to those dying with nothing meaningful to try. I am very familiar with Right to Try and Expanded Access. However, these are elusive for ALS.

I will however provide first-hand account. I was denied over 20 times through RTT. However, I was able to gain EAP to a treatment. Yeah, success you may say. I spent 684 days battling the FDA for approval of EAP. During those 684 days I quickly lost the ability to walk, hug my family, feed myself, go to the restroom, even breathe on my own or swallow. The FDA denied my EAP numerous times.

What concerns me the most and I hope you too, are the treatments that do work for patients yet we can't access them. Before ALS, I worked 20 years for Milliman providing healthcare consultancy. I built solutions for private insurers, Medicare, Medicaid, PBMs, and pharmaceuticals. I've become accustomed to viewing problems from different points of view and building solutions that benefited everyone. That was exactly my approach, helping build the Promising Pathway Act. This bill fills the community need, doesn't jeopardize science, and honestly provides the FDA with better tools. It's a win for patients, science, FDA, pharma, insurers, and Congress.

Time is of the essence for ALS patients as you can tell from what I lost playing by the current rules. We can no longer afford to kick this can down the road. You have the power to act now. My life and 30,000 lives of ALS patients like me are counting on you to resolve this now.

Kind regards,
Corey Polen



REID GLEESON

Davenport, IA

Reid was 27 months when he began having vomiting episodes and difficulty with balance. After a few weeks and multiple visits to doctors and a local ER trip, we ended up taking him to Iowa City. Our lives forever changed that day, August 26, 2017 when we heard those terrible words, "Your child has cancer". Reid had a large tumor located in the back of his brain and small tumors along his spine. He had emergency surgery due to hydrocephalus and two days later he had another brain surgery to remove the large tumor located in his cerebellum. We found out his cancer was called Medulloblastoma and began learning all of the things we needed to know to help Reid attack this terrible disease. Surgery was very successful, and Reid was back to walking, talking and eating within a few days. It was incredible. However, this was just the beginning of his journey. Reid then had surgery to place a hickman line and began 6 months of aggressive inpatient chemotherapy which included 3 bone marrow transplants. Brain cancers require very high doses of chemotherapy in order to pass the blood/brain barrier; so extra caution must always be in place for these kids. Reid's chemo cycles included a week-long stay for chemotherapy, home for a few days before developing a fever due to his white blood counts being so low, and back to living in the hospital for blood transfusions, platelet transfusions, and IV antibiotics until his counts recovered. During his bone marrow transplant rounds, Reid received even higher doses of chemotherapy and he was unable to leave floor 11 of the hospital due to fear of infection.

It was a long 6 months and these chemos were so tough, but our Reid was tougher. We were constantly chasing him around with an IV pole while he was dribbling basketballs, golfing, bowling, and playing volleyball in the hallway. No time for naps or complaining. Reid always had things to do. He loved exploring the hospital and checking out all of the garbage and recycling cans. He spent many Saturdays on floor 12 watching the Hawkeye games and participating in the wave. Reid loved to look out at the football field, but he really loved to point out all of the green and yellow garbage cans and the purple

port-a-potties around the stadium. He was a garbageman at heart. Reid soared through his treatments without a hiccup, and by March 2018 we were safe at home hoping everything was behind us. It was time to end the story and get our lives back to normal. Just 3 months later Reid began having difficulty walking. We had a scan done and were told he had relapsed all along his brain and spine. It was absolutely devastating, and our only hope for curing him was through radiation. Reid endured 6 weeks of daily anesthesia and radiation at Mayo in Rochester. He handled it like a champ and by the end was back to running and playing like his old self. We were so amazed at his determination and motivation. We then began another 6 month chemo regimen through St. Jude in collaboration with Iowa, and were hopeful that it would clear the rest of his disease. Reid finished his chemo in March of 2019 and was declared NED, no evidence of disease. We were thrilled! However, the very next day we got a call telling us that the radiologist had found a new spot on his optic nerve suspicious for disease. How many times could this happen to our sweet Reid? We kept an eye on Reid and 3 weeks later did another scan and were told that the spot had grown. Our sweet Reid had relapsed for a second time and options were running low. Over the next year Reid endured three different chemo regimens in hopes to keep his disease at bay. We chose lower doses of chemo to keep his quality of life high. We did not want Reid spending his nights in the hospital anymore. Reid did outpatient chemo and he was able to attend four year old preschool, visit Disney 3 times, and make many trips to parks, pools, trampoline parks, bowling alleys, and spend quality time with his family. He was a normal four year old enjoying his life despite many trips to "hotel hospital" for treatment.

In February 2020, following an awesome family Disney trip, Reid got sick and was in the hospital for almost 3 weeks dealing with fevers and seizures. On top of that, we had found out that his disease was progressing. We started a new oral chemo in the hospital but were told it would be a miracle if it did anything. We brought him home in the middle of March and were told he may only have days left with us. Well guess what? The chemo worked. We got 7 more months with our Reid. He made it to his 5th birthday in May, he was there when his baby brother was born in June, and he spent an extra 4 months with us making memories as a family. Our sweet Reid became an Angel October 13, 2020, and although we are devastated, we know he is now healed.

Why the Promising Pathway Act is Important to our Family: The Promising Pathway Act is something I wish would have been available to us three years ago when we needed it. We waited over four months to get a drug approved for Reid to trial on compassionate use. It was incredibly frustrating and agonzing for us as a family to have to sit and wait for a potentially life-saving drug. Our family was fortunate that we had another option, reradiation, while we waited for the drug to become available, otherwise he would have died waiting and we would have always wondered if this drug would have worked for him. If it could have saved him. Families dealing with relapsed cancers and brain tumors do not have time to wait. Brain tumors kill kids and they do it quickly. The Promising Pathway Act is an absolute step in the right direction for trialing drugs, and giving kids and their parents a hope for a future. In addition to getting these drugs approved more quickly, there may be answers for other kids fighting cancer! Please approve the Promising Pathway Act. Children with relapsed brain cancer have so few options, and passing of this act would provide them with so many more options to give them time, and will hopefully, lead to more cures for kids fighting these terrible cancers.

Megan Gleeson

Mother of Reid

Lesley K. | Iowa



Age: 58
Year of Diagnosis: 2018
Type: Limb Onset, Sporadic

It is very important to me. Every day is important and means more time with my family and friends.

Any chance of a new treatment is worth the risk. I have done several clinical trials and would like to participate in more.

It is not important to me at all to wait for FDA approval. We don't have a lot of time. I'm willing to take the risk.

I've gone from being a healthy active fitness instructor to needing a walker to walk. **I can't lift my grandkids. It has impacted every aspect of my life.**

My husband is impacted the most. I can't help him with our farming operation, he has to help with daily household chores. He has had to make changes to our home to help me function more easily. My kids and grandkids are impacted as well.

That anyone can get it, there is no cure. I didn't do anything to make me get ALS. I can't help that I'm tired all the time and I am getting weaker and slower.

I don't have a lot of time. I will decide for myself if a drug is worth the risk. Give me that chance.

Mike W. | Iowa

Age: 67
Year of Diagnosis:
Type:

We Can't Wait

If I were given any hope in slowing down the progression of this disease would truly be a blessing. It would depend on the condition the patient at the time the therapy was offered.

It's hard to answer that question not being in that situation. I would probably opt out unless there was a good chance, I would see some improvement.

Every drug on the market has its side effects. If I was given a chance on a drug that offered a good chance of reversing the effects ALS had given me, I would take the drug.

I witnessed my cousin live nearly two years with ALS. More research needs to be done to rid this terrible disease.

Norene B. | Iowa

Age: 64
Year of Diagnosis:
Type:

We Can't Wait

Very important to be giving ALS patients hope and more time to live is vital!

People with ALS know that the disease is terminal. They deserve to have every chance to extend their lives, especially if they choose to do so despite possible side effects or no effect.

The family of a person with ALS is highly impacted. The spouse and children see their loved one lose mobility and the ability to live a normal life, which is very traumatic.

People with ALS are willing to do most anything that they can to be able to live longer.

Because ALS is basically a death sentence, ALS patients should be able to have any and all treatments that could work to extend their lives. They should be allowed to try treatments that may not be fully tested or may have side effects because that is their only hope. I'm sure that they would be willing to sign a liability waiver in order to receive experimental treatments.

Manuel L. | Iowa

Age: 68
Year of Diagnosis: 2017
Type: Limb Onset; Sporadic



Click Here to Play Video

Will try anything. Been on Radicava for 3 1/2 years, and it was supposed to give me a couple months until something else came along. Well, it's here, give it to me.

I'll take that chance

Or important I took Radicava before trials were done

Horribly, just retired and found out

My wife had to quit her job and become my caretaker

It is a death sentence.

Give us a chance.

[redacted]

We are the Brody Family from Glidden, IA. My name is Tracy and my husband's name is D.W. Our son Bly is 19 years old and has Barth syndrome. We also have a daughter Willow (11) and a 9 year old son, Ty, who also has Barth syndrome.

When Bly was nearly 2 years old we found out that he has a rare disease called Barth syndrome. With Bly's diagnosis, we were able to more easily diagnose his younger brother Ty with Barth syndrome when he was born.

Bly has spent weeks in the hospital in heart failure as both an infant and a teenager.

Both boys struggled in different ways with eating and growing and Ty needed to have a g-tube placed as a toddler.

Ty has always been delayed. He was able to walk independently just before he was 4 years old and he didn't start using simple sentences until he was seven years old. One of his biggest struggles now is still his speech.

Both boys require heart meds and injections to strengthen their immune system.

Worries of falling due to weakness and fatigue is often a concern.

Headaches and body aches are also regular symptoms for the boys.

Having treatment for Barth syndrome is extremely important. Neither of our boys were part of this drug trial, but with the possibility of having elamipretide as treatment for Bly and Ty it could be life changing for them. It already is for many others.

Elamipretide could help in all these areas of concern and struggle. Please help us in our efforts to hold the FDA accountable for fair and equitable review of this drug for Barth syndrome and for all rare disease communities to be heard even though our numbers are small. We need you. Our boys' could depend on it, along with many others.

Thank you for your time and help!

Tracy Brody

Sent from my iPhone

[redacted]

Mitze Klingenberg AdComm PP.pptx

Dear Senate Committee on Aging,

My son has ALS - he is dying every day. I ask my friends who lost children suddenly what is worse? All of a sudden or a little bit every day.
There is no answer.

Changing ALS from 100% fatal to treatable requires urgency and flexibility by allowing a new time-limited approval pathway giving timely access to promising treatments for 100 percent fatal diseases like ALS. We can't wait a decade or longer for the FDA approval process when the average lifespan of an ALS patient is only 2-3 years. ALS has been uniformly progressive and fatal since the first reported case in 1869. ALS IS NOT RARE and is rapidly becoming more common. **We need the Promising Pathway Act to bring hope for effective treatments and cures in our / your lifetime.**

The **Promising Pathway Act** provides a pathway for provisional FDA drug APPROVAL for life threatening / terminal illnesses **(including future pandemics)** that have no meaningful treatment. **This approval needs renewal by the FDA every 2 years**.

ALS faces tremendous scientific hurdles to overcome in the currently available FDA approval pathways. These will further delay effective treatments if you don't pass the Promising Pathway Act. Most treatments approved by the FDA have thousands of trial participants and have very clear outcome measures which can easily detect efficacy. Our trials are small because people with ALS die so quickly leaving a small LIVING population at any given time. The outcome measure used for the trials is an extremely flawed questionnaire with 12 activity questions to measure disease progression. The disease is heterogeneous with significant clinical and biological variability. These reasons make it exceedingly difficult to show efficacy in a traditional ALS trial even for effective treatments.

The FDA does not have a Center of Excellence for neurodegenerative diseases like it has for oncology to allow agility and flexibility in trial design, evolving improved efficacy measures, and evaluating accelerated approvals of treatments that show safety and early signs of efficacy.

The unmet medical need for people living with ALS is critical. This community needs access to promising treatments. **Please cosponsor and pass the Promising Pathway Act.**

Please watch the PowerPoint about our family's experience with a recent FDA AdComm.
Please watch this video montage of just a few ALS patients: Https://clipchamp.com/watch/zSKoXUh26FL

Thanks for your time.

Mira (Mitze) Klingenberg
207 Crestview Drive
Marcus, IA 51035
712-229-0871

Jerry M. | Kansas



Age: 66
Year of Diagnosis: 2020
Type: Bulbar Onset

We deserve the right to try promising treatments

I'm living with a death sentence. What do I have to lose? The "side effects" of ALS are not pretty. I don't want someone telling I can't get access to a treatment that could improve my quality of life. If you were dying of thirst and came a across a puddle of nasty looking water. Would you drink it to save your life not knowing for sure what it might do to you? I sure would and wife and kids and grandkids would want me to.

Not important at all to wait on FDA. Who are they to make life and death decisions for me. Don't take my hope away from me and my family. Right my chances of survival is 0%. **If a treatment would have a 10% chance of improving my condition, I want to take that chance and don't want someone telling what's good for me. I'm dying for heavens sake.**

What kind of question is this. Someone that asks that question, hasn't had it or had loved with it. My gawd yes, it's impacted my life. **I can't talk. I can't eat food. I can't walk unassisted. I can't get on the floor and play with my 2 yr. old granddaughter. I'm having to sell our home and move into a home that's more wheelchair accessible. I could go but hopefully you get the picture and I ccx sure hope you already know how it impacts one's life.**

My wife is my caregiver and her dreams of traveling in our retirement years. She has to wipe me and clean up after my accidents. She has to drive me everywhere. My 2 children are watching their father wither away.

The things I've just explained about how it affects the PALS and their loved ones. I was a once proud and independent man. I now have to look to others to do things for me. My wife has had to call the fire department twice to get me off the floor, after I had fallen.

Let us make the decisions about therapies. Stop holding us hostage and letting us die. This is AMERICA and THIS IS INHUMANE!



Greetings, my name is Paul. I was born second of six kids; parents nor siblings have any lung issues. The bronchiectasis was likely due to an untreated or misdiagnosed lung infection as a baby/child. Sickly as a baby and child growing up.... Mother always took me to clinics and doctors. The initial diagnosis was allergies. Even though I enjoyed my childhood days, there were annual and biannual hospital stays. Pneumonias mostly. A Pulmonologist (lung specialist) finally diagnosed me at age fourteen with bronchiectasis in 1973 which was the year I had my first lobectomy - lower left lobe removed mostly due to abscessed tissue. Second lobectomy in 1975 which removed partial right middle. Every lung infection I've ever had is unmistakable and exhibits the same symptoms: headache, fever, fatigue, dehydration, loss of appetite, increased pulse, congestion. I don't routinely sputum culture, but if there were a problem then I would. I respond well to broad spectrum antibiotics.

I continued to have lung infections after both surgeries. Because the bronchiectasis was diffuse (widespread). Since birth, I've actually had over 50 lung infections. Both lungs are heavily scarred. All throughout my teens and on into my forties, I remained active. I love to play sports and did so on every occasion possible. Participating in physical activity was my physical therapy. I never liked taking medications or bending over a board and coughing. I let "playing" do all that. And it did. I lived on a cul de sac with six other boys around my age and we were always doing something... football, softball, basketball, ping pong, riding go carts, biking, climbing trees, roller skating, tennis, volleyball, on and on and on. I haven't been hospitalized for an active infection since 1988. As mentioned earlier, I respond well to antibiotics. And to all treatments. After 50 something episodes (infections), you know what to do. But there's always something new to learn.

Up until 2005, I was always "wet". Meaning I had a productive cough all the time. And the secretions were always yellow. A week of intravenous antibiotics in the hospital would clear the color but after a week or two, the color returned and stayed. I didn't have an active infection, yellow was just the default color. I made four major changes in 2005... moved to Florida for a year, healthified my diet, starting taking a daily vitamin supplement and began using Advair. I moved back to Kentucky in 2006, and by that time I had "dried" out. I don't have that productive cough I used to have and the sputum is colorless. Up until 2006, I averaged two bronchiectasis episodes a year, since then, I average one or less a year. I'll never know if it was just one of those things that caused the change, a combination, or all of them.

I had a CT in 2001. I've also had three bronchoscopies. Other conditions I have are scoliosis and spinal stenosis. The curve in my back is at 51 degrees but it's not currently causing any issues. The problem is the narrowing of spinal fluid around my spine in the neck. That started over five years ago and is being treated with meloxicam to manage pain. The surgeon wants to do surgery as a last resort. I never married but do not attribute bronchiectasis to staying single. I've had a number of relationships but much prefer the single life - it suits me. I'm happier. I've had a good career at office work. The bronchiectasis of course has prevented me from pursuing certain professions. I realistically wouldn't be able to keep up with co-workers in physical type occupations. But I've been satisfied with my career choices. I lost some work days of course due to infections but never enough

to threaten my job. There were many days I'd go to work while enduring an infection. Not while it was raging, but at the beginning or at the end.

I have an Albuterol inhaler plus a nebulizer. The nebulizer is fairly new for me. The only medication I take daily is Breztri. My FEV1 of a pulmonary function test is on the low end. I averaged between 21 and 29 for the last ten years. But keep in mind I've had two hunks of lung removed. I've never let bronchiectasis interfere with my fun. I likes my fun. One example is travel. I've flown to England twice to meet up with other bronchiectasis patients. I do fidget a lot on the plane. Can't stand sitting that long. The only negative is sleep, I usually arrive jet lagged when I get there. I've also taken a cruise to the Bahamas and have traveled to a dozen States. All with no ill effects.

It's crucial to find and maintain a sense of normalcy while having a rare disease or condition. I'm aware there is a difference and a variance between health conditions which obtaining a level of normal may not be as possible for someone with a different condition. Making attempts at living a "close to normal" existence is a priority. I don't identify as my rare disease. Meaning, I just live. I always have it, but it doesn't always have me. By doing that, it provides me with perspectives I wouldn't have had otherwise.

The unmet medical need for bronchiectasis patients is prevention. The current strategy is to treat it with antibiotics. New medications and therapies are needed to prevent infections before they start.

Sincerely - Paul Borders
3107 Wayside Drive #27
Louisville, KY. 40216
502-448-1120

Nina W. | Kentucky



Age: 67
Year of Diagnosis: 2016
Type: Limb Onset

I would participate in such therapy if it was not a major inconvenience such as daily injections or travel requirements

I would definitely take an untested therapy if it possibly had no benefit at all. I would have to waive the benefit against their significant side effects if that were the case.

Not at all

Why would you ask that? It has completely ruined my life and taken away many of the things I value. Also, it's going to kill me.

Most of my family and children feel helpless and sad. My husband who is my caretaker is depressed and completely worn out.

That it's a horrible disease and there is no cure

Hossein O. | Kentucky



Age: 70
Year of Diagnosis: 2016
Type: Limb Onset, Sporadic

Very important especially young pals with young spouse and children. It's empowering to most pals to know that they are doing something to fight back and not give up.

ALS is 100% fatal is not just a slogan for fundraising. Most pals are willing to take a chance with side effects and more complications just to have a chance specially if some of phase 3 trials show some benefits like NurOwn.

Totally unimportant. **By the time a drug is approved by the FDA, I would long be dead and buried.** I rather have access to AM0035 and NurOwn NOW while still here to potentially benefit from. How many drugs have been approved by the FDA in the last 50 years for treating ALS?

I no longer have a longer view of living my life. **I can only think of living on day at a time.** Working with my arms is challenging. Bathing and dressing is hard without assistance. I used to run long distances but I can't even run 200' due to weakened neck and upper body. I can't do routine home maintenance, cook and help my spouse with chores.

I have an amazing wife/CALS. Very mature individual. I am still enjoying an FRA-R of 35 but she still ends up doing most of the work around house and when traveling. Intimacy is a challenge. Our kids are grown and so far have managed life without their help.

I am not concerned with people's understanding of ALS. What can they do with a better understanding of ALS when the providers, insurance companies fail addressing our needs? FDA, Congress, ALSA lobbying efforts, all fall short.

Find ways to remove the obstacles so the RTT act can be better utilized to make promising drugs more accessible. Addressing the funding shortfalls that prevents pals to seek treatment specially if drugs not yet approved.

Craig K. | Kentucky (1 of 2 pages)



Age: 56
Year of Diagnosis: 2019
Type: Bulbar Onset

I believe it is extremely important to explore every avenue that may help slow the progression of ALS. Adding a few months to a person's life expectancy may not seem like a significant amount of time from the perspective of a healthy person who potentially has a long life ahead of them. However, from the eyes of a person with ALS whose life expectancy is only a few years, those few added months are equivalent to adding years to another person's life. In more personal terms it means more time with loved ones and participating in life's joys such as being there when a son graduates high school, or a daughter gets married or the birth of the first grandchild. The added months shouldn't be looked at in a dry statistical manner. It needs to be viewed from the eyes of the person with ALS and their family. **A few more months are a few more joyful memories.**

In my opinion those who have been diagnosed with ALS know what their outcome will be so if a therapy has no benefit all they've lost is the time they've put in. **The bigger question is the potential significant side effects. Everyone would have to weigh the choice of modest benefit with side effects versus not trying the therapy and knowing they wouldn't reap any benefit.** It is a hard choice however I would hope enough ALS sufferers would participate in new therapy research even if there are side effects so that medical advances can be made that could help others with ALS down the road.

Certainly, it is extremely important that any new drug or therapy go through a stringent clinical trial process and equally stringent FDA approval. However, the issue with ALS is somewhat unique. Because ALS is rare there are very few people worldwide who can participate in the clinical trial process. In addition, the overall clinical trial process, including the time spent perform non-human clinical trials before it can be tested on humans, can take years. People with ALS don't years. 80 percent die within 5 years of diagnosis. Consequently, those with ALS who are accepted in a clinical trial could potentially pass away before the clinical trial is completed. I believe that if a promising drug or therapy has shown to be safe and effective in clinical trials then the **FDA should take a hard look at allowing people with ALS to take that drug even though it is not fully approved yet. Consider the recent example of emergency FDA approval for the COVID vaccines. These vaccines have helped hundreds of millions of Americans. If the FDA can issue emergency approval for vaccines, it should consider that same strategy for other beneficial drugs and therapies that are critical to a person's health and longevity.**

Craig K. | Kentucky (2 of 2 pages)



Age: 56
Year of Diagnosis: 2019
Type: Bulbar Onset

From the time I was diagnosed with ALS in the fall of 2019 until now my life and the life of my family has been completely turned upside down. At the time of diagnosis, I was working full time with a wife and three school age children to support. Because of my deteriorating health we had to make some immediate hard decisions. First, I had to stabilize my rapid decline. This required the help of a number of wonderful specialists. At the same time, we had to plan an early retirement because it quickly got to the point where I couldn't physically work anymore. That was difficult considering I was not planning to retire for another 15 years after putting my kids through college. **My wife and I spent many nights quickly making one major life choice after another. We included the kids in on many of these conversations because their lives were being drastically impacted as well. Ultimately it meant we had to sell our home and move to another home that fit our new budget in another state.** It was extremely difficult to leave behind dozens of family and friends. As you can imagine this caused a severe emotional strain for our family and our marriage. We are still adjusting to our 'new normal' but hopefully we've put the worst of this traumatic situation behind us.

First there was the shock we all go through when a traumatic event affects our lives. Then there was the anger. Each family member and friend handled it in their own way. Ultimately everyone has been very supportive and rallied around us. However, the first year from the fall of 2019 to the fall of 2020 was the most difficult. My chief concern was how my kids would adjust. It was very hard for them over that first year. Emotions ran high and were all over the board. All we as parents could do was be supportive. We also sought professional and spiritual counselling not only for ourselves individually but as a couple and as a family. Without a doubt the professional and spiritual guidance that we received helped our family get through the worst of this traumatic experience.

There is a significant amount of collateral damage caused by ALS. It not only affects a person's physical health but also their emotional health and ultimately the emotional health and stability of their family. By attacking one member of a family, ALS has the power to drastically affect the lives of the whole family.

I believe ALS research can be thought of as the tip of the spear. ALS is one of many motor neuron diseases. I believe that research and development of drugs and therapies that benefit ALS sufferers could also be the key in helping others who suffer from other similar diseases so that all of us can lead long and productive lives.

[redacted]

To whom it may concern,

My name is Steven Graessle. I am a 37 year old male who resides in Edgewood, KY. I have had many proud moments in my life. I graduated Summa Cum Laude from Northern Kentucky University in 2008 with my Bachelor of Science in Business Administration. I have been a Medicare Risk Adjustment Analyst at St. Elizabeth Healthcare for eight years. I have had the honor of speaking with legislators on the advocacy of rare diseases resulting in the resolution of laws. However, my greatest accomplishment is to be able to tell you today I am one of the few adults living with Barth Syndrome.

Living with Barth Syndrome was not an easy journey. I experienced muscle weakness, the inability to gain weight and delayed growth. In the early stages, most individuals did not live past the age of two. If you were lucky enough to surpass that age, the majority of your time was spent in doctor's office, emergency rooms or extended hospital stays. Barth Syndrome causes your body to have reduced white blood cells and your ability to fight infections is non-existent. Barth Syndrome also affects your heart. Your heart has difficulty pumping blood to the rest of your body. This led me to develop irregular heart beats in my high school years. For others affected by this disease it has caused heart failure, heart transplants and even death. Growing up I could never have much of a social life due to the symptoms of Barth Syndrome. Every few steps would cause extreme shortness of breath. My legs would get heavy with exhaustion. I felt like I was wearing 15 pound ankle weights when walking. Wanting to play tee-ball for your grade school? I didn't have the energy to run. Your friends ask you to play a game of basketball in the front yard? That won't happen either. What about riding a bike? I didn't have the strength to pedal. What about dating? I looked considerably younger than my classmates. I entered my senior year of high school at 4 foot 11 inches. I did not have a growth spurt until I was in college. To this day I joke with my friends that I am a 36 year old with the appearance of an 18 year old with the ailments of a 72 year old. What about Covid? Three hundred and forty two days of isolation. 342 days of no family, no contact with friends, missing my grandmother's funeral and missing my nieces and nephews grow up. 342 days of an already shortened Barth life span that are gone forever because contracting any disease could lead to an extended hospital stay or death due to your heart issues and the inability to fight infections.

Although I grew up not being able to participate in sports, they still became an important part of my life. During an award show I once heard the late NBA Analyst Craig Sager say "Time is something that cannot be bought. It cannot be wagered with God and it is not in endless supply. Time is simply how you live your life." These words hit close to the heart of those suffering from ultra-rare disease, but it rings even more true for Barth Syndrome. Time is not on the side for individuals like myself who are diagnosed with Barth Syndrome. The unfortunate reality of Barth Syndrome is 20% of individuals die before the age of two, 45% before the age of 16 and 75% before the age of 30. I am often asked what a treatment for Barth Syndrome would mean to me. Access to treatment to specifically help with the symptoms of Barth Syndrome would allow us to live our life as close to normal. To be able to participate in activities with your friends and family without having to turn down opportunities to watch your family grow or build friendships. Normal would mean the opportunity to live a longer and healthier life.

Every morning I have to wake up wondering if I will see a black line placed over the Barth Syndrome logos on social media. The black line is the universal designation our community uses to state an individual with Barth Syndrome has passed away. Is that next black line going to be my friend, someone's child, someone's sibling or is that black line going to be me? In the world we live in, this should not be the normal we strive for.

Ann C. | Louisiana

Age: 42
Year of Diagnosis: 2015
Type: Limb Onset, Genetic

We Can't Wait

I lost my mother, grandfather, cousin and uncle to familial ALS. Because of the poor prognosis and lack of options for treating/curing ALS, I think it is extremely important to at least give ALS patients the OPTION to try experimental drugs that can potentially help. After all, what is there to lose when you have basically been given a death sentence with an average of 3-5yrs left of your life?

Again, due to the very poor prognosis of ALS, I think it would be up to the patient to decide if that is a risk he/she is willing to take.

Normally, very important. In the case of ALS, there is not enough time for that to happen and that's a risk I would be willing to take.

When my Mom was diagnosed with ALS, it was the most devastating moment of my life. To hear that it was familial was then the 2nd most devastating moment in my life. My siblings, uncles, cousins and I all live in constant fear that we may have the gene and one day start developing symptoms. We worry about the gene getting passed on to our children and possibly not being around to take care of them. It is one of the most awful diseases on Earth, and it is very disappointing that since my grandfather died in 1997, there are still no significant treatment options available. Something needs to change!!

As I stated in the previous question, everyone in my family has been greatly affected emotionally, mentally, and financially by those we have lost to ALS. We are constantly worried about who will be diagnosed or develop symptoms next. **We each have a 50% chance of having the gene and getting ALS in our lifetime.** Those aren't good odds, and our family could be wiped out. We worry about the financial impacts and the impact it will have on those who become our caregivers.

Although it is a "rare" disease and most cases are sporadic, when it is Familial, it is all-consuming for that family emotionally, physically, mentally and financially. I don't think people realize the cost of caring for an ALS patient for even just one year. It takes a very specialized team of caregivers and doctors, equipment, medical devices, handicapped vehicles and even home renovations to make sure an ALS patient is taken care of. Even then, many doctors don't have the knowledge to know how to help these patients-medications don't do much to keep them comfortable. Research is critically important and time-sensitive for these patients. Of course we would love a cure, but at this point, even a moderately successful treatment would be wonderful.

There is no time to waste trying to get these drugs for ALS patients approved by the normal standards-there needs to be a "fast track" if possible, with the understanding that there may be unforeseen side effects and/or no improvement.

Pam M. | Louisiana

Age: 62
Year of Diagnosis: Brother: 2020
Type: Limb Onset



We Can't Wait

I think it is very important. I see my brother's disease progressing pretty rapidly and everyone who loves him is helpless. There is nothing to help him. If there was something that could slow this disease, it would mean the world to him and to everyone around him.

As of now, there is nothing for ALS patients. I know that my brother would gladly take a drug that may not help him or even something with side effects. What is the alternative now? Nothing!!! So if something may potentially help him, he would take it.

It isn't that important other than what the cost may be. If it isn't FDA approved, from what I understand insurance wouldn't cover it and the drug would be very expensive.

It has impacted my brother greatly. He went from being a big strong working member of society, to now being confined to a wheelchair with family members having to feed him. It has affected everyone around him. **We cry all the time. We feel helpless.** There is nothing for us to do except watch my brother's condition get worse by the day. It is heartbreaking. I beg of everyone to make medicine available to ALS patients even though not approved by the FDA.

Everyone around him has given up free time to be a care giver. His wife can't do it alone. From fixing things around the house to just being with him so he won't be alone in case he needs something.

It is not just my brother suffering but the whole family is suffering. It is an awful disease. It takes everything from you. And you can not do anything for yourself anymore. You have to rely on someone for everything.

Every day that passes is critical. My brother needed medicine a year ago and he is willing to try anything. He has nothing to lose from trying medicine even medicine not approved by the FDA.

October 22, 2023

Dear Senator Braun,

I am reaching out to you in response to your request for stories on the unmet medical needs faced by people with rare, progressive, and serious diseases for a hearing by the Special Committee on Aging to be held on October 26, 2023.

I am a participant in programs offered by the Huntington's Disease Society of America (HDSA), a leading national organization dedicated to the care and cure of Huntington's disease (HD), a rare and fatal hereditary disorder that manifests as a neurological disease with both physical and psychiatric components. The mission of HDSA is to promote and support research to find a cure for HD; help people and families affected by the disease; and educate the public and healthcare professionals about HD. Currently, there is no clinically available pharmacological, biological, or surgical agent or method that slows or stops the progression of HD.

Sadly, multiple people in my family have HD. I was diagnosed in 2018 and my 26-year-old daughter was diagnosed in 2019. Here is a list of other family members who either have or had HD: my late father; my grandfather and more than half of his siblings; two of my uncles; and half of my cousins.

HD – which is described as having Alzheimer's, Parkinson's and ALS (or Lou Gehrig's Disease) in one disease – is a horrible illness, but what makes it worse is the high costs of dealing with it. My parents lost their life savings and then their home because of medical bills. And now, I understand why. I am starting to experience high medical costs as my symptoms get worse. I started taking a new medication this year. The pharmacy called to let me know the price for the prescription was $22,000 for a 90-day supply.

Any help you can offer to help those with rare diseases would be appreciated. Thank you.

Sincerely yours,

Jill Briceño

10 Delford Avenue
Silver Spring, MD 20904

[redacted]

Hello! I am writing to share some of my story specifically with my interaction with my son's doctors through the years. My son is diagnosed with multiple disabilities. Here goes:

My 24 year-old son Andrew is diagnosed with epilepsy. His epilepsy diagnosis is a rare one. Lennox Gastaut syndrome (LGS) affects only about 50,000 children and adults in the United States. One of the most difficult aspects of LGS is uncontrolled seizures. This is definitely the most difficult part for Andrew and our family. I've learned a great deal over the years from Andrew's neurologists, and now as a seasoned mom to a son who requires constant care, I would like to share my perspective in return. I want to maintain the relationship with Andrew's neurologist, and also continue our partnership in Andrew's care.

First and foremost, please understand there is nothing I want more than for Andrew's seizures to be controlled. That one thing is by far my greatest wish for him, and I cannot make that happen. That weighs on me every single day.

I started like everyone else as a new mom, and was immediately thrust into a world involving constant medical care, difficult decisions, medicines, medical equipment, therapies, dietary issues, seizures and so much more. In those early days, I had to do my own research. I found the need to connect with other families facing the same circumstances. I don't know of many other diagnoses where parents and their children live this kind of life. Day in and day out we live in constant fear of losing our children, and helplessly watch daily, sometimes hourly seizures, and medication ups and downs. This life can bring you down if you let it. As Andrew's mom for over 21 years, I can for certain say, I am an expert in "Andrew Care." Please don't question my decisions without experiencing personally our day-to-day lives.

To get to the medical appointment to see you, I've lost some sleep the night before as I have worried about every move I will make to get my son out of our door, and then to your office. I have other children at home I have to arrange care for as well. I drive over an hour to get to your office, and have to circle your building until a parking spot opens that will accommodate my larger wheelchair-accessible van. We wait our turn in the furthest corner of the waiting room so Andrew won't pick up germs from someone else. My son likes to make noise in quiet settings, and I frantically try to keep him occupied so he doesn't make too much noise in the quiet waiting room. Oh, and I pray he doesn't seize while he's waiting. When my son seizes his arms and legs shake violently, and he'll gasp for air. I don't want others to see him this way. Andrew deserves his dignity, and not to be stared at. Doctor visits are stressful even before they begin.

I waited six months or more for this appointment; please give me your undivided time to hear my questions and concerns. I know you've seen many patients today. I've been to enough appointments over the years to know you're on a tight schedule.

I have researched LGS online. I have attended conferences in person. I've made it a priority to educate myself as much as I can, and I don't see how that's a bad thing. It's OK that I'm an educated caregiver.

Medications do have side effects, especially anti-epileptic medications. We've learned this all too well. Sometimes when there's an issue, it's the simplest thing, not the most complicated. These medications aren't benign.

Consider me part of the team. My son had a procedure done recently at the hospital. A few days before the procedure, the nurse called me to go over pre-operative instructions. She asked me about Andrew's seizures, and admitted she'd

never heard of LGS. She made sure that my husband and I could be by our son's side in the hospital. Ask for my input, ask me questions. Knowing that you are interested and having your respect as someone who knows her son and his diagnosis validates the job I am doing.

Meet me where I am. When my son was 2 days old, he seized. He was whisked away from me and brought behind closed curtains. I saw the urgency in your care, we needed answers, and we entrusted his new, fragile life to your expert medical care. I was terrified. I knew nothing. You cared for my son, ran tests, shared results, directed me on what steps to take next. I was a new mom. I needed direction. You gave that to me, and even more, you gave me a shoulder to cry on.

When my son was 1 and seizures that were under control returned as clusters of seizures, Andrew was given the diagnosis of infantile spasms. Heartbroken and scared, you gave me options for treatment of this new diagnosis. Over the next few years, stopping the variety of seizures was now the main focus and you recommended medications, diets and alternative therapies. Andrew tried it all. Over 15 medications and alternative therapies to be exact. Once again, you directed me with all the knowledge you had available to you, and you were there to answer my questions as we introduced new treatments.

As Andrew grew older, his seizures didn't stop, but my knowledge and experience strengthened. This is when you agreed with me that LGS was Andrew's diagnosis. You ran more tests after those medications didn't control his seizures. You checked whether Andrew was a surgical candidate and whether the VNS would decrease or lessen his seizures. I went down any path I could just to stop the seizures and allow Andrew some freedom from the effects all those seizures have on him. I knew you were still offering your best medical tools for this difficult diagnosis.

Now, as an adult, my son still seizes. Unfortunately, very little has helped him. Seizures and medication side effects have taken their toll. I have to change my views now. I have no choice. There's life to be lived without as many medication trials. Now, what's important? I need to ask: Is Andrew happy? Is he comfortable? Does he eat well, sleep well, is he healthy overall? Does Andrew lead a full life? Does he stay out of the hospital? Yes. Your care for now is to maintain his quality of life.

Finally, please know that I chose you to be my son's doctor. I asked around. I researched your credentials. I am desperately seeking your input, your knowledge, your expertise on how to help Andrew. That will never change.

At this point I want you to hear my words, my experiences. It's been overwhelming. My hope is that you'll continue to treat Andrew's future care with your knowledge, medical expertise, compassion and understanding. Who knows, maybe my views will also help in your care for Andrew, and in the care of others as well.

THANK YOU! Please let me know if I can provide anything further.
Rachel Ablondi
Mount Airy, MD

Prasanna A. | Maryland

Age: 30
Year of Diagnosis: 2018
Type: Sporadic



Click Here to Play Video

We need access to NurOwn and MX0035 now. Even if it shows 1% improvement, we need it. We do not have time to wait. **I am waiting dying.**

I will happily try any potential treatments even if they are detrimental to my health. There are NurOwn and AMx0035 I want to try.

For me, it is not important. I want to get access to potential treatments that are currently stuck in FDA trials. **I do not have time to wait for a decade.**

I am not able to bath, eat, drive, speak and breathe!

My caregivers are tired of FDA red tape.

I wish FDA understood the importance of giving access to Patients with ALS. There are AMx0035 and NUROWN

ALS patients need access to experimental treatments right now! We do not have time. Please provide access to NUROWN and AMx0035 now.

[redacted]

Good morning. My name is Kevin Woodward. My wife and I are heavily involved in Barth syndrome (BTHS) advocacy and awareness. I sat on the Board of the Directors for the Barth Syndrome Foundation for the last nine years, and I would like to help you better understand the devastating effects that BTHS has on everyone associated with it.

My older son, Connor, has Barth syndrome. He was born on June 2, 2010, in Baltimore, MD. His actual birth did not go as planned, as he wasn't initially breathing on his own. Several terrifying and confusing minutes passed he was successfully intubated in the delivery room and quickly whisked off to the NICU, where he would spend the next four weeks before gaining enough strength to come home.

Over the next 18 months, there were many more questions than answers. Connor continued to have extremely low muscle tone and almost zero overall strength. He missed all the main physical milestones that normal babies hit. He was very floppy, he couldn't roll over, couldn't sit up, and he never crawled. He also was having difficulty eating enough. Then in February 2012, our telephone rang, and the doctors informed us Connor had been diagnosed with Barth syndrome. We were devastated as we began to read about it but determined to learn as much as we could.

Fast forward to present day, Connor is now 13, and more self-aware of his situation, but it has been a long and challenging road to get to where we are, and we realize the road ahead isn't any easier.

1. For starters, Connor still has heart disease – the threat of a cardiac episode is always present. We own a portable AED and bring it with us to many places. It is a constant worry for all of us. He takes 4 different cardiac medications 2X daily, and likely will for the rest of his life.

2. At this point, Connor also suffers from chronic severe neutropenia - unscheduled hospitalizations are a normal part of our lives. When Connor is neutropenic, he doesn't have enough white blood cells to fight off bacterial infections and needs to be hospitalized until that is resolved. So...Connor now takes a new injectable medication (Neupogen) at home to combat this. I wonder how many of his friends can say they need to get needles at home after school?

3. Connor has a permanent feeding tube surgically implanted in his stomach. He isn't able to eat enough food orally to sustain normal health and growth, so every night, he receives most of his food and nutrition through a tube into his stomach.

4. Some days, Connor can't physically get himself out of bed and needs to miss school. Between his hospitalizations, rest days and doctors' appointments, Connor missed 17 days of school last year due to BTHS. This not only negatively affects his schooling, but has an extremely disruptive effect on the entire family.

5. Every day, normal life for a 13-year-old with Barth syndrome presents many other challenges too. For Connor, most of those are focused around lack of endurance and his small size – he still weighs less than 65 lbs.

6. Connor also falls down ALL the time. It's a miracle he hasn't broken a bone yet. He lacks the muscle strength and dexterity that normal kids have. The smallest change in footing or in balance usually results in a fall. His tiny legs and knees are constantly scratched up and bruised. As his father, it's very difficult to see.

7. Connor is often the kid standing off to the side watching others run and play. Mostly because he just physically can't join them, but also to help protect himself from being knocked around too much.

8. Connor also can't ride a bike. Not even close. When we vacation with his cousins in the summer time, he stands by the side of the road and watches all of them (some younger) dash off to here or there on their bikes. He is used to it, and pretends like it doesn't bother him, but I think we all probably know deep down, it does.

9. He's not strong enough to open a bag of chips. He can't pop the top of the ketchup bottle. And on and on and on.

10. On a positive note, Connor does participate in the Cub Scouts, but even that comes with its own set of challenges. During a recent pack hike, something most little boys wouldn't even think about, but something Connor stressed about for weeks, I had to go along with him. And carry him up the hills.

11. This sort of thing permeates into just about every area of our lives. Connor just cannot walk long distances. We have an assistive chair we bring with us many places, or we just have to pick him up and carry him.

12. Connor is also a big brother. His brother, Ryan, is 10 years old and does not have BTHS. Yet the disease absolutely affects him too. There are times when we must focus much of our energy and time on Connor, and Ryan gets short-changed or must sacrifice to benefit Connor. He has a heavy burden to carry already as a 10-year old and we know that it will only increase as he gets older.

Another challenging aspect of this ultra-rare disease is that it is deceiving to the normal eye. Anyone who quickly looked at Connor wouldn't even be able to tell how devasting of a disease he has. That can be a blessing and a curse, as he often isn't given the time and attention he requires. So, he has to self-advocate, something difficult for a young child to do.

If someone asked me what kind of treatment I really wish we had, the answer would be something that would improve Connor's strength and endurance. There is virtually nothing we wouldn't do to help this happen.

Connor is a victim of BTHS who is stuck in his own body.

He wants to fly, but he can't even jump.

He wants to run, but he keeps falling.

He wants to hit a home run, but isn't strong enough to get the ball over the fence.

We hope his future includes overcoming some of these barriers, along with a cure and/or treatment for all the other wide-ranging symptoms associated with BTHS.

Thank you for your time today.

Kevin Woodward
kgwoodward@gmail.com
443-415-4711 (cell)

Leo M. | Bear Creek



Age: 72
Year of Diagnosis: 2021
Type: Bulbar Onset

It is extremely important to me to have a new therapy that offers the chance of a modest benefit even if it has no benefit or significant side effects. I would be willing to take the risk in order to have a chance of even a modest benefit.

In the case of ALS patients, if a potential drug is showing success in slowing down disease progression or improving quality of life, it should be available to patients to let them determine if they want to take the risk with only phase II complete. **Timing is crucial to NOT WAIT.**

Overwhelmingly affected by ALS. I can no longer eat or drink via the mouth and have a G-tube in place for nutrition and meds. Every day is a gift from God.

This horrible disease is heart wrenching for my family and friends, especially knowing there is no known cure at this time. All our future plans and day to day living have been affected. We pray for a cure every day.

That everything needs to be done to help find a cure and extend quality of life for those afflicted with this terrible disease.

Please hear us and take action NOW to approve use of AMX0035 for ALS patients, and any other treatments that are beneficial in Phase II trials and NOT WAIT for Phase III. **Please let the ALS patients have the dignity and right to make their own choice to take accept any risks and give us the hope of more time with our families and friends.**

Julie S. | Middletown

Age: 28
Year of Diagnosis: Bobby- 2014
Type: Limb Onset, Sporadic

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Janet M. | Arnold



Age: 60
Year of Diagnosis: 2014
Type: Limb Onset

It is very important I have a chance to try any medication to help me.

All I know, feel, and thinks about is death. Physical, mental and financial strain...

There is no cure

Don't be concerned with addiction until you find a cure



SELINA OEHMEN

Somerset, MA

On Feb. 21, 2018, our lives were forever changed. Just the night before we had gone snow tubing and had a lot of laughs as a family. Selina, our beautiful 9 year daughter had been complaining about headaches for about 6 weeks, we had taken her to the pediatrician and some blood tests were done and an appointment with the eye doctor was made. Blood tests were all negative and eye doctors showed an astigmatism. Glasses ordered but headaches continued. Pediatrician decided time to consult a neurologist. Before that could happen, we noticed Selina's gait was off. Called pediatrician and he said take her Hasbro Children's Hospital. A CT scan was performed and it showed a brain tumor in the brain stem. They told us they couldn't operate because the tumor tissue and brain stem tissue were intertwined. However, there was an area to do a biopsy. She was admitted to the PICU to be monitored to help bring down swelling and get her ready. On Monday, Feb. 26th, the biopsy was done. On Wed. Feb. 28th, we were told our daughter has DIPG. The worse cancer that exists. On Mar. 2, we were allowed to bring her home. She was to get PT, OT and speech therapy outpatient and start radiation the following week after we discussed her being part of a study in Boston. We had a good weekend at home with friends and family. On Monday, Mar. 5th while in the waiting room at PT, she started to vomit and seize. 911 was called and we were rushed back to Hasbro. She was intubated and rushed into imaging. Selina's tumor had hemorrhaged. She had slipped into a coma like state with only some eye movement and hand squeezing. The swelling had increased and an EVD was put in her brain to drain fluid and release some pressure. On Mar. 8th, she started radiation. By Fri. Mar. 9th, we had lost her squeezing our hands and synced eye movements. We know she can hear as she has ways of reacting like heart rate and some facial expressions. On Mar. 20th, swelling had gone down and they removed the EVD. On Mar. 23rd, an MRI showed the body was reabsorbing the hemorrhage and the tumor growth was stunted and possibly shrank. On Mar. 24th, her vent was removed and she did awesome breathing on her own. On Tues. Mar. 27th, we were moved to the regular floor from PICU, where we remained until May 8th. Although Selina could breathe on her own, she was "locked in", meaning that she could not move or

talk. She was never able to do these things this again. During this time, Selina turned 10. On May 8th, we took Selina home. She had some progress in her ability to move her head to answer yes or no questions, one of her hands and could swallow some soft foods like pudding or apple sauce. On July 19th, we got the unexpected and upsetting news that Selina's tumor had started growing again. We tried to do as many things together as possible like Ed Sheeran concert, the zoo, aquarium. On October 15, 2018, our beautiful Selina left us here on earth. We never knew how she was feeling, whether she was scared or what we could do to help her. We could only ask yes or no questions and hope she felt our love. Her biopsy was donated to DIPG research and we are working at keeping her legacy alive by helping to find a cure. Selina is the most vibrant, sassy, beautiful, and caring angel.

Why the Promising Pathway Act is Important to our Family: We had the biopsy done as we were told they needed to know the mutation of the tumor in order for her to qualify for any of the studies. It is often wondered if the biopsy is what caused the tumor to hemorrhage. We never got what they call a honeymoon with Selina because her tumor ruptured and she was locked in. If the PPA was available, we may have had more choices and she would have had a chance to enjoy the end of her life.

When your child gets a terminal diagnosis, you put all your efforts on finding something that can either cure or prolong the assumed outcome, or at least hope. At this point hope is all you have. When you try to get medicine to help make memories and told it will either take a while, may not be approved or cannot get it, nothing is more upsetting. I ask you out yourself in the above situation when thinking about the Promising Pathway Act. Our kids deserve better.

Ken & Michelle Oehmen

Parents of Selina

My name is Kate McCurdy. I live in **Boston, MA (zip code 02116)**, and I am one of the parents who **founded the Barth Syndrome Foundation (BSF)** in 2000. It is the **only worldwide organization that focuses on our ultra-rare disease**, and I now serve as the **Chair of the Board of Directors.**

But **most importantly**, I am the **mother of a wonderful son**, Will, who was affected by Barth syndrome. **Will died from the disease way too young**, so I deeply understand first-hand how truly **devastating** this disease is. And I certainly have experienced just how severe the **unmet need** is, **as there currently are NO approved treatments** for this disease.

Barth syndrome includes a **constellation of terrible medical issues** – heart muscle problems, skeletal muscle weakness, immune system vulnerabilities, eating and nutrition challenges, biochemical abnormalities, debilitating fatigue, and pain. All of these result from a mutation in a single gene that affects the way mitochondria (the critical energy and biochemical centers in most cells throughout the body) are shaped and function.

We started BSF because Barth syndrome is **SO ultra-rare** that, before the organization's existence, virtually **none of us knew any other families** contending with it. **Very few of our doctors knew of any other doctors** trying to care for a Barth patient, and there were no guidelines for treating the disease itself, only some of its numerous symptoms. We all felt **completely alone, without much information or hope.**

When Will was **born, he seemed fine,** though he had weak muscles and **missed many of his gross motor milestones.** For example, he could sit up at 6 months old if you put him in that position, but he couldn't get into a sitting position himself or roll over by himself until he was more than 3 years old. He endured many tests at several of the best hospitals in the US, but we got **no answers.**

At just over 2 years old, however, Will got what first appeared to be a bad cold but **suddenly went into heart failure.** When we arrived at the hospital, we were told he **might not make it through the night** but that, if he did, a **heart transplant** might need to be considered. Our world came crumbling down.

While Will was hospitalized in the Pediatric Intensive Care Unit, a geneticist talked to us about doing **genetic testing,** and we consented even though there was no evidence of any problem like this in either my or my husband's families. In a few days, the geneticist found a **single paper** by Dr. Peter **Barth** from the Netherlands about a disorder that sounded a lot like what our son had. The doctor wrote to Dr. Barth with many questions and eventually received a reply explaining that the last young boy described in the paper had **died while playing at home** and that there were **no treatments for the condition.** We were **devastated** and **left with nothing.**

Will had a **tough few years but eventually got a bit stronger while taking numerous medicines that tried to address the many symptoms he experienced. At age 14,** however, he began noticeably to go **downhill**

Like the FDA, those affected by our disease want treatments that are **safe and efficacious**. We are convinced by the data that this potential therapy is such a drug. Despite our best, multi-pronged efforts to find more patients, however, there are **only 136 BTHS patients alive in the US** and **318 in the world** today (as of 7/31/23). This means a huge proportion of our entire US cohort of any age was enrolled in the trial for this drug. Unfortunately, *by definition*, it is impossible to conduct a larger trial in our disease. But that does not mean that the drug is not a good one nor that the trial data cannot be well and appropriately analyzed and understood with small numbers in mind.

We don't have the luxury of time -- lives are being lost while we wait for the FDA to act. We know that the **Congress has given the FDA authority to exercise some flexibility in reviewing data for very serious rare disease with unmet needs, but we are being afforded NONE of that. This flexibility given to the FDA to use when reviewing rare disease treatment applications is only getting lip service in some areas of the agency and is not being applied consistently.**

Our Barth syndrome predicament has been cited recently as an **egregious example of** what we know is a **BROADER, SYSTEMIC REGULATORY ISSUE FOR ULTRA-RARE DISEASES**. We know there are other rare diseases, and especially ultra-rare diseases, that have had **similar experiences. There need to be regulatory pathways that work for ultra-rare diseases!**

We are extremely worried for our population. The fact that the **FDA will not** even **fully review the data form the trial of the potential only drug for our disease** that is in front of them means that **access to this very promising treatment will be kept from those who desperately need it.** In addition, this also will have a **significantly chilling effect on any future industry investment and partnership** in Barth syndrome.

We need ways that patients like those with Barth syndrome can have treatments developed for their diseases. Right now, the system is stacked against us, and that does not seem fair, right or equitable. Our kids should not be penalized simply because the life-threatening disease they were unlucky enough to be born with happens to be ultra-rare. Like the FDA, we too want safe and effective treatments. If existing congressional authorizations and regulatory pathways do not offer ways forward for these devastating diseases, then we need for new ones to be approved by Congress.

Thank you.

--

Kate McCurdy
Board Chair
Mother of Barth Son (Deceased)
Barth Syndrome Foundation (BSF)
www.barthsyndrome.org

Barth syndrome is a rare, life-threatening, genetic mitochondrial disorder. Affected individuals may suffer from heart failure, muscle weakness, and infection.

The mission of BSF is to save lives through education, advances in treatments and finding a cure for Barth syndrome.

Barth Syndrome Foundation

Becky M. | Massachusetts



Age: 57
Year of Diagnosis: 2020
Type: Limb Onset, Sporadic

I view new medication as something when now we essentially have nothing. I view it as a life preserver. At the very least it will buy me time while I await more effective drugs to make it through the pipeline. **I view it as Hope where there is little.**

I view a new therapy that offers the chance of modest benefit as not a risk at all. I am willing to take my chances regarding side effects.

I much prefer a drug be approved in a timely matter. It is important that it becomes standard of care so that people with ALS can continue to offer themselves to science. That being said access to any drug that has potential is better than no drug at all.

I am a musician who can no longer play her instrument in a runner who can no longer run. I am forced to process the loss every single day for the rest of my life. This started in my arms and hands, and when I lose them, I will lose my independence. And white why has it not impacted my life. I consider this a silly question.

My children will be forced to witness their mother lose a piece of herself day by day and die a cruel and inhumane death. My husband becomes my caretaker. Everyone who loves me is caught up in the week of this devastating disease.

I wish they understood that if it hit me, it can hit them too. The people not directly impacted by ALS need to be our champions. To raise awareness and funds for continued research.

I would like the FDA to know that this listening session is not enough. That it is time for action. Time for a change. Time to streamline the path to approval. That it is absurd that AMX 0035 is not going forward to approval. Absurd. Is your gold standard to deny us drugs? What could be worse than dying the death I will die from this disease.

Steve K. | Massachusetts



Age: 57
Year of Diagnosis: 2017
Type: Limb Onset, Sporadic

With a diagnosis of 3-5 years left to live a few months is a huge benefit to me.

I would consult my neurologists to weigh the risk/benefits but would be willing to accept more risk of side effects.

Since it is taking years and years of FDA red tape, I strongly feel after Phase 2 completion, ALS patients should be given the opportunity to have access to the treatment if it is proven to be effective.

It has impacted my life in every way. My families' lives have changed for ever! It is a very debilitating disease that progresses every day and there is no cure. Symptoms and progression time are different for each ALS patient.

ALS patients are grateful for the all the ongoing effort to find treatments and a cure, but we need regulatory urgency.

ALS cannot be viewed as a livable disease but ticking clock that results in people losing their life while waiting for approvals. Trial design should include innovative early access contingency plans.

[redacted]

To the Members of the Senate Special Committee on Aging
For Submission to the Congressional Record

October 23, 2023

Thank you for the opportunity to share my experience with you. I appreciate any time and attention you give to the critically important issue of the unmet needs of rare disease patients. I speak to you as a member of the Barth syndrome community; this genetic condition runs in my family. Barth syndrome is considered "ultra-rare" and there are currently fewer than 200 people in the United States living with the condition. There might be more - but, unfortunately, many die before reaching adulthood because there are currently no treatments and there is no cure for Barth syndrome.

Although no one in my immediate family has passed away from Barth syndrome, I know many who have lost loved ones too soon. Attending the funeral of a child is gut-wrenching. Attending more than one due to the same disease is almost overwhelming. And yet, we fight on!

Although our group is small, we have worked with a biotech company on a clinical trial of a drug that shows immense promise for our community. The data - which we have collected over 5 years - is incontrovertible. THIS DRUG - ELAMIPRETIDE - SAVES LIVES. And yet, because we cannot produce a large enough sample of patients for a bigger trial, FDA representatives refuse to provide a fair and equitable review of the results. We will never be able to produce a clinical trial of the size the FDA typically sees. Our community is too small. But this should not mean that the clear results of our clinical trial get ignored!

My appeal to you today is this: Demand that the FDA use the power Congress has given it to be more flexible in reviewing drugs for rare conditions.

Please help not only our Barth syndrome individuals but ALL of those who suffer from rare conditions in our country. Together, there are millions of us and we only ask for a fair shake.

respectfully,
Susan McCormack
18 Thackeray Rd.
Wellesley, MA 02481

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Why genetic testing should always be offered to children with neurodevelopmental differences

By Deborah OndrasikApril 10, 2023



The Ondrasik family attends the CACNA1A Foundation's 2022 Creating Connections Community Conference *Courtesy Deborah Ondrasik*

At 10 months old, my daughter Gabrielle had missed key milestones for gross motor, fine motor, social and communication skills. Following two seizures, Gabrielle had an MRI that showed brain abnormalities. When I was given the MRI results, I crumpled to the ground.

Over the next year, Gabrielle was diagnosed with epilepsy, global developmental delays, and autism spectrum disorder. While our diagnostic journey may have ended there, my husband and I, both physicians, wondered whether there was something deeper behind Gabrielle's diagnoses. So we were excited when we were referred to a pediatric geneticist who offered Gabrielle whole exome sequencing[2], which sequences all of the protein-coding regions of the genome, to determine whether there was a genetic cause.

should include whole exome sequencing in its board content so that current and future pediatricians are trained on when and how to offer it.

I know these systemic changes can take time. Until then, I urge my fellow pediatricians to learn more about genetic testing and to offer and advocate for whole exome sequencing for your patients with developmental delays. Our job is to fight for the health of each of our patients *now*, and we can't do that effectively without evolving our practice to embrace advances in genetic testing.

Deborah Ondrasik is a board-certified pediatrician in Massachusetts and the mother to three children. She is an active volunteer with the CACNA1A Foundation[12], whose mission is to find effective treatments and a cure for CACNA1A-related disorders.

About the Author

Deborah Ondrasik

linkedin.com/in/deborah-ondrasik-638665271/[13]

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[redacted]

Dear Senator Braun and the Senate Special Committee on Aging:

October 23 is International XLH Awareness Day, so it seems fitting that I should share my story about aging with XLH today. I have x-linked hypophosphatemia (XLH), a rare genetic disorder that causes progressive function/mobility restrictions, along with widespread fatigue and chronic pain. You can read more about it in "Whole Body, Whole Life, Whole Family: Patients' Perspectives on X-Linked Hypophosphatemia," published in the Journal of the Endocrine Society, and available here: https://academic.oup.com/jes/article/6/8/bvac086/6607648

I had relatively mild symptoms as a child, but once I hit young adulthood, they started to worsen and, over time, became severely disabling. By the time I was forty, I had the arthritis, spinal stenosis, and mobility restrictions of a not-very-healthy person in their eighties. By the time I was 53, I was totally disabled, even from significant, sedentary work. And the symptoms just kept getting worse until, at age 60, I started a new treatment, which couldn't undo the underlying bone and calcification damage, at least stopped the progression, and alleviated the pain/fatigue, making me more functional than ten years earlier!

Despite finally having an effective treatment, the problem that I, and everyone else with a progressive disorder, face is the prospect of having that effective treatment yanked away from us with no warning and without any medical justification. I'm referring to "prior authorization" requirements. (Step therapy requirements are a similar problem for children with XLH, who are forced to try an old, ineffective and potentially dangerous but cheap treatment before they can start the newer, truly effective, and more expensive treatment. This is particularly outrageous given that time is of the essence for bone growth and mineralization during childhood.)

Prior authorization may make sense initially, for the insurer to confirm the diagnosis and the lack of any other effective treatment options. That's annoying, but manageable. The problem comes when that prior authorization applies to renewal of the prescription every year (or sooner). Progressive disorders, whether rare or common, necessarily require treatment for the patient's entire lifetime. In the XLH context, once the initial authorization is granted, the scientific consensus is clear—the treatment should continue for the patient's lifetime (absent the development of side effects, in which case, the clinician and patient, not the insurer, would adjust the treatment).

It's particularly obvious that a lifetime of treatment is necessary for XLH patients. We do not (yet) have a cure, and there is only one effective treatment. If a patient has the genetic variant that causes phosphate-wasting, they will never have normal phosphorus metabolism without this new treatment, and phosphorus is one of the most critical minerals in the human body, necessary for the health of bones, teeth, nerves, muscles, and energy levels.

No one would doubt that a patient, once diagnosed with osteoporosis or a heart condition would require non-stop treatment for the patient's lifetime. It's only when the condition is rare and poorly understood, and/or the treatment is expensive, that the insurer imposes the "prior authorization" requirement, not just for the initial approval, but to annual (or shorter) renewals. In the XLH context, and presumably many others, there cannot be any scientific/medical justification for this requirement. It is just an attempt to delay incurring the cost, while the patient's health deteriorates. For a patient with XLH, the consequences of going off treatment (poor bone mineralization and increased soft-tissue calcification) can be permanent, with the effects lasting for the rest of the patient's life.

The harm goes beyond the physical too. Even if the treatment is authorized before any doses are missed, the stress of

uncertainty is overwhelming. Our treatment is a once-a-month injection, and many of us begin to feel an increase in pain and fatigue (signs that our phosphorus levels have dropped) a few days before the next dose is due. If we go a week beyond the due date, we experience severe fatigue and bone pain throughout the body, among other symptoms. More than a week, and I don't even want to think about how badly I'd hurt or how physically dysfunctional I'd be.

The prospect of suddenly having XLH treatment withheld reminds me of a short story by the acclaimed mystery writer, Dorothy Sayers, in which the inimitable detective confronts the mystery of a once-vibrant woman who had become a mental and physical mess over a short period, and he eventually determines that her evil husband had been withholding her thyroid medication. (The story is "The Incredible Elopement of Lord Peter Wimsey." See https://www.goodreads.com/en/book/show/40679677.)

That's the horror that XLH patients (and all patients with a progressive disorder) live with when they have an effective treatment that is subject to ongoing prior authorization requirements. We are constantly aware that access to the treatment that allows us to function is subject to the whims of a potentially villainous third party, and we cannot rely on having that access beyond the current authorization period. For us, it's not just a bit of fictional nightmare-inducing horror, but the reality of our lives, that our quality of life is totally controlled by the whims of a third party that is motivated by money, not by what's best for patients.

I'm sure the XLH community is not the only one suffering from the abuse of prior authorization requirements that are entirely profit-inspired, with no justification whatsoever in medical science. It's time to require insurers to follow the science, not the money. Patients with progressive disorders should not have to live in the constant and unnecessary fear that today, or next week, or next month will be the last time we'll ever have any reasonable quality of life before the lack of treatment sends us into a rapid decline.

Sincerely,

Gin Jones
Taunton, Massachusetts

[redacted]

Sorry if this is too late for today's session but it may assist you in the future.

My son Rob was born with a rare disease that went undiagnosed for 15 years. We were in a diagnostic odyssey for most of his childhood. It wasn't until this vascular disease, Blue Rubber Bleb Nevus Syndrome, eroded his spinal cord, leaving him a paraplegic, that we finally found answers. A little too late from where I sit!

But Rob is a champion and is thriving now as a 28 year old who lives his life to the fullest in a wheelchair while managing the symptoms of his rare condition.

Earlier diagnosis and access to information, education, treatments...all could have changed the outcome of his journey. My hope is that no other child and family would live through the agony of the unknown.

Thank you for fighting for my son and the community of rare diseases.

Sharon Drennan



CC: U.S. Sen Senate Special Committee on Aging
Sen. Bob Casey
Sen. Mike Braun
Sen. Kirsten Gillibrand
Sen. Richard Blumenthal
Sen. Elizabeth Warren
Sen. Mark Kelly
Sen. Raphael Warnock
Sen. John Fetterman
Sen. Tim Scott
Sen. Marco Rubio
Sen. Rick Scott
Sen. J. D. Vance
Sen. Pete Ricketts

Chris P. | Michigan

Age: 37
Year of Diagnosis: 2017
Type: Limb Onset, Genetic

We Can't Wait

Not quite what I'm looking for, but I'll take it. Perfect stopping progression.
I'd have to weigh against the severity of the side effects.

Not that important at this point. FDA seal of approval doesn't mean much to a terminal illness. Need treatments in our bodies. Now.

It has impacted every aspect of my life. Every second of every day. Work, family, kids, friends, mental health, activities, faith.

Negatively. There is no upside to ALS. Financially, emotionally, workload, family time.

It is the biggest monster around. **We need a glimmer of hope.** Something. Anything to try.

Biogen needs to release Tofersen now under compassionate care or expanded access. They need to understand their interpretation of impact on phase 3 trial results are wrong. **Something so promising doesn't need another phase 3. Do it now. Track it now. I'm dying waiting. 4-month wait could be difference of walking versus wheelchair, living versus dying.**

Dan P. | Michigan

Age: 37
Year of Diagnosis: 2019
Type: Limb Onset, Genetic



We Can't Wait

Extremely beneficial to have a chance. Hopefully by me time till some thing more advanced comes along. I need to stay around to see my kids grow up.

I'll take it. At least for awhile. I would weigh the severity of the side effects first though. I would want to make my life more miserable

Not important at all to get preapproved. I have no time to waste. This is not acne or ingrown toenail. What have I got to lose? Drugs in my body!!

How hasn't it impacted my life.???? You name it..... wife, kids, job, home ownership, friends, activities and it's different or nonexistent.

They hurt when I hurt. And I'm always sad. They have to go so much more. Pick up the slack and more. **This is a family diagnosis.**

Just how awful it is. How you're never given any hope. Just go home and get your affairs in order. A devastating disease like this needs fresh , out of the box approaches. Waiting 10 years for all the t's crossed won't cut it.

Put people before profits. Do for us what you'd do for your own family. One patient touches tenfold friends and family.

Candice P. | Michigan



Age: 37
Year of Diagnosis: 2019
Type: Limb Onset, Genetic

New medicine? Anything is good. Anything to slow this monster disease. **I have 3 children under 8 years old and I only have a few more months with them.**

Depends on severity of side effects whether I am willing to risk the worst. Modest benefit is good. Not important at all to have FDA approval. If it shows promise..... put it in my body.

I can't live a normal life. I can't play with my kids. I cry over not being able to see them grow. I am sad all the time.

Everyone is sad. Everyone has more work. Everything "normal" is curtailed.

It's a monster. Leaves you helpless while your mind dwells on what could have been, what you're losing

You have given us nothing. No hope. There must be a new and faster pathway for patients with ALS. We've seen you pull out all the stops for Covid. While not apples to apples , we deserve to live. Throw us a bone.

David H. | Michigan

Age: 44
Year of Diagnosis: 2020
Type: Limb Onset, Genetic

We Can't Wait

Very important. It could buy time to for the next therapy that might be better.

The alternative is nothing. Side effects would be a matter of how much one can tolerate them.

If there is sufficient evidence to show some efficacy, I would take it. I can always stop if side effects are too bad, or the FDA later finds a problem.

I am devastated. We are devastated.

ALS is the most complex disease and the least funded. A breakthrough for ALS could lead to breakthroughs in other neurodegenerative diseases.

How would you handle watching a parent or your child die from ALS? Imagine total paralysis, a feeding tube, loss of speech, ventilator and finally death by suffocation.

Patrick R. | Michigan



Age: 50
Year of Diagnosis: 2014
Type: Bulbar Onset, Genetic

Each new therapy that is identified safe and effective in extending life to any degree should be pursued at the behest of leading scientists given the leaps and bounds we can take in development today with a new maps and tools that can be game-changers for research, for families impacted by ALS, and pursuit of solutions for the wide set of currently fatal neuro-degenerative diseases.

I am more concerned with potential side effects, and not at all with the potential for what results might return. Even a program that fails to reach or is counter to expectations is valuable for future endeavors. Weighing the benefit of extended life versus types of potential side effects from the new therapy that provides is naturally a unique prospect each time. The most important thing is that a person who wants to answer "yes" to those potentially life changing, or life-saving therapies has the opportunity participate.

It's not important to me. I understand why it is for many people, but I've been educating myself on the disease that's now killed my mother, and three of her sibling, and is a fight to be had for me and potentially my children. I don't want to wait for FDA approval, I want to be a part of the process that makes lifesaving therapies easy to approve for the FDA and easy to access for people who need them in clinical settings.

My aunts', uncle's, and my mother's diagnosis and demise were brutal. Sad. My C9 status has both put me on alert and allowed me to be a resource for finding answers. So, in the end, I feel empowered by the charge to prevent ALS and other neurodegenerative diseases.

The people around me have learned a lot about the disease. My wife has been very strong throughout, but probably worries the most, about me and our kids. I don't worry about me because I don't want to, and I no longer worry about my kids because I know the work being done today will solve the problem for future generations -- If we keep our resolve and continue pressing to find answers.

My goal is for every person who ever heard of the Ice Bucket Challenge to understand that the campaign raised millions of dollars that are vital to the fight against ALS every single day. The person you tell, the dollar you send, and the research program you support WILL make a difference for people with ALS.

Thank you for all of your work in ensuring the safety and efficacy of the things we put in our body. We know that regulatory requirements and safety standards, like medical research and drug development, are complicated matters that require an immense amount of time, patience, funding, intellect. Thank you for what you do and know that families everywhere are grateful for the work being done to improve the well beings of the ones we love.

Dean C. | Michigan

Age: 61
Year of Diagnosis: 2005
Type: Sporadic



We Can't Wait

Let me have a choice. Let me decide what is best.

Very important to have a chance.

It has made it clear to me what is important.

They are all gone, they could not handle it. I came all along.

That it is a death sentenced. it may take a long time or be fast, but it process.

Diana H. | Michigan

Age: 71
Year of Diagnosis: 2020
Type: Limb Onset, Genetic

We Can't Wait

Any therapy would give a PALS hope. Very willing to try any therapy.

I have not seen many of my family. Hard to not do many of the things I used to do. My husband is tired.

No cure

Speed up use for PALS

Barry T. | Temperance

Age: 66
Year of Diagnosis: 2020
Type: Bulbar Onset

We Can't Wait

I no longer can drive a car, dress myself, or reach for anything. My food has to be cut up like for a 3-year-old. My balance is off. I have only been diagnosed with ALS for 6 months.

My wife must do most things for me now

How insidious this disease is and how anybody can get it.

Get off your ass. I should not have to die because of your ineffectiveness.

Please help me!!

Earl C. | Roscommon



Age: 63
Year of Diagnosis: 2018
Type: Bulbar Onset, Limb Onset

I am sorry but I cannot ask for more month of agony and suffering. **There come a point when your prayers change; and you ask for mercy instead of prolonging.**

I would not have asked my wife to risk more side effects and suffer for really no real benefit. They had a drug they said might prolong her life 4 months.. We asked when do you start counting ?? Are we adding to the "misery" or to the better day up front ?? (Still not good). Also, the range of life varies so much saying four months was a laugh ! No one recommended it, not even her doctors.

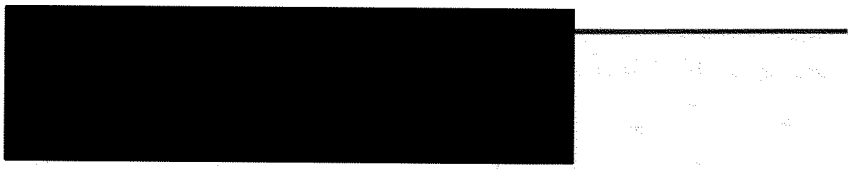
Depends fully on what the expectation are; You don't prolong a walk-through hell ! If you expect something that is real, then of course take the risk. You have nothing to lose!

My wife died ! So it was a great impact.

The death of my wife ! The death of a lady that brought joy to many, her kids included, was quite devastating.. But we expected no miracles from the beginning and in the treatment of 2016 none were forthcoming.

Very few caregivers have any experience. I nearly blasted a few people for their ignorance and lack of empathy!! Your walk will be very alone... Like Deanna Gage (Deanna's protocol) her father was a surgeon and tried to help with his knowledge of the medical world, because there simply was no alternative.

I think the illness is over whelming! and the benefits are not for the millions but for a much smaller number of people. So time and money is absorbed by bigger issues.. It might work, if a large compensation was offered to anyone or group that offered real medical breakthroughs in this horrible disease.



Ashley Hanson

Parent and caregiver of 14 year old son with Prader-Willi Syndrome (PWS)

Cadillac, Michigan

Because the state of Michigan fails to recognize Prader-Willi Syndrome (PWS) as a condition that automatically qualifies for Medicaid, our child, and therefore our family, are unable to access behavioral and mental health support from any public agency including what in Michigan is the construct to access almost all of this support—Community Mental Health (CMH). In our rural region, CMH is really the only option available for mental and behavioral health support for many conditions because it is supposed to be, as it's name implies, a source of support for the community. This is not actually the case; 'community' is actually is a misnomer as it only helps those in the community who have Medicaid. Since this is the only access point for so much of the support available within our community and state, we have been actively pursuing Medicaid waivers through CMH for our son but he has been denied for the Children's Waiver (even though his genetically diagnosed condition meets criteria in every category of the Developmental Disabilities Assistance and Bill of Rights Act) because it is rare and not easily understood. (Fifteen states do consider PWS as severe enough to warrant being automatically qualified for Medicaid.) Because he can walk, talk and does not need nursing care, it is not seen as 'significant' even though it requires 24-hour supervision in a way that is actually more dramatic than a lot of other qualifying conditions. At this time, his mental health is rapidly deteriorating as evidenced by the medical notes in his file but he is also not able to even be considered for the SED (severe emotional impairment) waiver despite having debilitating anxiety, for which he is currently taking three medications, as we are told that his intellectual disabilities automatically disqualify him from this waiver! Additionally, we have been told that CMH controls all the respite funds for the state so he denial means is excluded from respite too. He really needs a respite worker to help manage his anxiety. If he is to be able to be with a caregiver at home (because that is the most food secure environment for him and food security is paramount to managing his anxiety well) when the responsibilities of raising a family require both parents to be doing something other than focusing on his care such as working, caring for their other children or parents, etc. , outside of the school day, his mental health including anxiety will be better managed and, therefore, his behavior as well.

We would like to help build awareness of this situation—that the people who work and pay the taxes to support these public programs do not have access to any of them. They are disqualified because they hold jobs and are responsible citizens and parents! This a huge problem because these programs are often the only places that provide the kind of support that their child needs, and because, while the parents make enough to be disqualified, they often do not make enough money to pay for all the help their child's condition requires. As the needs become more pervasive, extensive and extreme, the financial burden on a family becomes overwhelming. There are a huge number of services and overlapping programming for the people who are under the income threshold. The same families get lots of help from many avenues and agencies but if you are above the income threshold, you are disqualified from help from every public program and agency—there is nothing! Why would there be a system in place that provides extensive support for people who may not even work, thereby disincentivizing those who do by making any and all support inaccessible? It makes no sense to us that people who have private insurance like us would be denied Medicaid because our child would require less coverage than someone who only has Medicaid as he would only be accessing the programs like CMH that are prohibitive to those without Medicaid. Please help responsible, hard working and high functioning

parents like us to be able to continue to care for their children. Additionally, it would be beneficial if support and help was accessible when needs are smaller and less dramatic instead of waiting until there is a progression of the child's condition to severe and extreme so that caring for them in the home is not feasible and potentially fractures the family by requiring placement outside of the home. Please hear our plight and take action to do something to help this overlooked and underserved population. Take action to preserve these families!

Thank you for your time!

Sent from Yahoo Mail for iPhone

October 23, 2023

Dear Chairman Casey, Ranking Member Braun, and Honorable Members of the U.S. Senate Special Committee on Aging:

My name is Andrea Vanbeek, and my son Crew lives with a disease called Facioscapulohumeral Muscular Dystrophy, or FSHD.

Different.

That is how we always defined our youngest of four children, Crew. He was an adorable, giggly, blonde haired, blue eyed boy of three. However, unlike his three older siblings he was uncoordinated and not interested in sports or activities. Misdiagnosis reigned as he progressed through grade school and included; speech apraxia, due to an awkward smile and muscle difficulties in the face, a stroke in utero, a mild form of cerebral palsy, and others. Not until Crew was 12 years old did we face the heaviest truth of our lives. On a warm spring day in May, Crew was at a field day for school and his father, his siblings, and myself were there to cheer him on. As an emergency room nurse for years, I simply watched him run across the field to get to his next event. His left arm bent up snug alongside his body, as he ran, made him look like a natural runner, but it was his right arm that made my heart sink. His right arm hung limply at his side and flopped in the spring air. Instantly, I knew something was wrong. Within weeks we realized that he had no muscle development in his right upper arm, and after seeing multiple neurologists at Devos Children's Hospital in Grand Rapids, Michigan we finally had a diagnosis. At the age of 12 years old, Crew was diagnosed with FSHD (Facioscapulohumeral Muscular Dystrophy). Imagine having to tell your 12 year old son, who is old enough to understand and to visualize his future that he will never play football or basketball like his older brothers in high school and college. Imagine for a minute watching your child take his shirt off, tears well up immediately at the disfigurement you see, and daily you watch his body and muscles decay and degrade as he grows. He is unable to fight against or stop it.

FSHD affects an estimated 1 in 8,000 individuals or 870,000 people worldwide. Ten percent develop symptoms before age 10, like Crew, and around 20 percent will need a wheelchair by age 50. These are children, men, and women of all races and all ethnicities. FSHD is not diabetes, it is not heart disease, a pharmaceutical miracle will not make big pharma billions like it does for these well known diseases. However a cure for FSHD may result in a cure for our disabled veterans with muscular disorders, a cure for a child who will go on to be our President, or a cure for many that will commit suicide due to the debilitating pain and fatigue that over 70% of those affected with FSHD will experience.

I am passionate in writing to you today, to simply say LOOK. Please look at this rare, progressive disease that will cause muscular degeneration in so many, in fact it is hereditary and could impact those you know in the future. We can't fight this without you. As a mom of four with two in college sports/activities, one that plays high school sports, and Crew, I sold my business last year to still be "mom" to my children but also to devote time to FIGHT FOR

CREW. With the help of friends and family I organized the first ever Walk & Roll Event for FSHD in Michigan in 2022. Not knowing what to expect, in 6 weeks we had 150 participants in pouring down rain and raised over $18,000. This year we increased that to over 170 participants and raised almost $27,000. Our family will never actually see this money as it goes directly to FSHD Society to help with research. However I am speaking not only for myself, but for all those who dedicate their time and efforts behind the scenes for this cause, and for every single individual affected with this horrible muscle wasting disease when I say we are pleading for your help! We are exhausted, but these are our children and family and friends. No matter how much we give up to help them, no matter how tired we are, we will continue the fight.

Today, at almost 15 years old, Crew is unable to smile fully, his scapula are winged and shoulders pointed forward. Recently he was told due to the concave nature of his chest he needs to sleep on a wedge to breathe easier. In spite of all the negativity, he is looking forward to the snow and ski season. Crew's legs are not yet affected by FSHD, and from December through February you can find Crew doing his passion on top of the ski hill. As a family, our hope is someday we don't ever have to take that away from him, that with help there will be a cure…

Crew does not let FSHD define him or acknowledge that he is different. Someday, with your help, he will embrace the fact that he is simply the same… as you or me.
You have the power to make this beautiful thought a reality.

Sincerely,
Andrea Vanbeek, RN
Grand Haven, Michigan



Dave D. | Minnesota

Age: 60
Year of Diagnosis: 2020
Type: Limb Onset, Sporadic

We Can't Wait

Very important to have a new therapy that offers the chance of a modest benefit. Depends on the side effects how much of a risk I will take.

I read quite often that people can't get into trials because the disease has progressed too far. It is somewhat complicated to find trials and sign up, or they take very few people around the world into trials. We have a cohort of many willing participants who want to live and will try most anything to do that. The FDA could be a leader in the promotion of new treatments and trial participants. **What is the worst thing that could happen? I am going to die, I know that. We all do.**

Not getting a chance to try these promising drugs, therapies, or treatments will not solve that issue of death, but just maybe, it can push the envelope of developing a tool that will allow people who have ALS to live longer. Or provide some hope to allow researchers to find the cure for future victims of this or any other terminal disease. **By trying treatments and new therapies, people with ALS can give back or be of some service as our bodies break down, showing if these treatments are working to prolong lives**.

ALS has slowed me down and I worry much more. ALS has made my friends and family sad and wonder how they can help.

We are not dead yet.

That I know I would like to live longer.

Stephen M. | Minnesota

Age: 72
Year of Diagnosis: 2020
Type: Limb Onset

We Can't Wait

It would have a large affect on illness cures for the future. Future research would better help AND WE HAVE NOT HAVE ACCESS to this.

We're dealing w/ a GRAVE disease here. Baby steps to a cure.

Not much. FDA supported Agent Orange.....

Greatly affected myeline in terms of the physical changes. Mentally I'm fine. I'm a recently retired Anesthesiologist.

Are you kidding??? **A GREAT IMPACT ON EVERYONE.** There hasn't been much medical treatment or improved therapies or a cure.

We need expanded access through clinical trials, compassionate release, less stringent inclusion criteria for ALS patients.

William M. | Minnesota

Age: 64
Year of Diagnosis: 2020
Type: Bulbar Onset

We Can't Wait

Important but willing to consider non approved trial. It is also important to have the chance to try medicine that could help.

Can no longer do anything I would like. Very limiting.

My wife has now become my caregiver

Don't pity me just treat me like I was before. I'm still the same person inside.

I have nothing to lose so would welcome trials to possibly help this disease.

10-15-23

Dear Committee on Aging-

My name is Megan Lilja. I am a mother to an eight year old daughter who has a rare metabolic disease called Galactosemia. Galactosemia is a rare genetic disease that can be life-threatening for newborns and can cause lifelong complications. My husband and I along with our two children live in Foley, Minnesota.

When our daughter was born in 2014 I was a healthy twenty-seven year old and fully expected to have another healthy baby. Unfortunately, that was not the case. When our daughter was diagnosed with Galactosemia at 3 days old I remember the doctors at M Health Fairview Masonic Children's hospital in Minneapolis, Minnesota tell me that there was no treatment for the disease. When I asked why they simply stated it was too "rare" of a disease to ever get a treatment in the United States. They said the National Institute of Health "would never" fund research for a treatment nor any drug company. It was an absolutely horrible feeling that no parent or family should have to face. As a young health care professional living in America I was astonished. Unfortunately, I was all too naive.

Fast forward to five years later and we were told of a company who was developing the first treatment in the world for Galactosemia. I immediately got in touch with the company and got our daughter on the list to be in the clinical trial. Our doctor did get in the trial and although we did not know if she was on the active or placebo drug and it was very demanding for her and our family with the traveling and treatments we were incredibly thankful to have her in the trial. Then in early 2022 the FDA blocked the company's request to utilize the accelerated approval pathway without explanation. The FDA has not been receptive to the Galactosemia community with our questions as to why this decision was made. It was the beginning of a terrible reality that all too many rare diseases in America face, that despite the drug trial and the drug working, it may not be approved.

I along with other parents participated in a Patient Focused Drug Development (PFDD) meeting in September 2022, and Voice of the Patient Report to the FDA, however they have been "business as usual". Our community then advocated for the passage of the HEART Act (Helping Experts Accelerate Rare Treatments) which thankfully passed in December, 2022.

To say this disease has been devastating for our daughter and our family would be an understatement. It has affected nearly all aspects of my daughter's life as well as our family's. As a result of having Galactosemia our daughter has struggled with speech impairments, cognitive/memory impairments, a decreased ability to complete basic self cares, impaired social skills, impaired gross/fine motor coordination, and sensory impairments. Her free time is spent going to Speech Therapy, Occupational Therapy, and private tutoring. However, the struggles remain.

Govorestat (AT-007) has been shown to be a safe medicine with the potential to impact many disease complications of greatest concern to the Galactosemia community. Clinical trial data has shown that the medicine is well-tolerated and has very few adverse events and no serious

adverse events, making the risk/benefit equation skewed heavily toward benefit. Clinical trial data has also shown statistically significant improvement on symptoms of the disease that are of great concern to our community, including adaptive behavior, activities of daily living, and tremor over 18 months of treatment compared to placebo. Additionally, consistent improvement was shown on measurements of cognition and fine motor skills.

The drug company had a Pre-NDA recently with the FDA to discuss submission for govorestat (AT-007) for the first ever treatment for Galactosemia.

Based on the tremendous burden of disease and the compelling evidence that govorestat (AT-007) may offer our children with Galactosemia a better chance of an independent life, we are urging the FDA to review and approve this medicine as quickly as possible.

As a mother this has been an incredibly difficult journey to watch my child be in a drug trial on top of all the things that already come with her having a rare disease. I can not explain how painful it is to watch your child have to take part in a number of medical tests around the country and cry and ask "Mommy why do I have to do this?" when they are not old enough to understand why. My daughter often asks me why she has this disease and why she has to have so many "pokes" (her name for blood draws). Then to have the FDA block the use of the Accelerated Pathway with no explanation and then now to have to live with the fact that there is a chance this drug will not be approved after all we have been through and despite it being safe and effective. I can not put it into words. I hope I never have to take my child off of this medication and watch her decline after all we have been through and then somehow explain to her when she is older why she had to stop the medication after she was so brave and went through all those medical tests for years and did her part in the journey.

Throughout it all I do feel as though I have a duty to continue to advocate for not only this disease but for all rare pediatric diseases in America. It is truly a shame that pediatric rare diseases have had such difficulty getting FDA approved treatments in this country. I obviously never wanted my child to have a rare disease but I do feel our family was picked for a reason and I was meant to help this cause.

I want my daughter to continue having access to this treatment as well as others with Galactosemia. I can not convey in words how important this treatment is and how devastated we will be if our daughter no longer has access to it.

Sincerely,

Megan Lilja, OTR/L

[redacted]

Hello,

My name is Sabrina Hadro and my daughter Eden Hadro is 5 years old and has Prader-Willi Syndrome. It is a terrible syndrome that affects every area of her life. She is anxious all the time, she is hungry all the time, she cannot be a normal child because she is always scanning the floor anywhere we go for crumbs of food even though she just ate lunch. She has scoliosis, a sleep disorder so the entire family cannot sleep peacefully at night, her speech, gross motor and fine motor muscles are delayed despite hundreds of hours of therapy. She has giant autistic tantrums when the smallest thing in our schedule changes. She has snuck out of the house in the night to find food outside. She pulls out her hair until she has a bald spot. She has so much potential, is so sweet at times, and is very smart. All we need is a medicine to help her. Please help us with regulatory flexibility to advocate for Prader-Willi Syndrome research and treatments.

Thank you,
Sabrina Hadro

October 25, 2023

Dear Senator Braun,

I am reaching out to you in response to your request for stories on the unmet medical needs faced by people with rare, progressive, and serious diseases for a hearing by the Special Committee on Aging to be held on October 26, 2023.

I am a participant in programs offered by the Huntington's Disease Society of America (HDSA), a leading national organization dedicated to the care and cure of Huntington's disease (HD), a rare and fatal hereditary disorder that manifests as a neurological disease with both physical and psychiatric components. The mission of HDSA is to promote and support research to find a cure for HD; help people and families affected by the disease; and educate the public and healthcare professionals about HD. Currently, there is no clinically available pharmacological, biological, or surgical agent or method that slows or stops the progression of HD.

I am a Caregiver for my husband Nathan. Nathan was diagnosed with Huntington's disease in April of 2016, He was 38 years old at the time. But looking back, we can see that he actually started developing symptoms about 4 years before at the age of 34.

HD has totally changed our lives. When we got married, we imagined a life of fulfilling dream careers, having a family and growing old together. Because of Huntington's, we have the family, but our other dreams of career and growing old together will not happen.

HD has taken a lot from our little family. My step daughter will never have the experience of her Dad walking her down the aisle. My 8-year-old son has and will never know a day his Daddy wasn't sick. Not long ago, our son, out of nowhere, while playing on the floor looked up at his Dad and said, "Daddy, I wish I'd known you before you got sick."

This truly is a family disease. We are all impacted by HD. My husband is looking at a future of being trapped in his own body. I'm looking at a future of caring for my husband's every need. Being more like his parent than his partner and his wife. Our kids basically being without a father.

Our Huntington's community needs so much. We personally have had troubles in the past of medical needs and tools because HD is so rarely known our medical professionals don't know how to handle the disease.

There's so much misinformation. For example, my sister in law, when inquiring about getting tested was told that she didn't need to get tested because women didn't get HD. Our medical community NEEDS to be more educated on the tools that our HD Warriors (which is what I call them) need.

We need more in the research side for ALL stages of Huntington's. If there were a medicine available that would stop Nathan's disease and he would not get any worse than what he is right now, we would take it in a heart beat and no questions asked.

That's how desperate our family and others like ours are. There's NOTHING to help with This disease and we need SOMETHING.

I always tell people that with awareness comes funding, with funding comes research and with research comes the hope for a treatment or a cure. We NEED this awareness, We NEED this help towards tools and medications to help our loved ones.

When Nathan first got diagnosed, we felt so alone. Like we were the only one's that were dealing with this disease. We don't want that to continue for others newly diagnosed. We're hoping with your help, we can make that happen.

Thank you so much for the opportunity to share our story and thank you for taking the time to listen to our story and the stories of others just like our family.

Sincerely,

Heather Thurgood Wilmoth
14 Old Nola Rd
Sontag, MS 39665

HI

MY NAME IS AMY WILSON. I'M MOM TO JACOB, AUNT TO CHRISTOPER WHO ARE BOTH AFFECTED.

I LIVE IN RANKIN COUNTY MS, WHERE I GREW UP.
I WANT TO THANK YOU FOR TAKING TIME OUT OF YOUR DAY TO BE HERE. THANK YOU FOR LISTENING TO OUR PLIGHT.
JACOB HAS ENDURED MORE IN HIS 23 YEARS OF LIFE THAN MOST HAVE BY THEIR 90S. HE'S BEEN POKED, PRODDED, TESTS, AMBULANCE RIDES, ER VISITS, AND HOSPITAL STAYS-SO MUCH SO- I'VE LOST COUNT. I'VE WATCHED HIM SEIZE AND TURN BLUE. I'VE WATCHED JACOB MISS MONTHS OF SCHOOL & HAVE TO BE QUARANTINED DUE TO HIS IMMUNE SYSTEM. JUGGLING WORK, DRS APPTS, BEING A WIFE, AND TRYING TO ALSO BE THERE FOR MY OTHER SON, ALL WHILE DOING MY BEST TO KEEP JACOB ALIVE.

THESE AREN'T THE THINGS THAT SCARE ME. THIS IS MY LIFE. IT'S BEEN A NEVER ENDING BATTLE TO MAKE PEOPLE LISTEN, TO GET HELP.

WHAT SCARES ME IS KNOWING WITHOUT THIS MEDICATION, QUITE POSSIBLY HE'S LIVED HALF HIS LIFE. STATISTICALLY SPEAKING. IT SCARES ME KNOWING I MAY NEVER SEE HIM GET MARRIED.

IT SCARES ME WATCHING HIS MENTAL HEALTH DETERIORATE ALONG WITH HIS PHYSICAL HEALTH.

BLESS HIS HEART, HE WORRIES ABOUT ME AND MY FEELINGS. MY MENTAL HEALTH.
IT SCARES ME KNOWING I WON'T HAVE GRANDCHILDREN. JACOB'S MADE IT ABUDANTLY CLEAR HE WILL NOT HAVE CHILDREN. HE DOESN'T WANT TO PASS THIS DEADLY DISEASE ON. THIS MAY CHANGE, SHOULD WE GET TREATMENT AVAILABLE.
WE'VE ENDURED MAY OBSTACLES WITH BARTH SYNDROME AND HAVE BEATEN ODDS.

WITHOUT YOUR HELP IN GETTING THIS MEDICATION, THIS TIME- WE WON'T.

I DON'T WANT TO SEE THE INSIDE OF ANY MORE AMBULANCES, ER ROOMS, HOSPITAL ROOMS. NO MORE MEMORIALS & PHOTOS OF THOSE WE CONTINUE TO LOSE. I'M SCARED I WILL HAVE TO BURY MY CHILD.
SOMETHING NONE OF US SHOULD EVER HAVE TO GO THROUGH.
I'M PLEADING WITH YOU ALL TO PLEASE HELP US GET THIS TREATMENT. OUR NUMBERS ARE SMALL IN OUR COMMUNITY BUT WHY SHOULD WE MATTER LESS? I KNOW THE FDA HAS APPROVED DRUGS WITH LESS PARTICIPANTS THAN OURS. WHY SHOULD OUR FAMILIES BE EXCLUDED OR MATTER LESS?

I KNOW THIS MEDICATION WORKS. I'VE SEEN IT WITH MY OWN EYES. I KNOW THERE'S NO SIDE EFFECTS. I JUST WANT THE CHANCE TO WATCH MY SON, MY NEPHEW, MY COUSIN, AND THE OTHERS TRY AND LIVE A QUOTE NORMAL LIFE. SO I'M ASKING YOU TODAY TO PLEASE HELP US MAKE THE FDA DO WHAT'S RIGHT BY OUR COMMUNITY. DO THEIR JOBS. WHAT WE'VE BEEN ASKING FOR 5 YEARS NOW.
DO RIGHT BY THOSE WHO ARE SUFFERING & DYING DAILY.

Thank you for your time,
Amy Wilson



I'm Kristiana Pena, Richland MS resident, mother to Christopher who suffers from Barth syndrome. Christopher was Mississippi's first pediatric hospice patient. The fact that 85% of those with Barth syndrome do not live to see their fifth birthday means that his life is no small miracle. He was the 157th boy to be diagnosed with Barth syndrome in world history. His journey has been highlighted across countless state and national headlines alike, including being a poster child for Mississippi"s only children's hospital and ambassador for the children's miracle network hospitals. We have participated in advocacy from mandating pulse oximetry in our state to the many hours in this plight for access to the only existing treatment for Barth syndrome and many issues in between.
In addition to Christopher, I also have a first cousin and a nephew both diagnosed with Barth syndrome.
I'm writing this testimony and imploring your assistance in asking FDA to review the positive data for the only treatment that exists for those living in this small community, all of whom suffer from this life threatening and life altering condition.

This disease impacts my son and others living with this condition in many extreme ways.
A trip to the grocery store requires multiple rest breaks from the parking lot to the walk through the store for basic life necessities. Stairs are his nemesis. Between OT, PT, ST, water therapy, horse therapy and even feeding therapy, if it was a therapy available, chances are Christopher has benefitted at some point. Attending school in person is out of the question. An illness that would be mild for us becomes life threatening for him with little to no warning. He's been a hospice patient, endured heart failure three times and is currently trending in a concerning way. He has suffered seizures, and a stroke at 4 years old. He requires 23 doses of medicine a day and two injections a week and is followed by 10 different specialists including complex care team.
Not only has this impacted him physically but also emotionally and mentally.
The older he gets the larger the void between he and his peers grows. Normally a very positive person, his most recent medical crisis found Christopher in so much pain that he asked me to let him die.
He is also old enough to remember all of the research he has participated towards the ultimate goal for a treatment or even a cure, He is old enough to understand the risk Barth syndrome places on his life, old enough to be afraid to die and know that the possibility living with barth syndrome untreated , that risk is very real. He feels its physical limitations and understands that its not normal to not have the energy required to live typical day to day life.
He feels very discouraged to think this treatment exists and the effort was made for nothing, all because how rare the condition is that he suffers with.
Not only does this disease take its toll on him, but it also affects his loved ones. This disease has impacted our entire family dynamics from employment, to the time it takes to be a caregiver, fighting every step of the way for every extra need, pa's referrals, medicine referrals and administrations....we never get a holiday fro. As a matter of fact many holidays we have found ourselves spending multiple holidays through the years in the hospital and separated from one another.

This journey has taken each of us through many traumatic experiences in many ways. It has cost each of us lost opportunities of differing magnitudes that will leave you changed for life.
Not only has this disease impacted my nuclear family, my sister's family, my aunts family, but it has impacted us for generations- with my own grandmother burying both of her sons, one of which happened on mothers day.
This example shows the treatment would impact many generations to come!
We aren't ungrateful of the burdens placed by Christopher's life because his existence is a blessing to us, but much of it has been unnecessary hardship and suffering for all of us, especially him.

I would love to see our son experience the normal quality of life that you and I take for granted.
One that includes comfort, good health, and less isolation.
This disease is extremely isolating for all of us.
I would love to see our son enjoy a life where the next medical crisis or worse.... Death is not looming over him. I dream of being able to see him be a productive member of society because I know he has so much to offer this world if only his body will give him the chance. I dream of him being able to attend school in person for the first time ever, a chance to attend social events without his body punishing him for days and even weeks afterward.
I dream of him having the ability to participate in sports... all of these are realities we never dreamed or considered possible before seeing the evidence of what elamipretide can do.
I saw with my own eyes my nephew thrive for the first time in his life, being an active participant in life, attending high school, working and a social butterfly. On this drug he gained 25 pounds. Since he has stopped taking the drug his health has declined. He is now a 73 pound 23 year old who lives on a feeding tube, because his muscles are too weak to digest food, swallowing and bowel control are also an issue currently.
There are other implications that don't get talked about simply because their dignity is already stolen living through it.

After being told repeatedly during my son's 15 years of life, "there's nothing we can do, Im sorry there's nothing we can do..." FINALLY there is something.
The very real possibility we may never be allowed to give our son the chance to try this miraculous drug, a medicine that would not only save but give him a quality of life is devastating to me, and that word doesn't seem to articulate the emotion I feel at the idea. To say that it is frustrating to me is an understatement. In never want to see another person I love suffer and die ESPECIALLY when its avoidable! The FDA agrees the drug is effective. They agree the drug is safe. They do not agree that there are enough people living with barth syndrome to justify taking the time to give a fair and equitable review of the data, something which they have been given congressional regulatory flexibility to do. This feels like a huge slap in the face and I feel what they are doing is egregious, and causing undue suffering and death. I do not want to play chicken with the lives of these precious individuals another day.
Thanks for your time.

Rankin County School District

Mission: *B*ring *E*veryone's
*S*trengths *T*ogether! We will all intentionally focus on empowering our students to reach their maximum potential by embracing opportunities and challenges while cultivating a tradition of distinction in education.

*Vision: *Continue a tradition of excellence by providing a world-class education that empowers all to grow through curiosity, discovery, and learning.

This email and any attachments to it may be confidential and are intended solely for the use of the individual to whom it is addressed. If you are not the intended recipient of this email, you must neither take any action

October 24, 2023

Dear Chairman Casey, Ranking Member Braun, and Honorable Members of the U.S. Senate Special Committee on Aging:

My name is Archer Sverdrup, and I live with a disease called Facioscapulohumeral Muscular Dystrophy, or FSHD. FSHD is a muscle disorder that causes progressive weakening of skeletal muscles. The most commonly affected muscles are face muscles, shoulder muscles, and arm muscles, but it is known to affect many more than just those three. It can sometimes cause hearing loss, and occasionally can cause breathing issues.

There are currently no treatments or therapies approved for the treatment of FSHD. However, there are multiple clinical trials currently happening with more expected to be announced. A treatment can't come fast enough for me. I am continuing to lose muscle function and am quickly losing my ability to walk even short distances. I can barely move my arm at the shoulder due to shoulder and upper arm weakness. I've had hearing loss since birth, and my breathing is also starting to be mildly affected.

Due to my declining muscle function I am having to transition to full time wheelchair use, but even that transition has its challenges. It took 8 months to get insurance approval for my everyday use wheelchair, and that is considered normal. Some people have to wait even longer. I still don't have in-home assistance, despite not being able to complete activities of daily living independently, such as showering or brushing my teeth.

I am also losing the ability to do some of the things I love. I love to bake, but due to upper body weakness I can no longer do it independently. Crafting is another hobby that has become more difficult for me. I have adapted a lot of my crafting tools and craft projects to be more accessible to me, but due to upper body weakness and weakness of my hands it is often difficult if not impossible.

The most debilitating symptom for me is not even the muscle weakness itself, but the pain. I am in severe pain all the time. The pain is an aching and burning muscle pain that feels like I'm constantly in a state of muscle overuse. The pain is the type that sucks the life out of me at times. It is from both the muscle breaking down due to the disease process, but also from having to push my muscles to their limits just to move at all. I fatigue super easily, and have to be careful about what I do in order not to increase pain and fatigue.

Living with FSHD is not easy. Between the physical barriers of pain and muscle weakness, and the barriers to getting proper care such as my wheelchair, there always seems to be a struggle. We need treatments and therapies for FSHD now. More and more people are getting diagnosed as testing becomes more widely available and physicians are more aware of the disease. More people now than ever need hope. What are you going to do to change the lives of people with FSHD?

Sincerely,
Archer Sverdrup
Lake St. Louis, Missouri

CC: U.S. Sen Senate Special Committee on Aging
Sen. Bob Casey
Sen. Mike Braun
Sen. Kirsten Gillibrand
Sen. Richard Blumenthal
Sen. Elizabeth Warren
Sen. Mark Kelly
Sen. Raphael Warnock
Sen. John Fetterman
Sen. Tim Scott
Sen. Marco Rubio
Sen. Rick Scott
Sen. J. D. Vance
Sen. Pete Ricketts

Rosa B. | Missouri

Age: 56
Year of Diagnosis: 2020
Type: Sporadic

We Can't Wait

There is nothing to offer these terminal ill patients. **Anything available is HOPE, each individual should have the right to choose if they want to participate in any clinical trials or therapies. It's there only hope, nothing else.**

Any option available is better than none.

There should be a loop in the restrictions for terminal ill patients. Why wait? These patients do not have the luxury of waiting.

It has affected absolutely every aspect of my life. My mobility, independence, lifestyle 100%.

My entire family has been devastated. **My daughter has had to quit her job, she has 3 little kids and is my caregiver 100%.** Its a horrible disease to everyone involved.

I wish people to understand how devastating it is. How fast a person deteriorates. How it rips the patient from everything they were.

Let the patient decide. They are terminally ill, it's their life, it should be their choice if they want to take alternative medication, therapies, clinical trials, anything.

Steven Y. | Montana

Age: 66
Year of Diagnosis: 2018
Type: Limb Onset

We Can't Wait

I believe that anything that will slow progression even in the slightest is worth trying immediately.

It is not important that the FDA approve the drug before I take it.

Any risk is outweighed by even the slightest benefit of a longer life even if it is just months.

ALS has basically ruined our life together. We had wonderful dreams of how we would spend our retirement years and now that is all gone. We are living day to day, and it is getting harder and harder to keep going.

It has put enormous strain on my wife who is my only caregiver. ALS is a death sentence unless they can come up with a new drug.

Angela F. | Montana



Age: 47
Year of Diagnosis: 2013
Type: Sporadic

Very important to me to get on the list for any drug regardless of any side effects.

Has limited what I can do and my quality of life has diminished

How it takes away your independence is awful.

Please let us try new medications, it takes too long for the FDA to approve



MADELYN SCHUMAKER

NE

Madelyn will be forever 8 years old to us. She was diagosed with DIPG on January 26, 2015 and she earned her wings in December 2015. Madelyn received treatment for DIPG as part of a clinical trial at St. Jude Children's Research Hospital in Memphis. Her initial response to treatment was positive and she tolerated the maintenance chemo well. She enjoyed seven symptom free months that we used to take trips to Florida, New York, Michigan, and an RV trip to South Dakota. We also researched additional treatment options during that timeframe.

In the fall, Maddie had a biopsy performed at Sloan Kettering in NYC due to the return of symptoms. Genomic analysis was performed as part of the Molecular Guided Therapy trial at Helen DeVos Children's Hospital in Grand Rapids, Michigan. The molecular analysis led to a combination therapy of four chemos that targeted the mutations in her tumor. Initial results where promising and we saw several weeks of improvement. When things then took a rapid turn for the worse we headed home to hospice since there were no more viable treatment options. Maddie's decline was mercifully swift and she passed away in our arms in December 2015.

Maddie had the warmest heart and a deep soul. We witnessed her compassion grow as she got to know many children battling cancer. Even with her extensive interests, her family remained the center of her world. Despite her young age, she understood the concept of heaven and was prepared for it. Her greatest loves, after her family, were her friends, her cat (Titan), her fish (Rosie), and pandas.

Why the Promising Pathway Act is Important to our Family: We know firsthand how important it is to gain access to new treatments as soon as possible. With such an aggressive disease, new treatments really are the only hope. It is crucial for pediatric therapies to be accessible for terminal

cases at the same time as conventional adult trials. The conventional FDA approval process simply is not practical for diseases such as DIPG/DMG due to the relatively small patient population. These children deserve a chance and should not be left behind.

The PPA provides a framework to expand access while collecting information that will also facilitate more informed decisions about next steps for therapy and ultimately improve safety. The PPA is a huge step forward and deserves the support from all of congress. Thank you for your consideration.

Jessie Schumaker

Father of Madelyn

Don N. | Nebraska

Age: 67
Year of Diagnosis: 2010
Type: Genetic



We Can't Wait

Any new therapy would be helpful and welcome.

I gladly accept no benefit or side effects. Not at all important to get prior approval from the FDA, Let's just have a chance!

It's become very difficult for others to understand my speaking to the point where my wife must speak for and make phone calls me.

My family's been extremely supportive of me, taking me to appointments and helping whenever I need it.

I went from an active, athletic father and grandfather to being wheelchair bound, unable to stand or care for myself over a short period of time. It's taken a lot of patience and Doctors visits to get me where I am today and couldn't have done it without help.

Please, please, please find anything that can help us!

Brian L. | Nebraska

Age: 55
Year of Diagnosis: 2019
Type: Sporadic



We Can't Wait

Extremely high. It's all about slowing the train down.

Better to have the opportunity than not

Moderate importance. Better to have opportunity for new treatments before the FDA is involved. They take way too long.

It's Impacted every corner of my life. Put it to you this way, I was able to walk with assistance a year ago and now not so much.

I'm humbled and lucky by all the support and help received by everyone around me

People need to understand once the diagnosis is given a clock really starts. Besides the physical things, **we don't have time to mess around with Traditional slow track medical research**

People with ALS and similar time sensitive diseases are more prone to take on higher risk scenarios than the general population. **Therefore, the FDA process should be fast tracked in a completely different way than other medication**

[redacted]

My name is John Wilkins and I live in Lincoln, Nebraska (68516).

As an infant in 1982, I was diagnosed with X linked congestive cardiomyopathy, a serious form of heart failure. This was treated with a number of medications and my heart was stabilized. I was so weak I was not able to feed enough to gain weight. At seven months I was started on tube feedings. I was hospitalized 20 times in my first 5 years of life, and suffered severe fatigue, muscle weakness, and chronic cyclic neutropenia. My growth was extremely delayed, I was much smaller than my peers until the end of high school. I was never able to participate in any physical activities in school. Once I reached high school I had to be homeschooled due to my growing fatigue. It took me six years to complete a two year IT program at the local community college.

In 1991, I was diagnosed with Barth syndrome. While it was good to have a name for my disorder, my symptoms remained the same. There was no treatment of any kind available.

Thanks to the Barth Syndrome Foundation, we now know so much more about this disorder. Yet we still do not have an available treatment and we now know Barth syndrome is progressive.

Because of Barth syndrome, I have never been able to live the life I dreamed of. Currently, I cannot work full time, I cannot walk more than 3-4 blocks without exhaustion, I have difficulty rising from a seated position due to the increased muscle weakness in my legs. The fatigue I experience is overwhelming.

An available therapy for Barth syndrome would hopefully allow me to have better health, more energy, to be employed, participate in activities, and overall live a better life. More importantly, a treatment for Barth syndrome would help the younger affected individuals live a much better life than I have.

John Wilkins

[redacted]

My name is Susan Varner Wilkins and I live in Lincoln, Nebraska (68512).

My son is now 41 years old and has lived his entire life struggling with Barth syndrome, a complicated X linked genetic disorder which is also ultra-rare. Barth syndrome is a mitochondrial disorder that affects his heart function, muscle mass, strength, stamina, bone density, and white blood cell count (his ability to fight bacterial infections is decreased because his ability to make enough infection fighting neutrophils is diminished). He also suffers from extreme fatigue and has been tube fed for most of his life.

My son's life has been severely affected by Barth syndrome, as have the lives of our family. From his early years when we had no idea what was causing his acute and dangerous health issues, (Barth syndrome did not get a name until 1991, our son was 9 years old) to his schooling, his inability to participate in school or social activities, or keep up with his peers. We needed to home school him for high school because he did not have the stamina necessary to attend in person. He has always worked as hard as he could and was able to pass the GED easily. Determined to continue his education, it took him 6 years to complete a two year program in our local Community College.

He has not been able to work full time, ever. He currently cannot work at all, very frustrating for a person who would love nothing more than to have a full-time career.

We now know that Barth syndrome is progressive, and we are seeing a physical deterioration in our son. He is weaker, his fatigue is worse, he is finding it difficult to get out of a chair or walk more than a few blocks without needing a break, and he must rest to conserve energy if he has something to attend, and then rest for several days following an outing.

Despite his lifetime of many challenges, our son is kind, compassionate, steadfast, and rarely complains. He is a proactive as possible.

For 41 years my family and I have dreamed of a therapy for this awful disorder. Our son has participated in numerous studies for Barth syndrome and the only clinical trial there has been for the disorder. We are desperate for a therapy for Barth syndrome before it's too late. Our Barth syndrome community have shared this dream for their affected family member (or members) right along with us. It is extraordinarily difficult and heartbreaking to watch your child (no matter how old) suffer, struggle, hurt, and on too many occasions in our community, die because there isn't any therapy available. This is why having access to a therapy that has shown potential to make a difference for our children is so critical.

Therapies for rare and ultrarare diseases like Barth syndrome are so difficult to achieve because there are so few people who can participate in clinical trials. Please help us. Lives truly depend on your help. Thank you.

October 25, 2023

Dear Senator Braun,

I have Huntington's Disease (HD), and would like you to keep my special – but not unique - story in mind when you meet next week for the Senate Special Committee on Aging. HD is an incurable, rare neurological disorder that resembles Alzheimer's, Parkinson's, and ALS.

I am 63, and inherited the defective HD gene from my father, who got HD from his father. As I've lost dozens of relatives on the Sweeten side of the family to HD, I would like for you to keep all of us in consideration.

There's real lack of appropriate nursing home care for individuals in my situation. While I'm in stage two out of four stages of HD, I can still advocate for myself. But as the disease progresses into later and final stages, I will need to have you use your position in government to protect seniors in nursing homes.

Part of the reason HD patients or residents are neglected or mistreated in senior facilities or group homes is that their behavior at times is unpredictable, erratic, and out-of-control. Sometimes medications and protocols alleviate some of the behaviors, but it's still challenging for an unprepared or inexperienced staff.

The staff should be well-trained to also handle a patient who has swallowing issues and know how to administer a feeding tube. Furthermore, HD patients have serious motor problems, and will need much help with walking. Finally, most also deal with significant cognitive decline and will need extensive assistance with activities for daily living.

I appreciate your time, and would like for you to contact me if you have any questions about my HD and where I will reside when I can no longer be cared for properly at home.

Yvonne Sweeten
HDSA Las Vegas Affiliate board member
230 Scotgrove St.
Henderson, NV 89074

Celisa M. | Nevada



Age: 55
Year of Diagnosis: 2021
Type: Limb Onset, Sporadic

A few months can mean attending your child's wedding or getting to meet a grandchild. When you have 36 months to live , 40 months is better, **it's the small things that begin to matter when your life has a known end date.**

When you are terminal, you have nothing else to lose and you are willing to try because not trying is giving up. There are always consequences to decisions, and I am willing to accept them for the benefit of saving my life or the next ALS patient.

I am an RN with 20 years of experience and conducted 4 clinical trials during my time. It is not important at this stage (living with ALS) to have proven drugs due to the time constraints. I'd be more than willing to start a Phase II approved drug and be tracked by whatever means.

Ended my 20-year nursing career. Ended my college studies for my advanced degree. I am not prepared to retire because I love my job and thought I'd work until I was 70. Relocating to be near my children because they are the most important now. I get to sit and watch them do what **I want to do so much!! I worked hard to be an independent strong woman but now my identify is "she is dying".**

I have 4 boys which I raised mostly alone and two of them are married. They are now having children (earlier) than they wanted so that I might get to know them. Careers are put on hold so they can spend as much time with me. Raw conversations occur about life that they weren't ready for.

There is no reason as to "why me" and it might be the most complicated, erratic and insidious disease a person can die from and those who can help with some hope, even just a little real hope, aren't or won't.

NurOwn passed phase 2 and was approved for phase 3. I have personally talked to some people who had benefit and reversed! I get that it didn't help all and they had a placebo effect. But I think the number was 34%? I know of 68 people who died last month, if they all had NurOwn, we could of saved 23 of them!! **Twenty-three lives lost because of "red tape".** If it's only producing those results for patients in early stages, then save them. You have to start somewhere, and the time is now! **Start with us, who are alive but living with a "tick tock" in our brains as we count down to our expiration.** Let us help you find a treatment or even a cure! Be humble and realize that ALS is different than other diseases and those that are suffering need to help you so that you can help us and future ALS victims.

[redacted]

To whom it may concern,

My name is Kathryn Michener, I live with my husband and two children in Wilmot, NH. My oldest son, Bryn was diagnosed with Barth Syndrome when he was two months old. He is now 11 years old and in sixth grade. He is about five inches taller but two pounds *lighter* than his six-year-old brother.

Bryn has all the classic symptoms of Barth Syndrome: cardiomyopathy, neutropenia, low muscle tone and reduced bone age – most people think he's about seven when they first meet him. He gets weekly shots for his immune system, and is on two heart medicines. He also has a feeding tube because it is too tiring for him to eat enough calories to sustain his body. Just the other night, we had to change Bryn's mic-key for his overnight feeds. He hates getting it changed – we have to pull the old, grungy one out of his stomach and put in a new, fresh one. He asked me, "what did I ever do to deserve Barth Syndrome?!"

I had survivor's guilt for a long time after my first-born, Rhys, died unexpectedly when he was six months old. My body betrayed me and passed on a defective gene that ended up killing my baby. Figuring out what happened to Rhys allowed us to save Bryn, as they were both identified to have the same mutation on the Tafazan gene, which causes Barth Syndrome. Bryn's question that night brought me right back into the depths of my guilt. No child deserves to live with any disease, let alone an ultra-rare disease.

Physically, we are managing Bryn's condition pretty well. However, as he gets older, it's the psychological impact of his limitations that really worry me.

About a month ago, we got a permission slip from school to attend Nature's Classroom. Bryn was SO excited. It's an overnight science and nature camp. We started looking into it and it didn't take long to realize that the camp was in no way equipped to manage medical disabilities. We were faced with the choice between advocating for equitable access and convincing him it wasn't worth trying. That is a really terrible position to be in as a parent. There have been instances in hospital when an attending nurse had to rely on my husband or I to manage Bryn's "rare" treatments – there is no way I could ever feel comfortable with a camp or school nurse handling his medications and overnight feeds. For example, his amino acid supplements are powders that I have to compound so that they can be taken via the g-tube... the camp requires a Rx for ALL meds. We have an old Rx for them but insurance stopped paying for compounding so currently, they are a "dietary recommendation," which would never jive with the camp's medical releases.

Thank you,

Kathryn Michener



October 25, 2023

Dear Chairman Casey, Ranking Member Braun, and Honorable Members of the U.S. Senate Special Committee on Aging:

My name is Gregg Lichtenstein, and I live with a disease called Facioscapulohumeral Muscular Dystrophy, or FSHD. The challenges of living with a relentlessly progressive disease are legion, but I want to focus on one issue facing everyone in the U.S. with a serious and chronic illness, about which your committee can and should do something: the overwhelming complexities of working with the health care system. As we age and our disease progresses, we take on a new demanding job: navigating the healthcare system in order to meet our needs. For me, this job has grown to a significant part-time job (now up to 2 full days a week), which I hold in addition to my full-time work. And I know that I am not alone; even fully able bodied people with occasional and acute situations are required to spend entirely too much time and energy, trying to get the health care system to fulfill our needs, not the needs of the providers and insurance companies.

The health care system is breaking down and we citizens are left holding the bag. I spent 7 months waiting for a critical appointment with a medical specialist. Last month, I spent 2 hours on the phone, attempting to fulfill a prescription which my insurance company and their utilization board (after 10 years) had decided was no longer medically necessary. I know how the system works – I am highly educated, extremely capable (except for my physical disability) and very organized – and I have a great deal of experience working with the health care system. Not only should this never have happened, but the system is designed to intentionally obfuscate the reasons for the denial so that customers will stop pursuing their needs. Two precious hours were spent when, at most, it should have taken 5 minutes. To someone with limited physical energy, that is a serious problem.

And this is just one or two among numerous indignities and problems I face every day. And I know that I am not alone. I share these stories with my friends – those who are disabled and those who are able bodied – and we are all spending too much time, energy and precious resources, chasing our tale in a system that no longer works for the citizens of this country who do not comprise the top 1%. And the situation is only getting worse, every year.

I am still working and mentally capable of making significant contributions socially and economically. But this challenge, this cancerously growing job of managing my health is eating into my ability to work (and those over other very capable members of our society) – which is something everyone on both sides of the political aisle should be able to agree, absolutely needs to change.

I urge you to undertake the necessary changes to make the job of living with a progressive disease, manageable.

Thank you.

October 23, 2023

Dear Chairman Casey, Ranking Member Braun, and Honorable Members of the U.S. Senate Special Committee on Aging:

My name is David Rubin, and I live with a disease called Facioscapulohumeral Muscular Dystrophy, or FSHD. Thank you for taking on the challenges of rare diseases. I am currently 66 years old. Growing up I was an athlete for most of my life. I was a competitive swimmer through college and raced motocross in my teens. Following unnecessary shoulder surgery in 2000, resulting from a misdiagnosis of my disease, my physical therapist noted winging in my scapula and suggested I go to Columbia Neurological Institute in New York City for testing. He thought I might have ALS. The physician at Columbia diagnosed my FSHD almost immediately and it was confirmed by a test. My personal family doctor was honest enough to tell me he never would have diagnosed FSHD. After much trial I found that the only way to find a physician with knowledge and commitment to working with FSHD patients was to go to New York. I live in NJ and would have preferred to find a physician closer to me. Some physicians were simply uninformed, others showed little interest in learning about the disease due to the limited number of patients. It is difficult to find knowledgeable physicians outside of a major metropolitan area or university hospital that focuses on FSHD.

When I was initially diagnosed, I had few symptoms, and I was in denial that I was facing a significant issue. I had a few falls over the years and always blamed them on something other than my disease. As I grew progressively weaker it became impossible to ignore my reality. The stairs became more difficult, the pain was always there, I was falling frequently, I could not get myself out of the water at the beach, I could not lift furniture and most obviously I was walking considerably slower than everyone else. I started working out more and more. While there was benefit to the exercise you cannot beat this disease by working out. The muscles are slowly being eaten away continually robbing you of more and more function. I eventually accepted my disease and became more involved in doing whatever I could to help find a cure. Today, I have trouble walking and maintaining balance, I cannot lift my arms over my head, I wear braces on both ankles, and I cannot lift or carry very much. That said, compared to others I am fortunate in that I can still walk short distances and use my arms for now.

My greatest personal pain with FSHD is that it is a genetic disease and the thought that I may have passed it on to my children or granddaughter. None of them are symptomatic at this point and they have decided not to get tested because there is currently no cure. The thought of what may lie ahead for them physically and psychologically possesses my thoughts. As a parent and grandparent, I don't want to burden my children. I want to protect them and. care for them. To the best of my knowledge neither of my parents was ever diagnosed with FSHD. They both died relatively young from other causes. It is possible they just never showed symptoms.

The burden this disease places on my wife is also quite painful. My FSHD not only limits her lifestyle it puts the burden of physical work that I would normally have performed on her. Thank God she is an incredible person with amazing skills and patience.

There is much progress on the scientific front regarding this disease. We have great hope that there will be solutions to manage or cure FSHD over the next several years. As with many rare diseases, finding the cure is only the beginning of the battle in getting treatment to those who need it. I worry that the cost of a cure will be unaffordable and not covered by insurance. That leaves patients with the choice of being untreated or facing a great financial burden or ruin. Not a great choice in the greatest country in the world.

Feel free to contact me with any questions.

Sincerely,

David Rubin

Toms River, NJ

Drubin257@gmail.com

201-370-2417

CC: U.S. Sen Senate Special Committee on Aging

Sen. Bob Casey

Sen. Mike Braun

Sen. Kirsten Gillibrand

Sen. Richard Blumenthal

Sen. Elizabeth Warren

Sen. Mark Kelly

Sen. Raphael Warnock

Sen. John Fetterman

Sen. Tim Scott

Sen. Marco Rubio

Sen. Rick Scott

Sen. J. D. Vance

Sen. Pete Ricketts

[redacted]

Hello there

Here is my daughters story...

My husband and I were so excited as we began our 10th year of marriage we were going to be a family of 3! Marissa was on her way. I remember the doctor asking me about testing as I was older and I said like I always said no worries. If something is needed we will make sure we get the right specialists, do our homework and we would be ok. I wanted to enjoy every moment and not worry what could or would be. The pregnancy was perfect I worked full time, got the nursery ready we had two showers and we were ready for this gift from God to arrive. After all we waited 10 years to meet her. My due date on St Patrick's Day had come and gone and we waited.

March 23rd began like every other day. I got up got dressed and went to work. I was sitting at work on the phone and my water broke. To my surprise no contractions and I drove to my doctors office like they told me to do and indeed as the doctor said yes I bought my ticket to the hospital. After 20 hours of labor and a c-section later Marissa was here! I knew I should be excited I really was but I remember the facial expressions first. As I was talking to the doctors I could hear my mom and my hubby talking to the doctor behind a curtain and they said no the redness won't go away. We will talk more tomorrow they said. Hmm I thought I knew I had gone through an ordeal what does this mean. I wanted to see her and hold her and check this out. As a mom you really check out a new baby don't you? You see everything ears nose eyes and differences. I looked at her port wine and her eye swollen shut and thought she can't go to school like this we are going to need help. That evening People came to see us and it was great. We were so excited. Our world was going to be different but how different I had no idea.

The next morning at the crack of dawn I call it the revolving door of crazy began. Doctor after doctor arrived. My doctor came to check on me first and said are you ok? I had lost a lot of blood so I needed a possible transfusion. Then that notorious facial expression told me that was not all. The dermatologist came next and I was like wow they took what I said pretty seriously and I already had a specialist for this birthmark but the same look was on his face. Then the pediatrician came and again the look. He explained what could, should and maybe would be was happening. I was screaming inside what does all this mean how it is just a birthmark and bruising that was what they said yesterday. Then they came and told me she was going for a cat scan. That can't be good I thought radiation not even 24hours old. The nurses hovered and my doctor came to check on me often. The results were in and my husband and I were relieved no calcifications whatever that really meant. But the looks started to relax and so did we. And we began to enjoy our new addition and couldn't wait to get home.

As the weeks turned into months she had check up after checkups. I consistently would say the same thing all these doctors but who is looking at her as a whole person. I reached out after some research and met Anne Howard at the Sturge Weber Foundation. There was a conference coming up and she said we had to come. I said no not needed as we don't have glaucoma or seizures but she insisted so we went. My husband and I arrived and out of no where bigger then life this lady came by and scooped up my baby and loved her so tight. No judgments for the first time, no staring at the birthmark just love. If you know me scooping up someone's baby and not knowing them well that could spell disaster. But that was Karen Ball and I knew that day was the day I came home. I never felt so comfortable and to talk about the syndrome and having others know was an experience I will never forget.

Fast forward Marissa was doing great she was progressing and then at 10 months to the day. Our world turned upside down. She wasn't feeling well not sure why but something was off. She cried and Moaned all morning and i called the pediatrician they said if It didn't get better I could bring her in. Then out of nowhere she vomited and the seizures began. One right after the other. As i began to count there was 10 then 15 I stopped counting as we approached 30. It took about 4 to 5 days to control these seizures. Each day the doctor would come in and that same look would come too. We went home on two meds for seizures and she was still having subclinical seizures. I have to say it was pretty scary. But as we began to breathe and Marissa got used to the meds the days again turned to weeks and months. She was again developing and doing great and 2.5 years later it happened again.

These seizures were even harder to control and again 5 days later now on three medicines she came home. Also around the same time had gotten glaucoma. We were scared everything they said could happen happened. We were talking brain surgery. We went to another conference in FL and there thankfully meeting with families and what we would find to be one of our best friends we were now equipped with a village. We talked and cried and laughed and we weren't alone. We decided on no surgery as the doctors explained that Marissa was bouncing back so well.

Fast forward to today and Marissa is now 14 years old and just started high school in the ninth grade. She had one breakthrough seizure 7 years ago, a concussion two years ago in gym class which caused paralysis and subclinical seizures. She is realitively controlled seizure wise. She has advoacated for herself with Congressman Norcross and has participated in a roound table for pharmaceutical drugs. Her seizure meds need to be the brand and we have had to fight to not go generic and she also needs a compound for her glaucoma which many insurance companies deny now as well.

Education is very hard and a big struggle. Her syndrome is multidisciplinary and in saying so makes it very hard to have the education system to understand what she needs. They continue to want to put her in life skills because her IQ is low and she struggles because her eyes and her brain do not communicate well due to the seizures and stroke like episodes. She learns differently and many times needs assistive technology. Actually as we speak we are having this conversation with the school she is in and I cannot back down because what I have learned as MOM is simply this...You may be a specialist in school, medical or the like but I am a specialist in Marissa and her needs. You must listen to the advocate, the caregiver and patient because they are the key to what they need. Placement is critical and you give in one time you will never get it back! Never!

Marissa is an amazing young woman with so much potential. She knows more then most because she has had to compensate from the beginning and knows the why to everything she does. She does struggle with school and what may seem like simple things but she is fierce and has tenacity to move forward at whatever motivates her. See she may have lots of doctors and our life does stop every time she gets sick and we always do things a little different then her friends. She has had 42 laser treatments too. But what we don't always talk about is what she has done. She has stayed at the best hotels ordered more room service then humanly possible. She has gone on vacations, met people, advocated on the hill, danced in recitals, she has her purple belt in karate, she is a Girl Scout, she plays many instruments at music therapy, swims, rides a horse and this year joined the bowling team at school. Will she struggle sure and she will tell you "you know I have Sturge Weber". She is not afraid to tell her story and she Believes in herself!! I am so proud of this gift from God everyday. Her village that stems all over now adores her too. We don't know what tomorrow will bring but right now we will celebrate her years of seizure free anniversary on April 19th and sit back in the best seat in the house to watch the rest of her story unfold.

Thank you

Julia Terrell, Proud Mom to marissa
6094250313

[redacted]

My father Jack was diagnosed with ALS in 2020. He's a man who has spent his entire adult life in the service of others. Someone who is truly the embodiment of the American Dream. After high school, he became a mail carrier for the United States Postal Service in his hometown. He then went on to the police academy while also putting himself through college in the evenings. He graduated from both and became a police officer in Newark, New Jersey. During his time as an officer, he put himself through law school at nights. Those were long days. I was around 9 at the time, and he would leave the house for work at 6 AM, only to get home around 11 PM. I remember staying up, just to get an hour or so at night to hang out with him. We would eat turkey sandwiches together at the kitchen table and talk about our days. I cherish those moments still. Soon after finishing law school, my father was elevated to the position of Undersheriff in Essex County, New Jersey where he worked for years. And despite all of these professional accomplishments; the long hours and busy schedules, he, along with my mother, raised three children. He coached little league. Never missed a birthday party. Took us on family vacations. He taught me about work ethic, integrity, and most importantly, he taught me to have empathy for others.

If this all sounds too good to be true, I get it. But I'm here to tell you it's the truth. The man is superhero. He's always been there for his community, his state, his friends and most importantly, his family. So, to see him suffer from a disease, which has a 100% fatality rate, and not be able to help him, has been devastating for those of us closest to him. See, the thing about ALS is that it's RELENTLESS. To put it bluntly, a patient loses their ability to move. They lose their ability to breathe. They lose their life. And while we've made some strides in the fight against ALS, there are still no therapies that halt or reverse symptom progression. That's 150 YEARS of diagnosing a horrific disease with an average survival rate of 2 to 5 years.

When someone you love deeply is diagnosed with ALS, you begin to see life as a collection of small moments that add up. Holding your significant other's hand, hugging your child, petting your dog when you get home from work, eating a favorite meal. These are moments that many of us, including myself, take for granted every day. The simple act of physically getting out of bed in the morning is so engrained in our daily routine, that we typically do it without even thinking. We're getting to the point where my father *can't* get out of bed without assistants. His legs are becoming weak. He's losing the ability to use either of his hands. Soon, my mother will have to cut his food for him. See, ALS strips away any semblance of independence you once had.

Mary T. | New Jersey

Age: 68
Year of Diagnosis: 2020
Type: Limb Onset, Sporadic



We Can't Wait

Very important to have a chance at making life better.

Significant side effects would keep me from trying it

I think if something is working with minimal side effects it should be approved quickly

Totally changed cannot work or walk long distances My hands are weak I cannot lift things or open bottles, or jars am not driving any more used to be the caretaker of my family. Now my family has to take care of me

Very upset that there is no cure. It is underfunded.

[redacted]

My name is Michael V. Dubuque, I live in Central New Jersey, and my Nephew Declan was diagnosed with the very rare, and very serious Barths Syndrome before his first birthday.

2022, on the eve of New Year's Eve, at eleven months old almost to the day during a Holiday visit home to New Jersey from Arizona, my younger Sister Jamie had to rush her Son Declan to the ER. He seemed to be fading away, as if his "power source" was gradually being turned lower as the day progressed. What began as concerning, soon turned into any loving parents absolute worst nightmare.

After being told by the first clinic visited my Sister needed to hurry her Son to the local hospital ER, Declan quickly went into cardiac arrest. He was lifeless for almost 20 minutes, his heart was still, the Dr's and Nurses fought tooth and nail to bring this beautiful eleven month old baby boy back to life. Thankfully, they were successful. He though was far from out of this detrimental trouble. Declan was airlifted to the much better equipped Jersey Shore Medical and then soon took a very slow, very foggy, cold and rainy ride via Ambulance out to the incredible Children's Hospital of Philadelphia (CHOP) in the University City neighborhood of Philly. Declan was hanging on by a thread and the immediate prognosis was beyond grim. His Father Jesse, who was still in Arizona as this happened, made it to CHOP by early the next morning. That very morning I drove my Mother, who was with Declan and my Sister as the initial drama unfolded, to CHOP. We met Jamie, Jesse, Jesse's Parents and one of his Brothers in the Pediatric Cardiac ICU waiting room. Knowing nothing about what exactly had just happened and why, only knowing that machines were keeping this little boy alive, we were starving for answers. Anything to possibly hold on to, anything to give some shred of hope. This took some time. His trauma was so devastating, the talk of a heart transplant was brought up quickly. Though it would take some time and the unfortunate loss of another young life, transplant seemed to be the only thing that could keep this kid alive other than the machines he was on and an emergency heart surgery that may or may not help. As shreds of light were slowly being shed on Declan's situation, one of the Dr's had a thought of something vaguely familiar. A genetic test was done and a diagnosis was made. Declan has Barths Syndrome. A rare disease found only in boys, that attacks the muscles and ultimately debilitates completely and almost always leads to death. As in 9.9 out of 10 times, death is certain. With the lack of known cases world wide, nothing seemed to remedy this disease. Up until a very small study done by Johns Hopkins based in Great Britain on a drug called Elamipratide, showed real hope. One of the Dr's at CHOP knew about this trial. After some phone calls and through the good grace of God, Declan was supplied with this wonder drug. With the help of a Ventricular Assist Device (VAD) called the Berlin Heart and most importantly Elamipratide, Declan went from certain death, to absolutely thriving back at home with his loving Parents in Arizona within the first half of this year.

My understanding, is that no child has ever come off of a VAD without the need for a heart transplant. Declan did, Declan still has his native heart. It is my understanding, that no child with this syndrome has ever recovered from such a trauma as quickly and strongly as Declan has. The report I got from Jamie on Declan's latest test results a couple of weeks back at Phoenix Childrens Hospital was, that if any Dr. or any Cardiac Specialist didn't already know about Declan's medical history looked at these test results and readings, they would "never be able to tell" he didn't have a healthy and normal heart. Declan has absolutely smashed any pie in the sky expectations for recovery and Elamipratide is to thank...

As you read this, know, though this kid is in the best possible shape a Barths boy could be in, especially considering the seriousness of what happened to him, he is NOT out of the woods. Far from it. Due to a complete lack of care and due

diligence by the powers that be at the FDA, Declan and any other Barths patient who does or who SHOULD be able to benefit from this unequivocally miraculous drug Elamipretide, are at risk of certain eventual death. Simply put, if the FDA does NOT decide to look into the efficacy of Elamipretide because this trial "lacks data", they will bury my Nephew...

Barths is an extremely rare disease. Extremely rare. The genetic pool cannot just produce an abundance of Children with Barths to add to this trial so the FDA has more "data", that's not how life works. In your face FACTS about this disease and this drug are being overlooked and it's wrong. Elamipretide MUST be given a REAL look. It is effective, I have a Nephew who is above the ground because of it... Other Uncles, Grandparents and Parents have kids they love in their lives who should be afforded this very same opportunity. Other Uncles, Grandparents and Parents who lost their little boys to this disease don't want to see other lives lost to this disease. Don't take it away from Declan. Don't take it away from those little boys who need it now and those little boys who will. Please. I implore you.

- Michael Vincent Dubuque
New Jersey



MADDOX JAMES PEARL

Albion, NY

Our son was diagnosed with DIPG in August of 2022. Maddox battled for 13 months and 6 days and gained his angel wings on 9/30/23. Our once vibrant, brilliant, loving and amazing little boy slowly turned into a shell of himself. By the end of his journey Maddox was no longer able to move his body or speak. Imagine being 5 years old and being hostage in your own body, it's torture. We looked into many trials and there were so many stipulations that made Maddox ineligible. How can you tell a terminal little boy that they can't try to live because their tumor isn't a perfect circle.. We eventually got on the PNOC022 trial and he was on it for 5 months until progression. After reradiation we chose to get on Everlimus and Ribociclib through compassionate use and the paper work involved meant that Maddox had to wait weeks for the FDA to sign off on it. During those weeks as a parent you are constantly thinking is this monster growing, and all because of paperwork it was so frustrating and heartbreaking not knowing.

Why the Promising Pathway Act is Important to our Family: If the Pathway Act is approved it will be instrumental in helping parents and giving them a piece of mind that people understand that time is of the essence. When your terminal there is no time to wait and the FDA makes that impossible to move things quickly. Every second counts for these patients and for these parents and we need all the hope we can get. As a mother who battled along side her little boy the Pathway Act has the potential to save lives, who knows what if Maddox had more than a week on the new trial meds. Would he still be here fighting? We waited 4 weeks because of red tape, 4 weeks that he could have been taking the meds, 4 weeks that could have changed the course, but we will never know because of paperwork.

Katelyn Pearl

Mother of Maddox



LUCAS HARASHIMA

Pound Ridge, NY

On September 17th, 2016, our little boy Lucas (age 5) was diagnosed with DIPG (Diffuse Intrinsic Pontine Glioma). DIPG is a terminal cancer residing in the brainstem - and one doctors hate because it is inoperable. We did everything we possibly could to combat the cancer and chase new science, light and hope for Lucas. In the end, it simply wasn't enough. Lucas died on March 21, 2018, just a few months shy of his 7th birthday.

As parents going through this, we can assure you there is no greater heartbreak. When something like this happens, you understand in an instant what truly matters in life. What matters to us now is doing everything we can to shine a bright light on DIPG and funding much-needed research towards finding a cure.

Why the Promising Pathway Act is Important to our Family: As parents learning about DIPG when Lucas was diagnosed, we were shocked that we had never heard of this deadly disease with no known causes or cures. It is both outrageous - and true - that there have been NO proven treatments developed for DIPG over the last 30+ years.

DIPG is a very difficult puzzle to solve for many reasons:

- It's rare: While considered rare, ~300 previously healthy children diagnosed each year in the US feels like too many when the certain outcome is death. Still, it cannot compete with high-profile pervasive cancers for attention and funding.
- It's quick: The tumor grows and spreads aggressively. The average lifespan for kids diagnosed with DIPG is 6-12 months. 6 months. That doesn't leave a lot of time for trial and absolutely no room for error.
- It's spread out: The disease doesn't form as a solid lump that can be surgically removed but rather as spread out clusters of cancerous cells located in the central stem where every single brain signal travels through.
- It is brutal: Children diagnosed with the disease are often pumped with steroids to manage the swelling effects of radiation. Kids with DIPG are often bloated, cross-eyed, unable to walk, talk,

eat, speak, etc. Regardless of our best human intentions, it is often hard to witness a child suffering in this way.

- It's likely to be the key: As one of the toughest cancers to beat, there has been much scientific speculation that finding a cure for DIPG could unlock important answers for all other cancers. That's why many researchers believe it to be the HOMERUN cure.

Through the passage of the Promising Pathway Act:

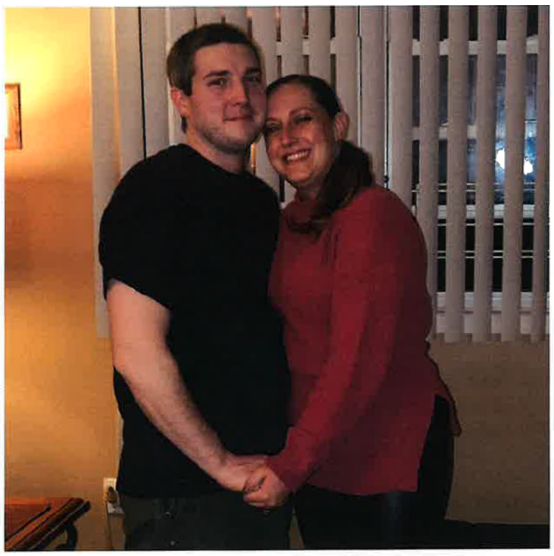
- Patients will obtain access to provisional treatments faster than current FDA pathways.
- Pediatric therapies will be accessible for terminal cases at the same time as conventional adult trials.

Each year, only a small percentage of research funds goes to pediatric cancers; a fraction of that for brain cancers, and an almost non-existent portion for DIPG. We ask for your support of the PPA to help with attention and funding that give kids a chance to live.

Hide and Sansan Harashima

Parents of Lucas

The Love4Lucas Foundation



ANDREW G. AUBRY

Staten Island, NY

My Husband, Andrew G. Aubry, was diagnosed with terminal brain cancer (DMG H3K27M) on February 17th 2022, at the age of 33. While he lay sedated in ICU, I was told by a neurosurgeon that Andrew had 12-15 months to live. It was an extremely overwhelming wave of pain, sadness, anger, confusion and more, that had completely consumed me from that second forward. I instantly started researching where to go and who to go to for this particular cancer. While yes, we found great Doctors and Surgeons, we also found out just how deadly this cancer is. Why? Why are ALL types of brain cancer treated the SAME? There is only ONE option. ONE!! One single regimen for every single brain cancer patient, regardless of tumor genetics. This is called the "Standard of Care". It's pathetic. It's 2023. Science has come so far and wide in 50 years, how are we still at ONE? I say 50 years because that is when this Standard of Care treatment plan was implemented on brain cancer patients. ALL BRAIN CANCER PATIENTS. My beloved husband Andrew, passed away 14 1/2 months after his diagnosis, on May 9th, 2023 at the age of 34. But not before he seized for over 5 hours. He didn't die until 15 hours after the seizure began. From the neck down Drew was fine, therefore his body refused to shut down. Had he not endured enough? All Andrew wanted to do was live and BEAT this cancer. He didn't want to "keep it at bay", he wanted it GONE. But there was no hope for Andrew. None. Again, WHY?

Why the Promising Pathway Act is Important to our Family: The Promising Pathway Act gives hope. Something that no one diagnosed with or have been effected by brain cancer has ever had after hearing the prognosis that is given to them. This Act will help research move farther along where sadly we have all been failed. While Drew's most valiant battle has ended, please let this Act begin.

Michelle Narducci-Aubry

Wife of Andrew

[redacted]

Good evening,

Attached you will find my son, Noah Murphy's, story living with Galactosemia without any treatment. From the bottom of my heart, I thank you for taking the time to read this and help us advocate for change. Please don't hesitate to contact me with any questions.

Warmest regards,
Tori Murphy

Tori Murphy | LMSW

His name is Noah and he is a miracle. I was 6 days postpartum as a new mom. I was navigating everything that had to do with having a newborn - diaper changes, feeding, and all of the firsts. The first smile, the first blow out, and the first set of doctor's appointments. Little did I know that I would have experienced a lot more firsts in the next coming days. Noah had gone for his first doctor's appointment and to my surprise, the doctor sent us to a geneticist to get bloodwork as he looked "a little yellow". Thinking everything was probably fine, I took him to get bloodwork and after 8 hours of doctor's appointments, I got news that I never had expected.

"We think he has something called Classic Galactosemia," Noah's pediatrician said.

When I heard those words, I knew my life had changed forever. The doctor explained that earlier blood work had come back, as well as his Newborn Screening Test done in the hospital. Both show his bilirubin levels being dangerously high and the results being consistent with the ultra rare diagnosis of Classic Galactosemia. We rushed him to the Children's Hospital where he would spend 4 days of his life hooked up to monitors, IVs, and sit under a light to break down bilirubin in his bloodstream. The doctors explained the aftermath may not be good. They'd said, "if he would've come in 2 days later, it may have been too late." This sentence put into perspective the miracle that I had just witnessed and lived through. Medical staff were able to intervene and they saved his life. However, they discussed the effects of this disorder being speech delays, learning delays, muscle weakness, developmental delays, poor growth, cataracts, tremors or seizures, vitamin deficiency, liver or kidney failure, and many more. They were not certain whether Noah would feel all or any of these effects. As we transitioned back home, Noah was switched to an all soy formula and I was not able to breastfeed him anymore. He frequently vomited after eating and had to be on multiple medications in order to stop spitting up and have a bowel movement. He was not able to comfortably fall asleep in his bassinet or crib on his back and would cry for hours, despite any intervention we would do, due to the gas, reflux, and constipation that coincided with soy formula.

Classic Galactosemia, or "CG", is categorized as an ultra rare disorder where individuals lack the enzyme in their liver to break down a sugar in galactose. If individuals with CG ingest too much galactose, that galactose in their body could build up and cause detrimental effects. There is currently no cure and this is something individuals with Galactosemia will have to live with their entire lives. One of the only ways we can somewhat "manage" this disorder and some ill effects is through diet - diet being the only thing we have.

Until, AT-007.

AT-007, or Goverestat, is a new drug that offsets some of the effects individuals with CG experience on a daily basis. The Galactosemia Foundation with the help of people all over the

world have been urging the FDA to take us seriously and look into this being approved for the community. Over the past several months, our community has been keeping up with everything that the FDA asked of us - clinical trials, research, meetings, PFDD (Patient Focused Drug Development meeting), Voice of the Patient Report, etc. Our community has reached out to countless representatives, senators, and other esteemed leaders of our country to advocate for us on our behalf to the FDA. All of us seem to be getting the same response from the FDA, if there is any response at all. While we are urging them to look at the drug, we are also cognizant that the FDA may not be able to disclose with us about drugs and drug trials. This is not what we are asking. At this point, given nothing seems to be changing with the FDA, we are wanting confirmation that they understand our rare disease as a whole especially when reviewing present and future treatments. We have heard next to nothing regarding this. Working with the FDA on this has been frustrating, given their mission statement is one of "promoting and protecting public health," two things of which they have not shown to us. We have not seen any evidence of promoting our health or protecting it. We are part of the public, albeit, a small portion of the population, but we still deserve to be heard. The people living with Galactosemia everyday deserve a treatment that could help their health in unimaginable ways ("consistent and sustained clinical benefit on activities of daily living, behavioral symptoms, cognition, adaptive behavior and tremor") We deal with rare disease every day and like me, I have to watch my child be affected by a disorder that sets him back milestone after milestone compared to his peers. It is difficult knowing that there could be a potential treatment out there for us that could make Noah's future different.

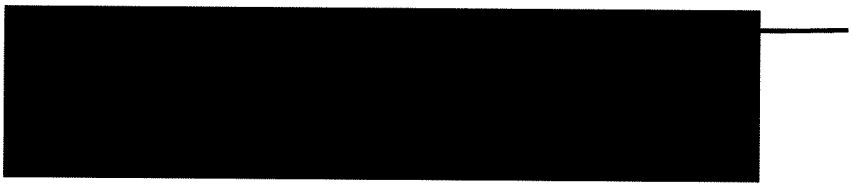
Over the past 28 months, we have started to experience some of the long term effects from Galactosemia. When he was around 12 months old, he started to fall behind in growth. He was the 5th percentile in both height and weight compared to his peers. He was also diagnosed with a vitamin D deficiency and will likely be on his vitamin D supplement the rest of his life. Currently, Noah has been diagnosed with a "severely impaired speech delay" and his expressive and receptive language is functioning around a 12-month-old level. Today, we see 6 doctors in total on a frequent basis (pediatrician, geneticist, endocrinologist, dietician/nutritionist, eye doctor, and allergist) and 2 speech and language pathologists 3 times a week. We are also participants of 2 research studies to further the knowledge and data present about Galactosemia. Given these things, we count our blessings as he could have more severe effects from his disorder. In the years to come, as he moves closer to puberty, we will have to intervene more as he is expected to begin a rapid decrease in bone density, as many Galactosemia individuals experience. Doctors also predict at some point he will have to be placed on a calcium supplement, as well.

We stay vigilant about his diet, doctor's appointments, and speech therapy sessions, but we also hold onto hope that one day there will be some sort of treatment available to us to offset some of the effects felt from being diagnosed with Galactosemia. We are thankful and blessed

to have him here with us, as he is the most amazing little boy I have ever met. He is kind, genuine, smart, loving, hilarious, and so social despite his speech delays. He loves fire trucks, playing outside, reading books with family members, and everything Disney including Cars, Toy Story, Elemental, and Turning Red. He plays soccer in a soccer league for 2 year olds and has a social speech group once a week where he interacts with other little kids that have speech delays. He is my whole heart and he deserves the world. He deserves to have his story heard. He deserves change and action.



Tori Murphy (mother), & Noah Murphy (patient with Galactosemia)
From: Smithtown, NY



To the members of the Aging Committee,

Our names are Joseph and Joanna Gattuso, and our son, Alexander, has a rare genetic disease called Barth Syndrome. We are a family of four living in Long Island, New York.

Barth Syndrome is a rare metabolic disease that affects all the muscles in the body, primarily the heart, causing cardiomyopathy, feeding issues, and extreme fatigue. It also causes recurring infections due to small numbers of white blood cells (neutropenia).

Due to his condition, Alex is exclusively fed via a feeding tube everyday, and will require heart medication for the rest of his life. What is most distressing to us as parents, is the fear of what the future may bring, unless advancements in treating his condition are not made. Not only are we concerned about the physical limitations he faces, it will also create obstacles from a social and mental aspect. As times goes on, and he becomes self-aware of his limitations, it will be challenging for him to maintain a certain level of confidence.

We will continue to do everything within our power to help Alex, but we really need your help in order to make ignificant, and a meaningful impact on improving Alex's quality of life. Knowing that there is an effective drug in existence with virtually no side-effects, our children deserve the opportunity for advanced treatment to be readily, and easily accessible.

Sincerely,

Joe and Joanna Gattuso

Deborah G. | New York

Age: 53
Year of Diagnosis: 2019
Type:

We Can't Wait

We need a Cure. It doesn't matter if it's approved prior to trying.

I was diagnosed with PLS and impact on my daily life is terrible. **Life is not good.**

It's hard to live with. Please help.

Adam S. | New York

Age: 41
Year of Diagnosis: 2017
Type: Bulbar Onset, Limb Onset, Sporadic

We Can't Wait

Extremely important to have access to medicine.

Not important to me to worry about anything else that could happen by taking this medicine.

It has destroyed my life

It has destroyed the life of my family

That there is no cure

Please give us a chance to try new medications that have passed Phase 1 and 2 trials

Todd W. | New York



Age: 56
Year of Diagnosis: 2019
Type: Bulbar Onset

Any help would be a positive, give hope where there is none.

Anything is better then nothing, right now there is NO hope to live, née drugs may not help but there may be a chance which is something ALS patients don't have now.

Todd would have tried anything for a chance to live, he died only 14 months of being diagnosed. I don't feel the FDA has to approve something when there is no hope.

There is NO life anymore, ALS took his life.

Losing Todd has been a nightmare for myself and his children. It's a death sentence, and it doesn't have to be- whether it be through drugs or herbs

I'd like them to help people not their pockets.

Lucyna D. | New York

Age: 58
Year of Diagnosis: 2020
Type: Bulbar Onset

We Can't Wait

A new therapy would give hope.

ALS itself is a death sentence. It is worth to try any treatment. It was not important to wait for FDA approval.

It was devastating news for the entire family. We can't take this much longer.

That anybody can get it and also that it can impact cognitive skills.

People with ALS diagnosis cannot wait long time.

Michael O. | New York

Age: 59
Year of Diagnosis: 2015
Type: Limb Onset, Sporadic

We Can't Wait

ALS has Changed everything. I cannot walk and I am in a wheelchair. **Any medicine is important.**

It has made my caregiver life more difficult

That it is terminal, and we need therapies to slow it down

Give me access to experimental drugs now

CQ. | New York

We Can't Wait

Age: 60
Year of Diagnosis: Brother: 2018
Type: Bulbar Onset

Imperative!! It is imperative to have a chance to try something that will help my quality of life.

Current therapy has side effects and current therapy has limited duration too but better to have it than not have some options.

Death sentence and frustration that a cure cannot be found. My brother's life expectancy is nearing the end of a torturous 3-year period

Devastated our family. My Brother is currently 60 years young ALS is also a very expensive disease and often people always need to wait for insurance approval which Is very frustrating. Waiting for approval for breathing equipment can take weeks !!

It is a devastating generally short-lived disease that therapies cannot stop the progression. **People with ALS are the most determined and strong fighters I have ever witnessed. They deserve any consideration for any new medication therapies to give hope to those fighting this monster.**

Find a cure.

Henry C. | New York

Age: 73
Year of Diagnosis: 2003
Type: Bulbar Onset, Sporadic



We Can't Wait

Every improvement is a blessing, and I would prefer no advanced side effects.

I would like to try before full FDA approval

ALS has devastating changes in Lifestyle and perspectives. It is simply daunting. It is torture.

Give us an option to try new medicines.

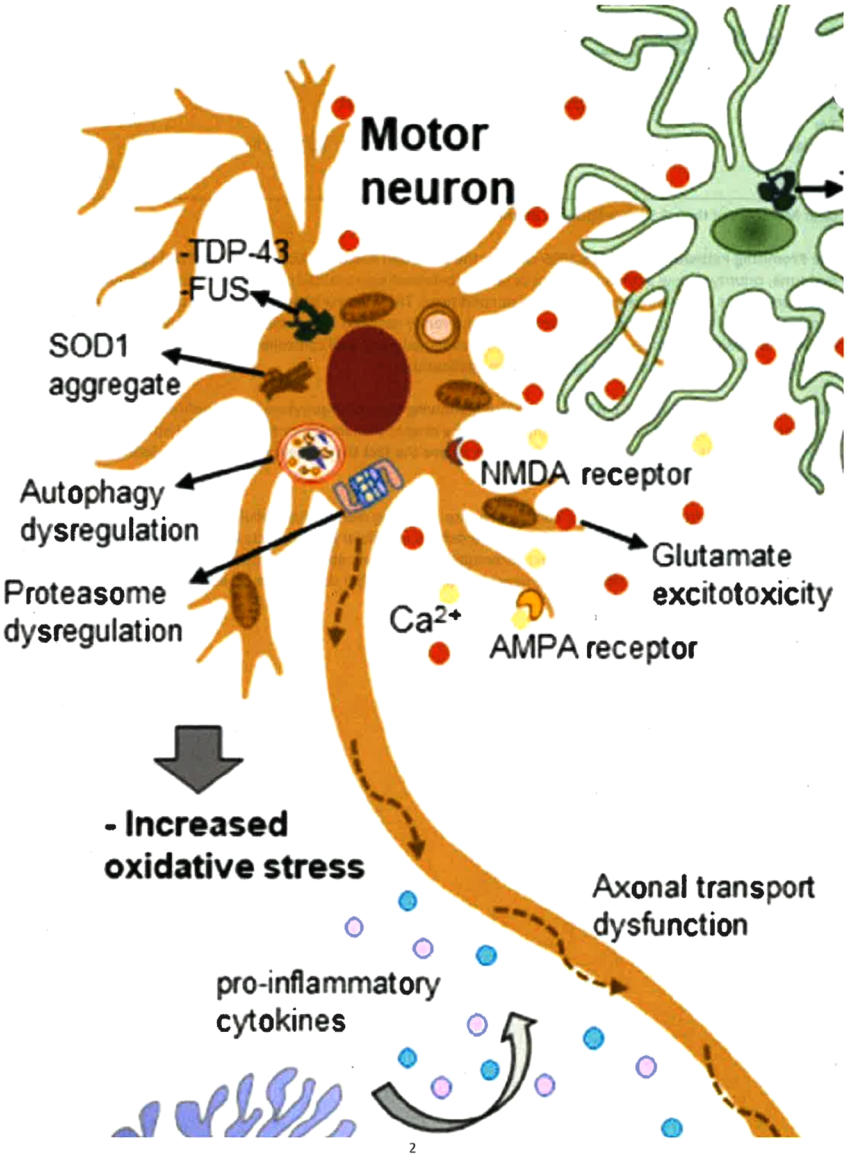
[redacted]

Dear Members of the US Senate Special Committee on Aging:

The **Promising Pathway Act (PPA) S.1906** calls for the U.S. Food and Drug Administration (FDA) to establish a rolling, real-time, priority review pathway to grant or deny provisional approval status for drugs intended to treat, prevent, or diagnose serious or life-threatening diseases or conditions. The granting of provisional approval requires demonstration of substantial evidence of safety (the same level as currently required for standard FDA approval) and relevant early evidence of positive therapeutic outcomes based on adequate and well controlled investigations. **The PPA also allows for the use of real world evidence to support an application.**

"Real world evidence" means patients are clinically showing signs of improvement, as confirmed by their health care providers. "Real world evidence" means that if during a drug trial a laboratory test does not improve, or statistical parameters are not achieved, then **the FDA cannot ignore the fact that patients and their physicians are testifying to clinical functional improvements.**

ALS (amyotrophic lateral sclerosis) is a complex disease, affecting many varied cellular functions, and **science does not yet know the definitive cause ALS.** In ALS there are defects in cellular DNA, defects in mitochondria (the energy powerhouses of the cell), abnormal protein accumulation in the cell, abnormal vesical transport in the cell, too much of the excitatory compound glutamate at the nerve junctions, and other defects (see attached diagram).


Motor neuron
-TDP-43
-FUS
SOD1 aggregate
Autophagy dysregulation
Proteasome dysregulation
NMDA receptor
Glutamate excitotoxicity
Ca2+
AMPA receptor
- Increased oxidative stress
Axonal transport dysfunction
pro-inflammatory cytokines
2

The need for the new – but not new - approach is obvious once all realize that "we do not know the math yet – we need to invent the math".

In the movie Hidden Figures the NASA chief tells his staff: "What I'm asking everyone in that room to do, all my geniuses, **is to look beyond the numbers.** To look around them, through them, **for answers to questions we don't even know to ask."** The movie focuses on the first manned Earth orbit by John Glenn in February, 1962. John Glenn agreed to the launch only after he knew that Katherine Johnson had calculated and confirmed the trajectories.

We are today, in this meeting with you, looking for answers to questions we don't even know how to ask. The answer is the patient is improving. The question is "what causes ALS?" We don't know what causes ALS. At this early stage of trying to cure this disease, a disease that has minimal federal funding dedicated to researching its cause and cure, many times all we will initially have, as patients and researchers, to show the FDA – is that we are improving. **But I can't tell you why – because we don't know what causes the disease, and I don't have any laboratory test to show you I am improving. Stop it ! – and just look at me !**

The PPA provides for *provisional* approval only, for two year periods up to eight years. Patients must participate in an observational registry. The FDA must review the registry annually and shall withdraw provisional approval if a drug has serious side effects or is ineffective. Drugs must meet existing standards for full approval. In sum, the PPA provides a pragmatic pathway for the FDA to provisionally approve drugs for **individuals with rapidly progressive terminal illnesses who will die of their diseases waiting for the usual FDA approval pathways to unfold.** Provisional approval would be subject to full FDA guardrails and oversight.

For individuals with rapidly progressive and 100% fatal diseases like ALS, timely access to promising therapies is essential and offers an opportunity for survival. **Even the FDA's current expedited pathways are insufficient. For example, the FDA's "accelerated approval" pathway allows for drug approval without evidence of direct clinical benefit in certain circumstances if a drug's effect on a biomarker (a biological measurement) is likely to predict clinical benefit. Over 95% of ALS cases do not have an accepted biomarker. Withholding promising and safe therapies until evidence of efficacy under current FDA standards is met means certain death for those with ALS.** The status quo can result in an unwarranted loss of life. The PPA affords patients access to safe therapies that have shown promise while the process of gathering additional evidence of efficacy proceeds. The PPA requires the FDA to withdraw provisional approval if such evidence is not provided. The PPA also preserves efficacy standards for final drug approval. **Please support efforts to bring safe, promising therapies to more people living with terminal diagnoses pending full FDA approval.**

Marcus Noble is 36 years old, and had spent 3 courageous years living, and fighting, against the worse disease known to man.

I have been through a series of lasts with Marcus: Last time he walked without a limp. Last time he walked without a cane. Last time he walked without a walker. Last time he climbed stairs. Last time he could walk at all. Last time he could use hands to control his power wheelchair. Last time he could cut his food. Last time he could swallow food. Last time he could use fingers to play his video game controller. Last time he hugged me. Last time he talked ..... I was not there when he spoke his last words ..... to his wife Emily ..... who only 5 years ago he spoke his wedding vows to. Last time he thought about starting a family of his own. Last time he laughed.

Marcus can still breathe. Marcus can still communicate with eye-gaze. Marcus can still drive his wheelchair with eye-gaze. Marcus can still obtain all nutritional needs via his gastric tube. Marcus can still feel happy and feel hope and bring joy to all.

Margaret Mead, the renowned anthropologist stated: "Never doubt that a small group of thoughtful, committed, citizens can change the world. Indeed, it is the only thing that ever has."

BE THE FIRST TO STOP THE LASTS. SOMEONE HAS TO BE THE FIRST.

I share with you for reflection, another dialog from the movie Hidden Figures. Mary Jackson (the mathematician) to the Judge: "And I, Sir, plan on being an engineer at NASA, but I can't do that without taking those classes at that all-white high school. And I can't change the color of my skin. So.... I have no choice but to be the first, which I cannot do without you. Your Honor, of all the cases you hear today, which one will matter in a hundred years? Which one will make you "the first?""

OF ALL THE DECISIONS YOU MAKE IN YOUR LIFE, WHICH DECISIONS WILL MATTER IN A HUNDRED YEARS? WHICH ONE WILL MAKE YOU THE "FIRST"? ..... THE FIRST TO ENABLE PATIENTS TO ACCESS THERAPIES BASED ON THE FACT THAT THE THERAPY WORKS FOR THEM, EVEN IF THERE IS NO ABILITY YET TO PUT DOWN ON PAPER WHY THE THERAPY IS WORKING.

The patients you are hearing from, and about, today have within themselves the capability to create meaningful improvements in their own health. However, these individuals, these beings, cannot do it without you. Give hope. For those who only have their thoughts left, let those thoughts be full of hope. There is a long way to go still, to cure this beast of a disease ALS. This small committee can change worlds.

Attached are photos of Marcus and wife Emily Noble and a photo of younger Marcus. We are asking you to let us help ourselves get back our time.



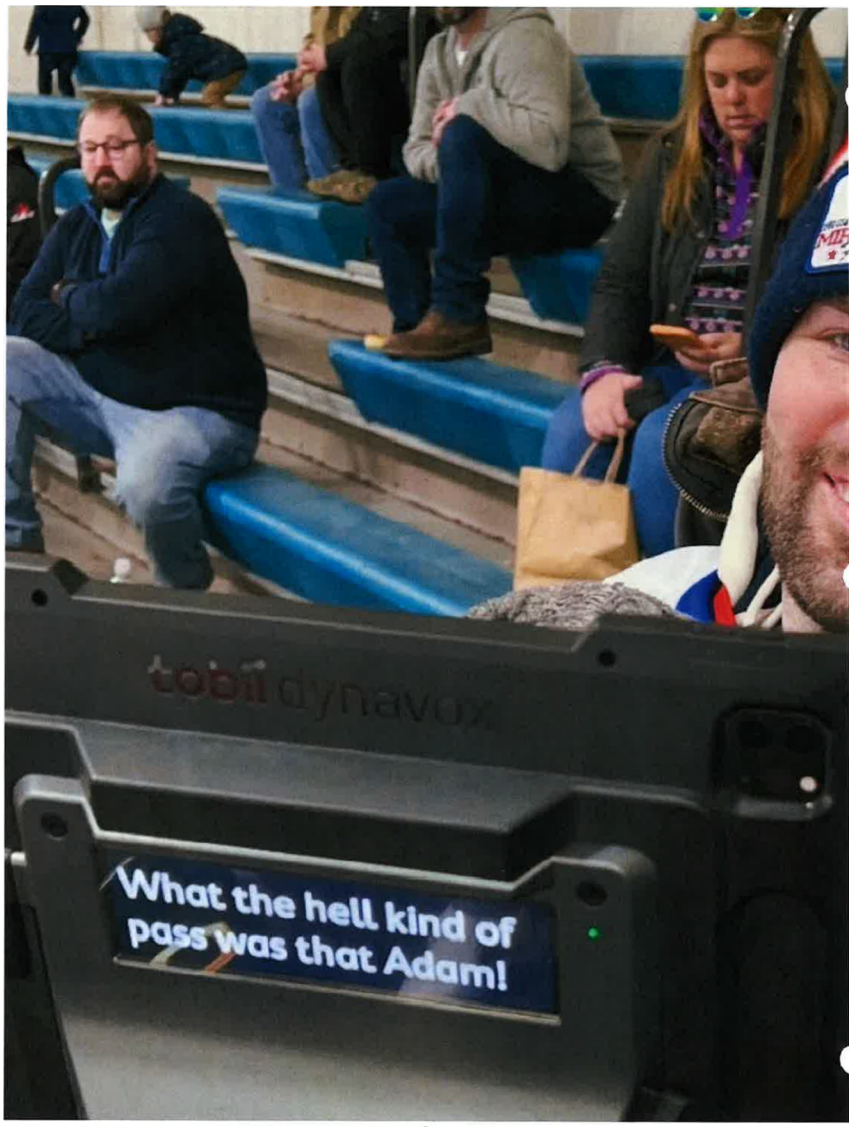
5

"Oh I don't know
What's around the bend
All I know is that my love
It knows no end"

📸: @Whiting Photography
Stephen Whiting



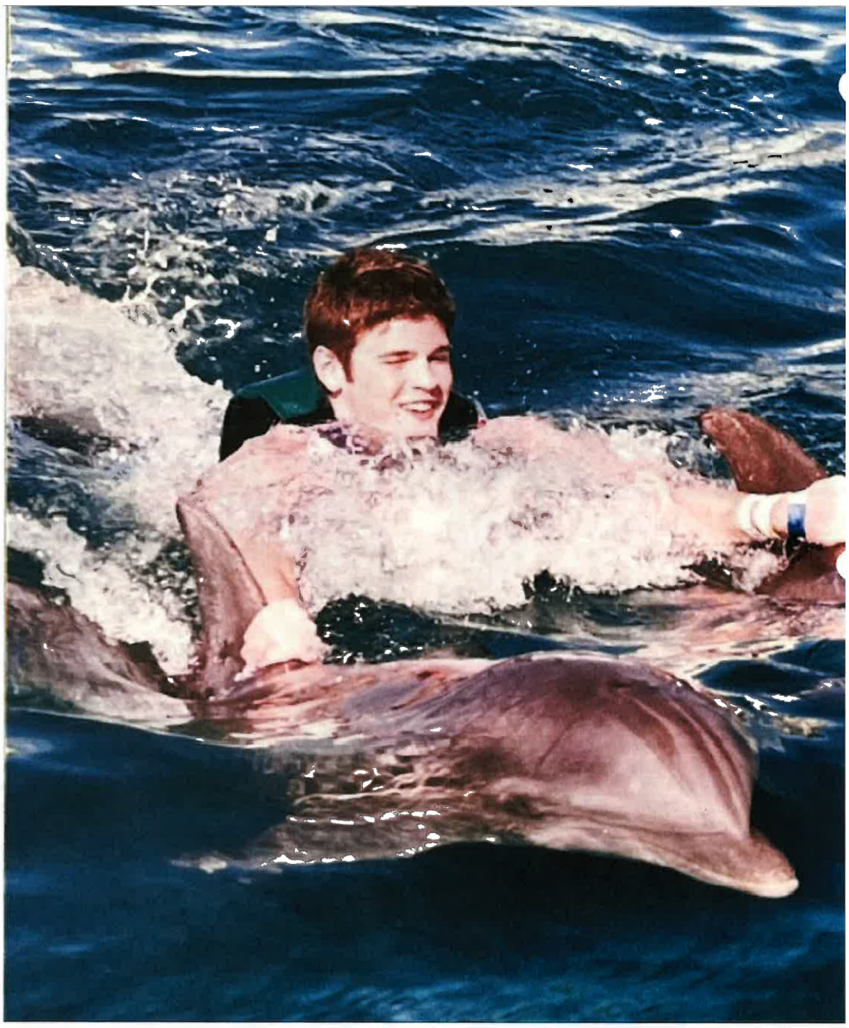

Happy Thau



8


4:42
NORTHSTARS
"When you pull on that jersey, you represent yourself and your teammates. And the name on the front is a heck of a lot more important than the one on the back!"
ADIRONDACK YOUTH HOCKEY ASSOCIATION
NYDER'S

9



Regards,
Mary Frances Kusior MD
Marcus Noble's Mom

Board Certified Internal Medicine, Anatomic Pathology, Clinical Pathology
2 Brentwood Drive
South Glens Falls, NY 12803
518-744-8299

Sent from my iPhone

[redacted]

I was a late friend of Corey Polen; it was clear we had similar viewpoints, language, and shared a dark humor. Through Corey I became more familiar with the Promising Pathway Act, which resembled a model I'd cobbled together. ALS is an exceptionally dismal disease and as such deserves exception when it comes to treatment. Social Security and Medicare already recognize ALS as a special circumstance and approve coverage automatically. Similarly, the FDA should make exceptions for safe and promising treatments for ALS instead of applying stringent, universal criteria that virtually no ALS candidate could meet, given the heterogeneity of the illness. The most recent example of course is NurOwn, which was hammered viciously in its recent AdComm with the FDA. In fact, evidence has arisen of collusion between the FDA, the National ALS Association and at least one patient advocate to ensure NurOwn's demise. (This is an admittedly incendiary statement that I hope will be validated by investigative reporting and lead to a congressional investigation.) As a PWALS I was optimistic about a possible lifeline with NurOwn; now I'm back to end-of-life planning. I only wish one or two of the exhaustive, condemning statisticians with all their charts and graphs could spend ONE day in my body and grasp the bigger picture.

It is enough to be hurled into a tortuous and rapid demise for apparently no reason; it is inconceivable that so many forces exist to push back against "possibility" to maintain a status quo of "reasons why not."

I truly hope the PPA will be passed and provide some renewed hope to PWALS and other rare disease sufferers. I ask only one thing: please hurry.

Thank you.

Pete Macnamara
NYC .

[redacted]

Ranking Member Senator Braun and Honorable Members of the Senate Special Committee on Aging

It's been a while since we've been in touch. We wanted to offer an update on what my big sister Mayuri is up to! As you know she has advanced stage ALS.

Mayuri had to take a step back from advocacy because of health changes. She was influential in the passage of the Act for ALS Bill, signed by President Biden. But these days, she gets tired from using her eyes to do everything; from typing her medical needs, to conversing with caregivers and loved ones, to browsing the web, social media, and even calling for help. In essence, Mayuri's eyes are her only connection with her outside world. So she's understandably trying to rest them whenever she gets a chance. Day and night, she only gets to rest her eyes for a maximum of 3-4 hours of unbroken sleep at night. So we're trying to ensure her eyes get some TLC while she interacts with you (You can follow her on X, formerly known as Twitter, @Mayuri_Saxena)

In regards to her care, we continue to experience chronic staff shortages that continue to affect our mother's health. Our mother, now in her mid-70's, still pulls multi-day shifts (some lasting up to 48 hours or more) when aides/nurses are "no shows", or if the shift simply isn't staffed. Since being forced to retire, this ongoing demand has started to take its toll on our mother - with sciatica, accelerated arthritis, and sleep deprivation / exhaustion. This is why we rely on a privately paid caregiver who stays committed - though it's only part-time.

Time and time again, we are shown that there is no actionable steps being taken to give terminally ill ALS patients access to treatments that can help. Time and time again, the silent torments we caregivers experience is never accounted for when we fight for our own livelihood, for our own mental health, and pursuit of autonomy and happiness. Time and time again, we are left on islands - by insurance, CMS, by our government, by agencies that provide nurses and home health aides. We're always fighting, and feel like no one cares for our chronically ill, and medically demanding tasks of our dying loved ones.

With many thanks,

- Mayank Saxena (brother of Mayuri)

Dear Senator Braun,

I am reaching out to you in response to your request for stories on the unmet medical needs faced by people with rare, progressive, and serious diseases for a hearing by the Special Committee on Aging to be held on October 26, 2023.

I am the Senior Manager of Disability Programs at the Huntington's Disease Society of America (HDSA), a leading national organization dedicated to the care and cure of Huntington's disease (HD). HD is a rare and fatal hereditary disorder that manifests as a neurological disease with both physical and psychiatric components. The mission of HDSA is to promote and support research to find a cure for HD; help people and families affected by the disease; and educate the public and healthcare professionals about HD. Currently, there is no clinically available pharmacological, biological, or surgical agent or method that slows or stops the progression of HD.

I have been working with the HD community for eight years, first as a disability attorney who specialized in representing HD families, and now as the Senior Manager of HDSA's Disability Program. It is truly a privilege to work with the HD community.

From my work as a disability attorney, unmet medical needs are a huge issue for the community. So many of my former clients went years with a misdiagnosis, delaying incredibly important care. An equal number of former clients were told by medical professionals that there were no options and there was nothing they could do for their HD. While there isn't a cure for HD, early medical intervention in the form of clinical care, physical therapy, occupational therapy, and behavioral medication management can improve quality of life for years. Starting medical care also creates a medical record for HD families when they inevitably have to apply for disability.

So many of the HD families I have work with had to fight tooth and nail for Social Security disability because of delayed or limited care. Incomplete medical records and limited treatment plans have a detrimental impact on the HD community. Families who do not see an HD specialist do not get the true level of care they need, which often makes it appear that their HD is not as progressed or "bad" as it truly presents.

Working closely with medical professionals, HD specialists, and reading thousands of pages of medical records, it is clear that most primary care physicians and unspecialized neurologists do not have the expertise necessary to treat HD patients. They fail to order beneficial HD tests, like neuropsychological testing or other cognitive testing, and fail to refer patients out for therapy, physical or behavioral. HD is a physical, cognitive, and behavioral disease, but most unspecialized physicians only see it as a movement disorder, which ignores 2/3rds of the disease. Many HD-impacted individuals are denied treatment options that could help with symptom management and quality of life simply because they are not given the option. This is not a critique of the medical profession, but an honest observation that there is a limited understanding of HD and only a limited number of specialists truly trained in the vast complexities of HD.

HD families also face discrimination regarding unmet medical needs by doctors and care providers who refuse to participate in the disability process. The people best equipped to speak

on the complexities of a patient's medical condition are their doctors. Expecting a disabled individual to successfully apply and navigate the complex disability system without help is discrimination and ableism at its finest. Approval for disability is also closely tied to continued access to medical care because of the healthcare benefits that accompany the financial benefits. When a patient cannot afford to get medical care they often do not continue to seek medical care.

The average onset of HD is between 35-55, meaning people who have HD will have to stop working as a result of this disease and will require disability benefits. No one can get approved for disability without a medically determinable impairment or medical proof the condition is disabling. With a rare medical condition, this burden is even higher because individuals have to show they have a medical condition that impacts their ability to work and live and often bear the burden of educating the reviewers on the disease itself. The disability process is made substantially easier with assistance and support from a treating physician and care team that is willing to write a letter, assist with medical record retrieval, and provide general support.

Additionally, HD-impacted individuals often have a hard time finding placement at care facilities. They are denied access because they are too young, have too many behavioral health concerns, or pose a physical risk, which leaves families without care options. Late-stage HD requires highly specialized help and 24-hour care. One family couldn't find a facility because their HD-impacted loved one was considered a flight risk and had gotten out of three facilities. Recently, another family was trying to find a facility for an HD-impacted loved one before they were discharged to the street.

Furthermore, unmet medical needs in the HD community can lead to homelessness and jail time. HD is progressive, but appropriate medical intervention and treatment can help with coping mechanisms, care plans, and necessary safety measures. HD-impacted individuals who do not get medical care for their HD are more likely to struggle legally and financially and lack safety measures. They struggle with impulse control, issues with judgment, and lack of insight and awareness. A specialized medical care team can help with appropriate interventions.

While the ultimate goal is to find a cure for HD, providing resources to meet current medical care needs will go a long way for the HD community. Access to specialists, appropriate treatment plans, physical, occupational, and behavioral health therapy, and care facilities will improve the well-being of the HD community, both impacted individuals and caregivers.

Thank you for the opportunity to share my experiences and for considering the needs of the HD community.

Sincerely,

Allison Bartlett, Esq.
Senior Manager Disability Programs, HDSA
505 8th Ave, Ste 902
New York, NY 10018

Cristina M. Brennan, Esq.
STXBP1 Foundation Board Member and Mom
30 School Street, East Williston NY 11596
cristinabrennan@gmail.com 516-782-4276
www.stxbp1disorders.org

To: Hon. Sen. Mike Braun (R-IN) and all members of the U.S. Senate Special Committee on Aging

From: Cristina Brennan, parent/caregiver of rare disease patient

Date: October 25, 2023

Re: Story Submission for hearing on October 26, 2023, re: Unmet medical needs experienced by people with rare diseases

Thank you for your interest in our rare disease story. The subject of this tale is currently only 11 years old, but his story should still be of interest to the Aging Committee because, without a cure or treatment, he will need 24 hour care and supervision until his death.

My son, Tristan Brennan, is 11 years old. We live on Long Island, New York. Tristan has the cognitive ability of a 12 month old. He is in diapers. He cannot speak or communicate. He has seizures. He cannot feed himself and is a choking hazard. He can walk – but has no safety awareness and will run directly into traffic if not guarded at all times. He cannot understand or express "yes" or "no". If he is hurt, he cannot tell us where the pain is. If he is hungry, he cannot tell us he wants to eat. Despite the fact that he is the age of a 6th grader, he cries like an infant until we guess what he needs.

He is diagnosed with: STXBP1 (rare genetic mutation), HARS genetic mutation, Autism, Intractable Epilepsy, Cortical Vision Impairment, Global Developmental Delays, Hypotonia, and more. He is categorized as Profoundly Intellectually Disabled.

Our story:
Tristan was born on October 23, 2012. As our baby grew, it became clear that he was not meeting the milestones of a typical child. He was not speaking, sitting up, giggling or attending to the people around him. This was the start of a 5 year debilitating diagnostic odyssey. No doctor could tell us what was wrong with our son, why he was having seizures, or why he could not speak.

Month after month, year after year, appointment after **DIS**-appointment, every doctor sent us away with a shrug. "I don't know what's wrong with him, but it's not Autism," was the most prevalent prognosis.

Trying to get therapies like speech, PT and OT, as well as services, like ABA or financial assistance, was so difficult because we had no official diagnosis or ICD code. We had no proof of his disabilities.

As torturous as those 5 years were, we never lost hope of finding the source of his delays. We were going to find it and we were going to fix it. Then this happened in March 2018. A lab tech from a geneticist's office called and said this, "Your son has an incurable, unknown genetic mutation that will cause him to be profoundly mentally retarded, autistic, mobile-ly challenged, and he will develop progressively worsening epilepsy that will eventually take his life. In addition, he has a second gene mutation that may take his sight and hearing from him as he grows. Lastly, we don't know anything about his rare condition; there is no known course of treatment. Call us if you have questions." CLICK.

In one run-on sentence, that lab tech stole our HOPE, which was the only thing that had carried us through each day for 5 long years.

But, we finally had a diagnosis. Our son's delays are caused by a mutation of the STXBP1 gene. At the time of diagnosis in 2018, there were 300 cases worldwide. Today, there are more than 1,000. By the way, **6 years post diagnosis, we still do not have an ICD code!**

We were left alone and unsupported as we processed the shock that comes with hearing that your child has a permanent disability. Doubled by the fact that it will worsen. Tripled by the fact that there is no cure. Quadruped by the fact that no doctor had ever heard of it, and most didn't even bother to Google it. We felt abandoned by the medical community.

In the 6 years since Tristan was diagnosed with STXBP1, thanks to Facebook, we have connected with other STXBP1 families across the globe, and have created our own routine of therapies to attempt to address our son's symptoms.

To cope, and to create action, I have joined the board of the STXBP1 Foundation to raise money and awareness for research to treat or cure STXBP1. Made up of parent volunteers, we recently had an FDA PFDD meeting and are gaining momentum for potential drug trials and gene therapies for STXBP1. We are running a Natural History Study for STXBP1 in coordination with major hospitals including Childrens Hospital of Philadelphia, Texas Childrens Hospital, Weill Cornell Medicine (NY) and Childrens Hospital Colorado. But, we need so much more money than our small group of parents can raise.

I have found a neurologist and a neurogeneticist who want to help people with STXBP1. My son is currently in a drug trial through Weill Cornell repurposing a drug that costs $1.2 million per year. Once the trial ends in 2024, we do not know how we will continue to get access to this drug. It is called glycerol phenylbuterate, aka Ravicti. It is mostly controlling Tristan's epilepsy and may help boost cognitive improvement.

Without a cure or treatment, the children with STXBP1 get sicker as they age. Some die in their teenage years. The worst symptom, intractable epilepsy, slowly takes away what little progress these children make. Soon, Tristan will not be able to point to things he wants, then he will lose the ability to swallow, to walk, to breathe. We are in a desperate race against time to find a treatment or cure for this ultra rare disorder and improve Tristan's quality of life.

We have encountered multiple unmet medical needs along this journey to date.

The first unmet medical need is **a lack of education and resources for doctors about rare diseases.** Throughout our search for a diagnosis, we felt abandoned and ignored by most of

the doctors. It was hard for us to understand at the time, but the doctors had no idea what to do either. Simply starting with genetics testing could have taken years off our search.

Another unmet medical need is the **lack of guidance given to our family once the diagnosis was finally identified.** Even if the geneticist did not know how to treat our son's genetic disorder, the very least he could have done was tell us in person and let us ask questions or speak to a social worker.

A third noticeable unmet need is the **unwillingness of the FDA to assign an ICD code to this rare disorder.** Lack of a code prevents us from identifying other patients, prevents researchers from collecting and analyzing data on this disorder, and curtails the services that insurance companies will cover. My son is "lucky" to have an Autism diagnosis, which is the only way his behavioral services are covered. I still pay approximately $1,500 per month for copays and non-covered therapies.

Daily care is another unattainable and unmet need. We cannot find competent caregivers, called "community habilitation workers" in NY, because the pay is so low. Nonverbal children are ripe for abuse, so I have given up my career to care for my son.

Perhaps the biggest unmet medical need is a **lack of research and funding for research.** Rare disorders are often ignored because they cannot be monetized. Pharmaceutical companies cannot profit from curing only 300, or even 1,000, children suffering with STXBP1. There is no incentive for pharma to fund research for these patients. If the parents don't do it, no one will. Full stop.

October 25, 2023

Dear Senator Braun,

I am reaching out to you in response to your request for stories on the unmet medical needs faced by people with rare, progressive, and serious diseases for a hearing by the Special Committee on Aging to be held on October 26, 2023.

I am a participant in programs offered by the Huntington's Disease Society of America (HDSA), a leading national organization dedicated to the care and cure of Huntington's disease (HD), a rare and fatal hereditary disorder that manifests as a neurological disease with both physical and psychiatric components. The mission of HDSA is to promote and support research to find a cure for HD; help people and families affected by the disease; and educate the public and healthcare professionals about HD. Currently, there is no clinically available pharmacological, biological, or surgical agent or method that slows or stops the progression of HD.

As a young mother, I helped to care for my mother with Huntington's disease. She could no longer feed herself nor walk nor talk to me on the telephone. Now I am 48 years old and my own Huntington's disease symptoms have progressed to the point that I rely on my husband, who works full-time to care for me. We cannot get modifications made to our home, nor hire a care assistant to care for me while my husband works

I was diagnosed in 2013 and applied for SSDI. It wasn't until early 2016 that I was able to 'qualify' for Medicare. That was 2 years that I didn't receive critical therapy services. Please support immediate Medicare qualification for those who have neurodegenerative diseases. We can't afford to wait 2 years for medical care and therapies.

My sons are now 22 and 17. They are both at risk and I pray that they have an easier time procuring services than I have had. I was a taxpayer for 20+ years while I worked as a social worker. Please do whatever is in your power to provide quality life for my remaining years.

Thank you for the opportunity to share my story.

Since I can no longer use a keyboard, I have given permission to my friend and advocate, Ruth Stanton, to relay my story.

Sincerely,

Adriane Burdette Robinson
8106 Mapleway Lane
Greensboro, NC 27455-9265
and
Ruth Pridgeon Stanton
13 Donnybrook Ct
Durham, NC
919-451-3234

Shelly Hoover
Clayton, NC



I'm a daughter, wife, mother, grandmother, sister, and friend. I'm a US Navy Veteran and have lived with ALS for over ten years. I'm now paralyzed from the neck down and rely on a tracheostomy and ventilator to breathe. My husband, Steve, quit his job at the height of his career to care for me. My children have altered their lives to take care of me.

I'm using my eyes to type this statement with eyegase technology. I use the same technology to advocate fiercely for people living with ALS.

I was an educator and a middle school principal. ALS forced me to abandon the career I had worked for all my adult life. I was a runner and athlete, and in the best shape of my life since bootcamp. ALS has robbed me of every physical function. I can't scratch my nose.

I've observed a deadly slow drug approval process for ten years, providing zero disease-altering treatments. There must be a different drug approval process for fatal diseases with unmet treatment needs. ALS is not erectile dysfunction or toe fungus, yet the FDA treatment approval process is the same. That is simply cruel.

Solid science is paramount. But the science is feckless if I die waiting. We must find a better way.

Thank you for taking time to hear my story. Thank you for finding an efficient, humane way to approve effective treatments. -

With hope and gratitude,
Shelly Hoover, EdD

Diane C. | Matthews

We Can't Wait

Age: 51
Year of Diagnosis: 2020
Type: Limb Onset, Genetic

I think this is very important to have access to drugs now. A diagnosis of ALS often means a diagnosis of a life expectancy of 3-5 year. A few months can increase the possibility for eligibility for further treatments until there is a cure or a treatment that can slow symptoms even more.

At this point I feel like I don't have much to lose. I am dying either way. Again, I am in favor of trying something rather than just letting ALS win with no fight. I took the COVID vaccine that was developed very quickly and provided emergency dosage use authorization and would easily do the same for ALS treatment.

ALS has had a dramatic influence on my life. I have had to stop working as a school social worker (a job I loved). My family has had to move because of having too many stairs. I have not been able to help with making our new house our home (unpacking, painting). I can no longer cook, clean, or walk the dog. Everything I do requires so much planning and effort that I just don't want to do them. Even typing this is as struggle as my hands and fingers are weak and clumsy.

My family has been great, but it is hard. My children are 16 and 19. I've always been the primary caregiver but now they have to help me with so much. My husband now does most everything around the house and it has been very stressful for him. **We can't wait. That's the bottom line.**

My father was diagnosed with ALS in 1998 and died in 2000. I was shocked and disappointed that there was still so little in therapies (only one new one) for treatment 20 years later when I was diagnosed with ALS. **I can't wait for the long drawn out processes the FDA uses because I am dying. My siblings and children can't wait either as they are at high risk for receiving this diagnosis too.**



CONNOR GEORGE

Jamestown, ND

Connor was diagnosed with Medulloblastoma in October 2020 when he was 2 years old. Three months after finishing treatment he relapsed and he underwent treatment once again.

Why the Promising Pathway Act is Important to our Family: Scans today are currently clear but we know that can change at any moment, which is why the PPA is so important to us. If Connor relapses again, we are basically out of treatment options. Currently, promising trials have to be tested on adults first, for a series of phases. Only at a certain point can it be offered to children. We don't have that type of time. We need promising options to be offered immediately or more quickly to our children as time is limited. Our children are our future, we need to do whatever is possible and as quickly as possible to save them. The PPA gives us the chance to attempt trials that otherwise would not be an option.

Brooke George

Mother of Connor

KEATON SUNDEEN

Jamestown, ND

Keaton was diagnosed with DIPG on May 6, 2022. Doctors told us that we had 6-12 month with him. DIPG is an incurable cancer. We could try a few things, but basically, there is no cure. Keaton received 10 rounds of radiation at Mayo in Rochester, MN as part of a clinical trial. Keaton's tumor was shrinking during his last scans on June 9, 2022. However, after flying to Florida for a family vacation, Keaton brain's starting hemorrhaging. There was really nothing left to be done, and Keaton passed away in our arms on June 13, 2022, the day after his 9th birthday.

Why the Promising Pathway Act is Important to our Family: Why the Promising Pathway Act is important to me because all children need a chance to live. Parents should not have to bury their child. We need to do everything we can, use every resource we can, to do the best for our kids to give them the longest and best life possible.

Jennifer Sundeen

Mother of Keaton



ELENA DESSERICH

Cincinnati, OH

The fight for the "homerun cure" and DIPG research, in many ways, started to gain momentum with Elena. Diagnosed in 2006 at the age of 6 with Diffuse Intrinsic Pontine Glioma, her public battle and determination from her parents formed the basis of The Cure Starts Now Foundation, 135 trials and $30 million invested in both research and support. Learning that many experts felt the future of cancer research might come from DIPG research, but that it was generally considered a "lost cause"; her parents wrote what they considered to be a private blog questioning how we prioritize cancer funding in April of 2007. The last words of this journal were the words "the cure starts now" and with it started the cause that today is the largest funder of not only DIPG and DMG research but also the only "homerun cancer research" organization in the world.

Elena's lessons during her battle were more private. In the 9 months after her diagnosis, she quietly left behind notes of love and support for her family for them to find after her passing. Her heart picture, "I Love You" came to symbolize not only her love for her family but today is the logo for the charity. During her battle she lost the ability to speak and ultimately turned to her notes to express her feelings. She died in August of 2007. After her passing, her parents shared the notes they found, urged by friends to combine this with their blog in a book to tell the world the importance of this cause. Several years later, they did, ultimately becoming a New York Time bestselling book translated into 22 languages worldwide.

Why the Promising Pathway Act is Important to our Family: Elena's story isn't about the cancer. It is about the resilience of these children and our need to do more. During her fight we were told that we should "go home and make memories" because there were no options available to us and no trials that were open to her type of cancer. The Promising Pathway Act, had it been in effect earlier, might have helped with this – thus allowing pharmaceutical companies to see promise in those cancers

that the experts believe might just offer us clues to cure all cancers through those that we can learn the most from. Instead of excluding our children from trials, this will allow our society to prioritize those "rare" pediatric cancers that have no current path beyond the lab – and allow families to never again be told to "make memories" rather than to have the power to fight the cancer.

Brooke Desserich

Mother of Elena



MADISON SEYFRIED

Cincinnati, OH

Madison was diagnosed at 15 months old with anaplastic ependymoma. She had two brain surgeries one to remove the tumor, proton radiation 33 rounds and 4 cycles of chemotherapy at Cincinnati Children's. She is now 4 years old and has had stable scans with no tumor recurrence. She continues to be monitored every 6 months.

Why the Promising Pathway Act is Important to our Family: Why the Promising Pathway Act is important to you- It is important to me as a parent with a child with pediatric brain cancer that we do everything in our power to eradicate pediatric brain cancers of all types. Including increased funding and research. Every child deserves a chance to grow up free of cancer. I ask for your support in passing the Promising Pathway Act.

Carrina Waneka

Mother of Piper



ASHTON HAWKINS

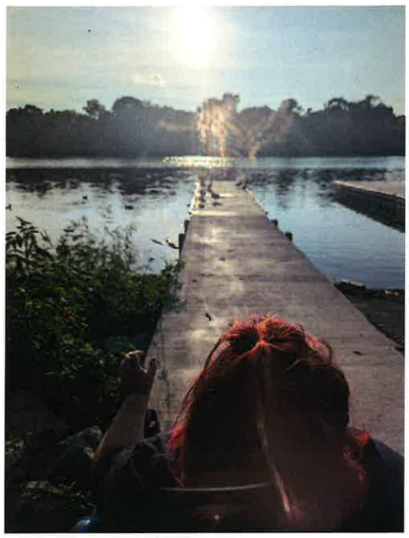
Morrow, OH

Ashton is our sweet and beautiful 7-year old daughter (our second born) who was diagnosed with medulloblastoma brain cancer at the end of August. Since her diagnosis, Ashton has undergone two brain surgeries and began radiation this week on October 16th. She will continue radiation for a consecutive six-weeks, followed by Ovarian Tissue Preservation, and nine rounds of chemotherapy, which is expected to take at a minimum, one-year. Today, Ashton is suffering from Posterior Fossa Syndrome, brain damage from her two surgeries, and is unable to walk without significant help, a walker, or her wheel chair. Her cognitive abilities, emotions, and reactions have all been affected and we don't have any answers to when or if she will ever return to the girl she was before cancer. The road ahead for us is going to be unimaginable. We don't know if she will ever be healed from cancer, live a normal life, be able to have children, or if it will or won't come back again. No kid deserves to be diagnosed with cancer. No kids deserves the pain. No kid deserves this battle.

Why the Promising Pathway Act is Important to our Family: Most people don't think about their child dying. But, when your kid has cancer, it crosses your mind every day. There is far too little funding and research being allocated towards childhood cancers, specifically brain cancer. While the frontline doctors, nurses, oncologists, neurosurgeons and other staff dedicate their lives to beating and eradicating cancer, congress and those who are supposed to represent the American people do not. Congress should be putting more effort and support towards protecting our kids from cancer. This would include not only funding, but the attention, and advocacy that is so desperately needed. With the childhood cancer diagnosis's increasing on a yearly basis, there needs to be decision makers and leaders who are fighting the fight with us. This bill is crucial. No parent wants to lose their child, ever. No parent ever wants their child to suffer the last years, months, weeks, or days before their child dies in a hospital like kids with cancer do. But, this happens every day in the lives of families dealing with cancer. This would be a step in the right path to helping gain interest, funding, and the resources that childhood cancer deserves.

Amanda Hawkins

Mother of Ashton





HARLEIGH VANHORN

Pickerington, OH

July 5th, 2022. That is when I was told that my daughter will die. That she had a brain tumor that was in her brain stem. They told me she will probably die in the next 9 months because that is the average life of a child post diagnosis but if not in 9 months then she had a 20% chance to live 2 years. And then well, only a 2% chance of living 5 years. If we wanted, they could do a surgery to extract a portion of her tumor so they can genetically mark it to possibly open more trials for her. But these trials were all phase one. There was nothing that showed more promise than another. And THIS was their biggest failure as doctors. Radiation may shrink her tumor. Or not. Because there are some cases where it does not work. And it was aggressive so, her first symptoms were likely a few weeks to a month or so after it started. But because of it's aggressive nature, we needed to make a decision...soon. How were we going to go forward with treating her? We had 2 trial options at the hospital we were at. One was a radio sensitizer to try to make it so the radiation had a greater effect on the tumor and the other was where they were using recombinant DNA to try to make the immune system recognize and attack the cancer cells. We discussed the options and decided to do the radio sensitizer. It really did kill a lot of the tumor. But the amount of dead cells it created also created a different problem, clearing out the dead cells. She was on that trial for 6 months until her tumor showed progression.

Why the Promising Pathway Act is Important to our Family: There are things out there that show promise. 2/3rds of mice are cured with this treatment, this is showing promise in the first adult trial, this drug combination works to suppress the pathways the cells are using to hide from the body. But these are not available to Harleigh.

Because you see, she does not have the right to try experimental treatments. She is 8 going on 9. The trials happen in adults. Then they are expanded to 12 - 18. And then to 6-12. And then down to younger children. And each trial phase takes years. And she does not have years. The average age of a child who is diagnosed with DIPG is 7. Any promising treatment for these children is beyond their reach because they can't get access to the treatments. How they were able to get AIDS/HIV treatments out to the public so quickly is because the rules were changed so the patients did have the right to try experimental treatments. We just want the same for our children. We don't want to have no guardrails. We just want to get some hope. Wouldn't you want hope for your child? What would you do if you were told your child was going to die and there is nothing you can do about it?

Jill Hines

Mother of Harleigh

JTHF
Jeffrey Thomas Hayden Foundation





JEFFREY HAYDEN

West Chester, OH

My name is Tim Hayden and my wife Cindy and I live in West Chester, Ohio. Our 12 year old son Jeffrey was diagnosed with a DIPG brain tumor in January of 2004 and passed away in September of that same year. It has been over 19 years since his passing and researchers are making progress to identify and treat this disease, however there is still no cure and federal funding is severely lacking.

Jeffrey was a smart kid who loved school. Learning new things came easily to him, and his knowledge impressed everyone he met. He loved to play sports and excelled in baseball, football, basketball, soccer, and golf. Jeffrey's neighborhood was filled with children. They would gather in the cul de sac and plan the day's newest adventure. Capture the flag, street hockey, kickball, hide and seek, and generally running around until they dropped. Today, we remember Jeffrey as the intelligent, playful, and generous 12-year-old who left this world too soon. 19 years after he conquered his battle against DIPG, his presence is grieved by all the hearts he touched.

In 2004, we established the JTHF Foundation to increase awareness about pediatric brain tumors, specifically DIPG, and to take a proactive approach to raising money to support pediatric cancer research. We are proud to partner with The Cure Starts Now organization (www.thecurestartsnow.org) to serve families affected by pediatric cancer by funding clinical research as we are a Leadership Partner in the DIPG/DMG Collaborative.

Why the Promising Pathway Act is Important to our Family: The Promising Pathway Act is important to us because it offers hope to parents whose children are fighting DIPG/DMG. 19 years ago the medical community had little to no options to offer our son. The PPA would open the door to allow patients with terminal illness to try promising drugs, therapies and treatments not normally offered. We support the Homerun Cure that The Cure Starts Now and the

DIPG/DMG Collaborative are pushing, and the PPA would go a long way to help speed up the timeline to cure this deadly disease. We urge you to support the PPA.

Timothy B. Hayden
Cynthia M. Hayden



WYATT REBER

Loveland, OH

We were living and loving life when our son started having episodes of dizziness. In an instant every aspect of life changed when our Wyatt was diagnosed with a rare and aggressive form of brain cancer at 3.5 years old. We have been told the recurrent rate of this cancer is HIGH and usually not treatable if it does recur. Our son endured a lengthy brain surgery, recovery and 30 rounds of radiation to his brain and brain stem to help ensure it doesn't return—but that often isn't enough. He will be monitored for the rest of his life and we will always live in fear it will return. We have to do whatever we can to ensure we have treatment options for our son and countless other children battling brain cancer.

Why the Promising Pathway Act is Important to our Family: We will never stop fighting to ensure our son is able to live a long and healthy, fulfilled life and this is step in the right direction

Alexa Reber

Mother of Wyatt

[redacted]

To Whom it May Concern,

I am forwarding this email that I sent to Keith at the Pediatric Brain Tumor Foundation. I am also sending to this email address, as advised by Jacob Chebowski to ensure its received and gets the attention it deserves.

As an advocate for my daughter and children's brain cancer, I would love to discuss in more detail or get involved in any way I can.

Feel free to reach out anytime via email, phone, or text - 513.519.8509

The email copy is below:

Your Full Name: Amanda Hawkins
Your City and State: Morrow, OH
Your Child's Name: Ashton Hawkins
Your Story:

Ashton is our sweet and beautiful 7-year old daughter (our second born) who was diagnosed with medulloblastoma brain cancer at the end of August.

Since her diagnosis, Ashton has undergone two brain surgeries and began radiation this week on October 16th. She will continue radiation for a consecutive six-weeks, followed by Ovarian Tissue Preservation, and nine rounds of chemotherapy, which is expected to take at a minimum, one-year.

Today, Ashton is suffering from Posterior Fossa Syndrome, brain damage from her two surgeries, and is unable to walk without significant help, a walker, or her wheel chair.

Her cognitive abilities, emotions, and reactions have all been affected and we don't have any answers to when or if she will ever return to the girl she was before cancer.

The road ahead for us is going to be unimaginable. We don't know if she will ever be healed from cancer, live a normal life, be able to have children, or if it will or won't come back again.

No kid deserves to be diagnosed with cancer. No kids deserves the pain. No kid deserves this battle.

Why the Promising Pathway Act is important to you

Most people don't think about their child dying. But, when your kid has cancer, it crosses your mind every day.

There is far too little funding and research being allocated towards childhood cancers, specifically brain cancer.

While the frontline doctors, nurses, oncologists, neurosurgeons and other staff dedicate their lives to beating and eradicating cancer, congress and those who are supposed to represent the American people do not.

Congress should be putting more effort and support towards protecting our kids from cancer. This would include not only funding, but the attention, and advocacy that is so desperately needed.

With the childhood cancer diagnosis's increasing on a yearly basis, there needs to be decision makers and leaders who are fighting the fight with us.

This bill is crucial. No parent wants to lose their child, ever. No parent ever wants their child to suffer the last years, months, weeks, or days before their child dies in a hospital like kids with cancer do. But, this happens every day in the lives of families dealing with cancer.

This would be a step in the right path to helping gain interest, funding, and the resources that childhood cancer deserves.

(Note the cheer picture and family picture are before cancer. The one with Ashton in the hospital bed is her with cancer)

Ashton's CaringBridge: https://www.caringbridge.org/visit/ashtonstrong









Hello,

My name is Laura Manhardt and I am the primary caregiver for my mom, Patricia, who has been living with ALS since her July 2020 diagnosis. Two years before her diagnosis, in 2018, my mom was an active individual who ran her first half marathon. Today, three years into her journey, she does not have the use of her feet, legs, left arm, and left hand. Her right arm and hand have enough strength for her to operate her phone and in-home hospital bed remote, but they are quickly going. She needs complete assistance with personal care and some help with eating. She cannot lift her head up if it falls, and uses a portable ventilator almost constantly through the day and night to support her weakened breathing. She had to leave her job this summer when typing with one finger finally became too tiring.

As each part of my mom's body has fallen victim to ALS, I and her other caregivers replace that function with our abilities. Every day, I strain my own body to complete lifts and transfers, maneuver assistive equipment, and complete care tasks. Imagine your longest days - when you are moving from the moment you wake up to the moment your head hits the pillow, completely and thoroughly exhausted. That is every day for me. I am 27 years old and doing my very best to not let go of my own life despite of the horror that ALS has placed upon my family, and the challenges of caregiving. But the price of that is that my days are overflowing. I work a full-time job, which is luckily remote so that I can be around for my mom. I have friends, family, a dog, and a boyfriend that I love and spend time with during the all too few elief hours I have. I do my best to care for my body given how much stress it is under, which sometimes mean sleeping 7 hours instead of 6. I have passions and interests I spend time with daily, for the few minutes I have to spare. Keeping these good things consistent in my life, even just a little, is a challenge I have to endure, because the price of failing is that all I have left in my days is care and watching my mom die before my eyes, and I refuse to let ALS take any more from us than it already has. I say all this to try and convey how completely draining this illness is on the patient AND everyone around them, but in truth, you will never truly know this tragedy until you've been as close to it.

Roughly a century and a half after ALS was first identified, this is an insane position to be in. We've seen results for numerous other illnesses completely transform in that time, primarily cancer. And to be honest, I wish my mom had cancer instead of ALS. Because for the most part in cancer, you can still have the dignity of caring for yourself, or traveling to fulfill your bucket list (my mom can't fly with her breathing problems), or holding your first grandchild (my nephew was born in April and my mom's hands were too far gone to hold him). This illness is the same horror it was 150 years ago. We have a few treatments that extend life a few months and technology that helps immensely, but the disease progression is the same. The outcome is the same. My mom will die without intervention. After 150 years of this, the situation is more than dire. Patients need options and will do anything to get them. My mom spent $10k for two weeks at a functional medicine clinic in Miami. She's currently signing up to let Elon Musk plant a chip in her brain with Neuralink. We've seen others in this community fly across the world for stem cell treatments. The ALS community has suffered so greatly for so long, and the desperation grows with each new generation of patients that is diagnosed with and soon dead from this illness.

This is where you come in! Remember when you (hopefully) got into government with the idea of serving the people? This is that moment! ALS patients need access to new and emerging therapies ASAP. Us caregivers need it to, not just for the hope that our loved ones will get better, but also for the chance that we'll have more time to adjust between the unctional losses that add more to our responsibilities. We are asking for you to help. ALS moves quickly and violently, and our current system is not set up to get patients access to treatments that they are willing to try. Our current system isn't even set up to listen to patients, which for ALS patients is especially devastating given how shrouded in uncertainty

so much of this disease still is. We need to operate on the ALS clock, which moves at a pace of killing an ALS patient and diagnosing another every 90 minutes.

'f my mom had access to treatments, the difference in our lives would be, quite frankly, heavenly. I of course hope for access to treatments like NurOwn, which patients reported incredible results on. I doubt any emotion, even the birth of my child, could compare to the joy of seeing my mom regain function. My daily fantasy is that she'll suddenly walk into the room - and that's a possibility when patients can quickly access emerging treatments and start seeing what works for them. On a smaller note, I get my time back! I can actually think about getting married and planning a future, I can work on projects, I can spend an hour alone on a Saturday morning before I have to take care of anyone! That's the best case. At worst, I have more time to spend with my mom, my best friend, a person I hope I keep around in every lifetime. She gets to live a little more of the life she deserves to live. There are no downsides to changing up the status quo, and the consequences of not taking action is that we'll continue down this path and my mom will die and I'll fall into a few years of grieving depression and lose even more of my time to ALS. And that's not a joke.

So here I am, writing to you in the middle of the night (I told you my days were overflowing), begging you to please URGENTLY help these patients access new and emerging therapies, and provide plenty of flexibility to developers so that we can start fighting this illness at the same rate it moves. Help me and my mom, in our little corner of the world, so we can get back to the goals and dreams and richness of life that at this point we have earned the opportunity to live. So much of your days are the chaos of politics and witnessing the worst troubles in this nation and in our world. This is a moment to combat that horribleness with joy. Please seize it and run until patients have constant access to new therapies, until my mom can find something that improves her symptoms, until I can go to bed at night (as I am about to) and not wonder if today was my last day with my mom.

God bless,
Laura Manhardt



To the members of the Senate Aging Committee:

Thank you for accepting stories from people like me, people impacted by ALS. My family has the C9orf72 genetic mutation of ALS and FTD (Frontotemporal Degeneration). We have been fighting these awful diseases for over 30 years.

I lost my Mom, Karen, at age 65, to bulbar onset ALS. She was an incredibly independent person. She cleaned houses and businesses in her small community and became friends with the elderly people she worked for. She ran errands for them and supported them. She loved gardening and her flower gardens rivaled any you could find in our great country. She enjoyed being a grandma and she loved cooking for her husband. She sat with me Easter weekend of 2007 and told me, "I think I have ALS." Then she said, "I hope I can handle it with the grace sister Jean did." She was 62 years old. ALS is a devastating disease. It took away my Mom's ability to swallow first. On Thanksgiving Day 2007, we sat down to eat the meal she cooked and she choked. Everyone at the table, her children and grandchildren, cried. We all live with that awful memory. There were so many more awful memories. ALS took away her ability to walk and use her hands. She couldn't work and she couldn't tend to her flower gardens. Do you know how difficult it is to give up your keys because you know it isn't safe to drive anymore? Do you know how hard it is to give up the ability to eat? And then to continue making meals for your husband and to watch the Food Network because it's your favorite? Do you know how difficult it is as a daughter to watch your Mom use a feeding tube and mime "yummy" when you are eating a sandwich right beside her? It was the most difficult time I ever had eating, because I felt such guilt.

How did my Mom know she had ALS? Because she had already lost her sister Betty (in 1993), sister Jean, and brother Jim. She already had another sister, Carole, who was in her own fight with FTD. By 2014, our family had lost 5 people out of one generation to ALS/FTD. And there was only 1 drug to help them, and it only improved a person's lifespan by a few months. So, over a period of 21 years, there was almost zero progress towards treatments for ALS.

Now ALS is in my generation. In 2022, we lost my cousin Vonnetta to ALS and FTD. Now her brother Steve is in the final stages of FTD. ALS is just getting started in my generation. I'm aware of two other cousins who may be impacted and are considering genetic testing and neurologist visits. My grandparents have over 100 living descendants, that's blood relatives, not spouses. My family can't wait another 21 years for more treatments for ALS and FTD.

Here we are in 2023, and we have no treatments for C9orf72 FTD - none! And our mutation is the biggest piece of the genetic pie. For my family, there are 3 medical treatments for ALS now: Riultek, Relivryo, and Radacava. None of these cures ALS. At best, together, they may extend a person's life up to a year. One year! How many more of my family members will not see their children or grandchildren graduate from high school or college? Will not see them get married or have children? How many more of my family will pass this awful disease on to children that haven't been born yet? We need more treatments and we need them yesterday!

For people with rapidly progressive and 100% fatal diseases like ALS, timely access to promising therapies is essential, critical, crucial, etc., and offers an opportunity for survival. Current FDA approval pathways take far too long to help those currently suffering from such diseases! People living with ALS do not have the luxury of time. We need this legislation passed - please.

I've been in the fight for nearly 20 years, as a Team Captain for the Walks to Defeat ALS in Columbus and Cincinnati (we've raised almost $150,000), as a volunteer for The ALS Association Central & Southern Ohio Chapter (board

member, board secretary, board chair), and as an advocate (coming to DC multiple times to ask Congress for money for ALS research and to pass key legislation to help those with ALS). Now that I'm retired, I've become a Northeast ALS Consortium Research Ambassador. I'm co-chair of the Familial ALS Team with I AM ALS. I'm a contributor to the Roon app for ALS. I volunteer at our local ALS support group. I'm not asking you to do anything different than I'm doing - and that is to help people living with ALS and their families.

Thank you Senator Braun for your work to support those living with ALS and our families. Thank you for the ALS Caucus and so much more!

Thank you for listening and acting.

Debbie Lower
Cincinnati, Ohio

Jennifer B. | Ohio (1 of 2 pages)

We Can't Wait

Age: 52
Year of Diagnosis: Mom: 2020
Type: Sporadic

I helped take care of my Mom, who was diagnosed in late October/early November of 2020 and sadly passed away in April of 2021. She had been diligent in her health concerns, spending years going to doctor appointments, etc.. to see what was causing her foot drop. **When she was finally diagnosed with an advanced stage of sporadic ALS at age 79, she was determined to fight. I tried to get her enrolled in clinical trials, but she was denied based on the advanced stage of the disease, unfortunately**. We continued researching therapies and drugs/medications to slow down the progression, as she had so much more to share with us and so many more lives to impact. Providing her with a choice in her battle is benefit enough, in my mind. So, a modest benefit such as slowing the disease or providing a few months of additional life was not offered to her, the choice in what she wanted was a luxury that was abruptly taken away upon receiving the diagnosis. This choice should be given to those that are battling this disease, as I believe that any person in my Mom's position would welcome an alternative to what they are given with this diagnosis, such as a new therapy.

I would weigh the benefit of any therapy that might end up having no benefit at all or has a significant side effect to my ability to have a choice in my approach to my fight. My Mom was given the choice of taking Radicava or Riluzole, both drugs used with ALS patients. She chose Riluzole, understanding that the drug might not have any benefit or cause side effects for her. She made this choice to aid in the fight for her life.

The clinical trial process and the FDA have rules and regulations in place for keeping people safe. However, if given a diagnosis, such as ALS, with no known cure or cause, my Mom, and possibly others, would welcome the advancement of determining if medications could prevent their outcome of a death sentence in their fight. Suffice to say, my Mom was interested in clinical trials, if they could offer some insight, breakthrough, or an alternative to what ALS did to her.

I can only answer for how this diagnosis impacted her based on my time with her. Upon hearing the diagnosis, she stated that this diagnosis was a death sentence, and she knew what her future held for her. I recall sitting with her one day and she looked at me and said, **"I miss my life." ALS is cruel, taking away her independence, dignity, and her voice. Your mind and soul remained unchanged, so you are keenly aware of all of the abilities you find are no longer part of your routine. You miss conversing, expressing your joy, feeding and bathing yourself, walking into the room and so much more. In essence, ALS impacts the person and all of those who love them, as we are all left to watch helplessly as the disease progresses.**

Jennifer B. | Ohio (2 of 2 pages)

We Can't Wait

Age: 52
Year of Diagnosis: Mom: 2020
Type: Sporadic

Since my Mom is no longer with me, I know how being diagnosed with ALS impacted our family. We all began to fight with her to help her, advocating for physical therapy to maintain what strength she had left, finding ways to raise money to help with the 24 hour care that soon became the norm, and spending 4 hours driving in the car to provide assistance and time with her for encouragement and aide in her care. Due to the pandemic, this created a whole new hurdle for us, as our family knew the importance of keeping her safe, but also how important it was to spend time with her. ALS did not define who she was, but instead proved the value of her legacy.

My wish for what people understand about ALS is that it is not curable, there are no treatments available to stop the progression. Those with ALS will not get better. ALS is more commonly sporadic than hereditary, anyone can be diagnosed, at anytime during their lives, as this affects old and young alike. ALS is cruel, as it takes away what so many of us take for granted, while you sit and recall in your mind the things you were doing a year before the diagnosis. My wish is that those with ALS are given more, in terms of studies, money for research and funding to find a cause, they deserve better than what they are given. Those diagnosed are so much more than what others see in pictures, they are full of life, with many adventures left to explore, and many more holidays and family celebrations to enjoy, and so much love to share with others.

I would like the FDA and pharmaceutical companies to know that my Mom was more than a statistic, she was more than one of the many that pass away from ALS. More than the Member ID number on her Medicare account. She was in the fight for her life and was not given the adequate supplies to wage her battle. The cost of her one and only medication, Riluzole, was astronomical. She and her husband are retired educators and cannot afford the cost of the many medications she required with her diagnosis. I would like them to know that waiting on approval for a new therapy or medication costs lives, ALS patients do not have the luxury of time on their hands. **I appreciate your job and the responsibilities that come with your line of work, but please remember your impact on those fighting for their life and discover ways to improve the process of approval or costs for those that may need it.**

Robert S. | Ohio



Age: 62
Year of Diagnosis: 2017
Type: Limb Onset, Sporadic

I am advocating for this. I want to continue to be a part of my family. I would be in favor if the benefits outweigh the side effects. If the drug won't kill me, I don't care if they have approved it.

It was devastating. I tried to take the drug on tap, but it made my liver angry. I tried to keep active. My family didn't expect me to be there two Christmases ago. But with my vent helping me breathe I am still here, and I got to meet my 4 grandkids

My daughter doesn't like to visit, she doesn't like to see me degrade, my wife has to take care of me, totally. I am now a quadriplegic I am really sorry she has to do everything for me, my Son convinced me to write stories and I have.

There is no cure, it is devastating to a family and friends.

Every moment counts.





Bobbi A. | Ohio

Age: 67
Year of Diagnosis: 2020
Type: Bulbar Onset

We Can't Wait

It would give me the chance to live longer to enjoy my family & friends. It would give me hope, which is better than what I have now.

I would still want to try the therapy. Everyone is different, I may not have any reactions. It's a chance I'm willing to take.

The clinical trial is important for 2 phases. I don't need FDA approval.

It's changed my whole life. I can't talk or walk. I depend on my husband & children for getting through my day. I no longer can do what I enjoy. I miss going out to eat, gardening, & talking.

Sadness all around. Lots of tears & prayers for some kind of cure.

That it's so hard to lose your independence & having to rely on others for daily tasks. Your body experiences different symptoms like muscle spasms, mouth chattering, legs shaking & your talking is hard to understand. You can't drive anymore, you can't go to places that have steps or if the bathroom isn't on the first floor.

Please give me the chance to try different therapies. Let every ALS patient try, forget about qualifications. It shouldn't matter how far along a ALS patient is, open up access to all patients.

[redacted]

Hello, Senator Braun and Committee Members,

My name is Patricia Manhardt and I have ALS.

When I was a teenager, I interrupted an armed robbery at the movie theater where I worked. I had surprised the thieves as they thought they had already accounted for all the employees. They held a gun to my head, told me to be quiet and do as I was told. Strangely, even though they had control of the situation, I knew I had some control too. I did not panic. I knew if I followed their instructions, I would be OK.

ALS is holding a gun to my head. However, the trigger is being pulled very, very slowly. At some point soon the gun will go off no matter what I do.

I am writing this letter to ask you - no, beg you - to try to put the safety lock on that gun and give me a chance to live longer. I don't want to die.

I need someone to intervene to give me a longer life. We, in the ALS community, need someone to intervene.

We need Congress to pass the Promising Pathway Act (PPA) to give us fast access to promising treatments. Our time to death clock is ticking. The current drug approval and access process is too lengthy for us. We are literally dying waiting. The PPA allows a drug to get to market based on "early evidence of efficacy". There is an amazingly promising treatment called NurOwn which has shown early evidence of efficacy since the Phase 2 trial in 2015. Thousands upon thousands would have had the opportunity for a longer life if we would've had access back in 2015.

I personally have been fighting for NurOwn since I first heard of the amazing phase 2 and phase 3 results. Below in this email is the majority of my statement to the AdCom members for NurOwn. Unfortunately, the FDA did not provide the correct background and rules to guide the committee as they have done in other drug trials . The Committee members were not even advised that they could or should take into account patient testimony or that they could exercise flexibility on their decision making process. 17 out of the 19 members did not listen to patient evidence or take it into account in their decision-making. To make matters worse the patients who receive NurOwn were not all allowed to speak at the AdCom including a Navy pilot named Matt Bellina, who, after treatment with NurOwn was able to stand up on his own out of his wheelchair and even take a few steps. Dr Windebank from the Mayo Clinic was able to testify, but obviously no one listened to his real world evidence. Almost 2000 people submitted testimony asking for NurOwn to be approved. Still the FDA did not listen. Instead, they chose to depend on the data that was calculated using a very flawed system of progression measurement. We even tried to explain the huge flaws in this measurement to the FDA, but again, they did not listen .

On October 18 of this year, Brainstorm, the manufacturer of NurOwn, pulled their application for the approval of NurOwn apparently due to the obvious negativity and lack of support from the FDA. Please see this pertinent local news story:

https://wlwt.com/article/manufacturer-experimental-als-treatment-fda-approval/45578505

These 6000 people who die each year of ALS are your neighbors, your family, and your friends. They are citizens of the United States of America. They, we, need your help.

Below is the majority of the statement I submitted for the NurOwn AdCom which was held at the end of September of this year:

5 years ago I was eating right, no smoking, no drugs. I was exercising and I even ran a half marathon. Then I broke my toe, and had 2 surgeries on my toe. My foot healed but I knew something was wrong. I was having trouble walking in heels. I took my 93-year-old mother home from a family dinner and I fell lifting her out of my car. By April of 2020, I could no longer run sprints with my son while he was training for football. My legs just wouldn't move fast. The physicians at University Hospital in Cincinnati diagnosed me fairly quickly after that. The first neurologist I saw, held my hands and just stared at them. I didn't know what he was looking at. Now, I realize it was the wasting in my left hand. I was diagnosed on July 23rd, 2020. I told my children that day, and I also told them I would get tested to see if this was genetic. The one person I could not bear to tell was my mother, but she would find out soon enough, because I would no longer be able to help my sisters care for her.

I went to Mayo Clinic not for a second opinion, but to ask about a trial I had heard about. It was for NurOwn. Unfortunately, the trial was closed.

I started researching to find a supplement or medicine that could help me - Anything that could slow this high speed ALS train down. I am constantly contacting physicians for their recommendations. I have even (legally) purchased a medicine (Clenbuterol) from another country that has shown some efficacy in a trial. I worked with functional nutritionists. I joined the Healey trial for CNM-Au8. I did and I am doing everything I can to help myself.

Even with everything I tried, my legs became weaker. In the summer of 2021, I squatted down just a little too far, and my thigh muscles gave out. I fell backwards but, as my body was no longer working correctly, my foot stayed where it was planted and I snapped 9 bones in my foot. I argued with the doctors because I did not want a cast on my foot. I did not want to have to stop walking. I had no choice though, and I knew I would never walk again. It was traumatic. It was devastating.

But I collected myself. I was "OK". I had to crawl up the stairs to bed at night, and in the morning, I went downstairs step by step on my bottom. I was able to get into a wheelchair because I could still stand on my left leg to transfer. Then my left leg got too weak and I had to use a slide board to transfer from wheelchair to my chair, bed, shower chair or car. My arms and hands were strong "enough" so I was still "ok".

Last year I was hospitalized for malnutrition, and also for two pulmonary embolisms. I started using a bipap to breathe at night. I had a feeding tube installed. I was still "ok".

Well, I am not OK anymore. I have no use of my left arm or hand. I have very little use of my right arm and hand. Now I need help to get dressed, brush my teeth, use the bathroom, get a shower, and I can barely feed myself. My children, my friends, my sisters, and my caregivers have to help me in every aspect of my life.

I use a bi-pap almost 24 hours a day because I can't breathe easily without it.

I had to quit my job.

This whole situation is not ok.

The most frustrating thing is that I believe in NurOwn and if we would've had NurOwn approved back when I was still walking, I believe I might still be walking today, like the people in the NurOwn EAP who were diagnosed years before

me. Even if it had been approved a year ago, I would still be able to take care of myself. Now I'm hoping that NurOwn is approved so I can regain some of my independence again. I know NurOwn isn't a cure, but it will improve my quality of life and give me more time. When you have ALS, time matters. We are on the ALS clock.

In 2015, when NurOwn worked in Phase 2, my motor neurons were already dying but I had no ALS symptoms. I was going to my son's football games, taking my daughter to college, running 3 miles 3 times a week and working at a challenging I.T. job in the banking industry.

Me in 2015:

With my beautiful daughter. I'm on the right. :)

In 2019 when Navy Pilot Matt Bellina stood up out of his wheelchair after receiving 6 doses of NurOwn, I was experiencing some unexplained cramping but my life was really not effected, yet.

Me in 2019:



In Paris with my new company. I'm an IT project manager.

Me in 2019 at my nephew's wedding before I was diagnosed:
https://youtube.com/shorts/pE2yxvlBkGY?feature=shared

In 2020, when some people in the Phase 3 trial reported that it had halted their progression and helped them regain some function, I was just diagnosed.

My daughter and I in 2020 on our trip to Mayo Clinic:



Me in 2020:



Trying to do the impossible of pulling the sword from the stone.

In 2021, when Congress held a Congressional hearing asking the FDA what it was doing to expedite ALS therapies, I was able to walk with a walker when I did an interview with Sheree Paolello of our local NBC station:
https://wlwt.com/article/cincinnati-als-patients-lawmakers-drug-access/38163503

Me in 2021, walking out on the field at my son's college football senior night. My boys are holding me up so I can walk without falling: https://youtube.com/shorts/DSTxmM2ygZg?feature=share

Me and my children in 2021:



It was a once in a lifetime trip. I knew that without treatment it would be our last all together.

Me in 2021, documenting my ALS progression:
https://youtube.com/shorts/7slpeyL55kA?feature=share
https://youtube.com/shorts/4En3yK-FW-8?feature=share
I broke my foot a couple weeks after this video was taken and have never walked again.

Me with friends and family in 2021 asking Congress to help us:



In 2022, people in EAP again halted their progression for the third time. By this time, I could no longer transfer on my own and had my feeding tube placed.

Me in 2022:

My son moved to Phoenix and the family went to help him move in. It made me feel awful not being able to help.

Me in 2022 to support the fight against MS:

In 2022 at the Flag Event in Washington DC asking for help:

In 2022 at Lou Gehrig day to raise awareness:

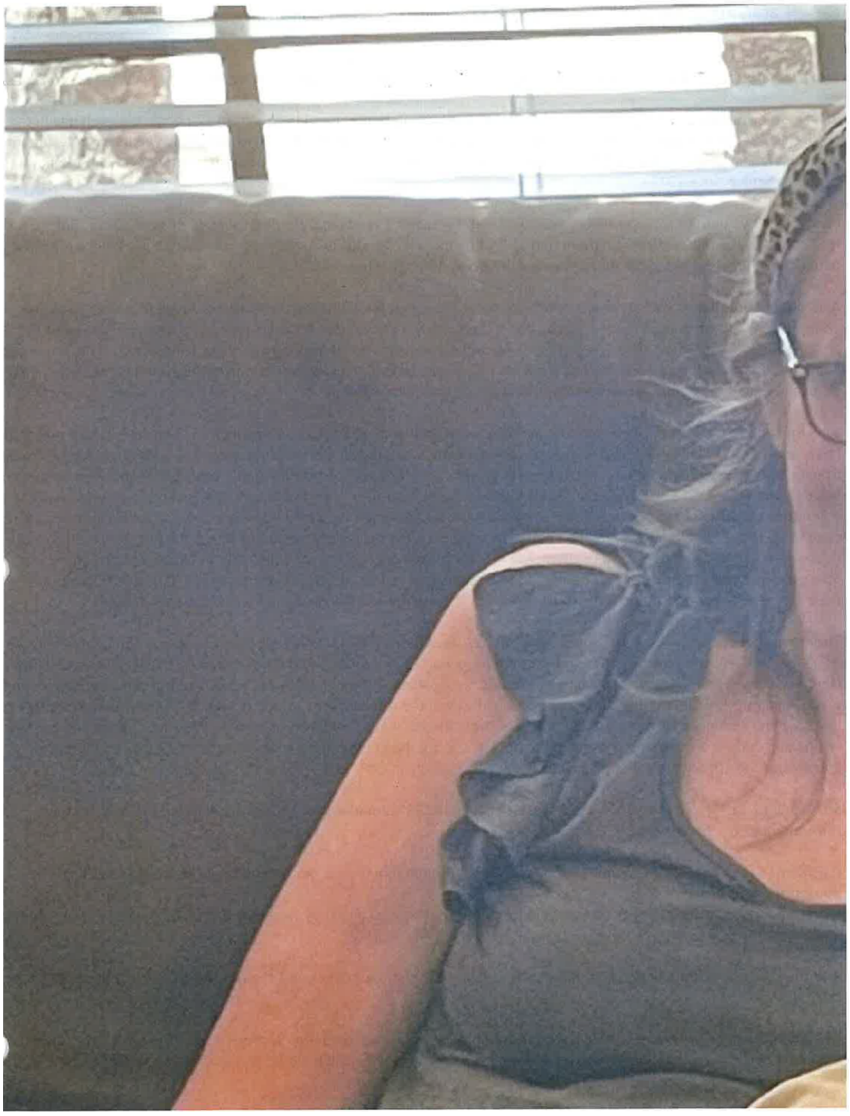
Now in 2023, we drove from Ohio to DC for the Flags on the Mall event with I AM ALS. This time when Sheree interviewed me, I was having a lot more trouble breathing and lost the use of my left arm and hand: https://wlwt.com/article/local-patients-national-awareness-als-faster-treatment/43869936

In 2023 in D.C. with my family and caregiver, lucky to get a quick pic with Brian Wallach

...and honored to meet Senator Murkowski.

At Lou Gehrig day with the Reds:

Me in 2023 with my grandson:



Because of my ALS we had to drive two days (instead of flying) to Phoenix to meet my grandson. I couldn't pick him up or bend down to kiss him.

This illustrates why the FDA must act with urgency. Every year, month and day of delay, more of my motor neurons die.

Why hasn't NurOwn been approved already? There is an urgent, unmet need here. About 17 people die each day in the US of this disease. Everyone involved should be acting aggressively to get treatment to patients. Type II errors result not just from failing to approve a drug that works, but also from delaying the approval of a drug that works. That is what has been happening since 2015.

I know NurOwn didn't meet its primary endpoint, but if you aren't familiar with the ALSFRS-R, do you realize that that endpoint is a massive improvement and 35% of people met it? NurOwn did meet its secondary endpoints for patients in a prespecified subgroup, showing a 2-3 point difference from placebo.

And what about that ALSFRS score that was used to assess progression? Researchers acknowledge and have published about its many flaws. It does not track progression accurately. For example, it doesn't measure when my left hand -- which is my non-dominant hand -- is getting worse as I can still do most things with my right hand, which is my dominant hand. It didn't measure when I switched from walking with a cane to walking with a walker. And it didn't measure when people regained the ability to use one finger to operate their wheelchairs.

Why must patient testimony be taken into account when approving ALS drugs or treatments? Well, here is one reason. If I have a zero score on walking, and I have no leg movement whatsoever, yet the drug or treatment is affecting me, I may then be able to wiggle my toes, or adjust my legs at night, or lift up my foot off the bed. These are small things to some but they are huge to me. Yet my score for walking would still be a zero. How I wish I could adjust my own legs at night when they get sore from being in the same position. Another example would be if I have a zero in handwriting and if I cannot move my right hand. If I then had a drug or treatment that will allow me to just move one finger, I could control my power chair and get around on my own. My ALSFRS score would be the same but this would be a huge help to me. These are just two examples of why physicians and scientists need to include patient testimony. There is no accurate measurement of our progression. We must be heard because the ALAFRS data itself is not accurate enough.

This is why patient testimony is so important with ALS. I am friends with several people who were in NurOwn EAP as we have spent dozens of hours on calls together. We have walked and rolled the halls of Congress. They have shared how NurOwn allowed them to stop using bipaps. That is not a placebo effect. I didn't miraculously stop using a bipap when I was using imported Clenbuterol, no matter how badly I wanted it to happen. I didn't regain the ability to move parts of limbs when I was in a trial, but a friend in the NurOwn EAP did. Patients know our bodies. We knew something was wrong long before we were diagnosed when medical science didn't. We know when we are losing function and we know when we are regaining it. Believe us. Believe the people in EAP.

So what about biomarkers? NurOwn did cause a change in CSF biomarkers for those who were on the drug, but not those on placebo. That's a fact.

CSF biomarkers hit target engagement of decreasing neuroinflammation & neurodegeneration, while increasing neuroprotection. That's a fact.
CSF biomarkers showed changes across the entire disease spectrum and they were not limited by the floor effect. That's a fact.

And the UNC13A biomarker showed that 65% of people with that biomarker met the massive primary endpoint. That's a fact.

ALS is a 100% terminal disease which has a critical unmet need for a treatment. Without a treatment, I will die. I will suffocate because I will not be able to breathe and the carbon dioxide will build up in my blood.

NurOwn is not a cure. What about that? Well, let me tell you, if I can gain one point back in my ALSFRS score I might actually be able to hold my new grandson. If I had one point back on my ALSFRS score I might be able to brace to transfer myself and my daughter and son would not have to pick me up. If I had one more point in my ALSFRS score I could use the bathroom on my own. I could go on and on with examples. I would be so happy with one more point.

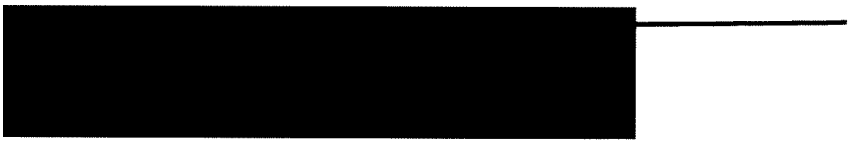
NurOwn is safe. It has shown positive results, at the very least in some... and based on the CSF biomarkers, likely in most.. Just like cancer, there are many different kinds of ALS. I don't expect one treatment to be a miracle cure at this point. But I know NurOwn works on some... and it gives some more time. I know cancer as I have watched my sister battle multiple myeloma while I have been battling ALS. Multiple myeloma is not curable but her doctors gave her treatment options. Her chemo has a lot more side effects than NurOwn. What she has experienced so far is Neuropathy, Chronic diarrhea, Muscle cramps and possibly Cataracts. And that chemo treatment is not successful on all types of cancer - just hers. I expect the same kind of situation with ALS. Her physician caught her cancer very early so a treatment would have a better chance of extending her life than someone with stage 4 cancer. It's only logical to assume that the longer a person has ALS the less likely they're able to make positive progress with NurOwn – but that doesn't mean NurOwn should be withheld from anyone to try. My sister's stem cell transplant is giving her more time. All I'm asking is to let the NurOwn stem cell therapy give me more time too.

So what are the drawbacks in approving this treatment? Maybe you should think about what is the drawback of NOT approving it. Well, I will surely die and so will 30,000 other people and that is a fact. Probably at least another 30,000 or 60,000 will die as there are no other promising treatments in the pipeline at this point until 2026 or 2027 -- and that will be with only one phase 2/3 trial. Drug trials and approvals take years and years. We don't have years and years to wait. When the Titanic sank, they filled lifeboats knowing not everyone would be saved. We are asking you to approve NurOwn knowing that NurOwn will not save everyone, but it will save some, and therefore all patients deserve to try it.

I don't wish ALS on anyone, but the facts are that one in 300 people will be diagnosed with ALS in their lifetime. If you don't already know someone personally who has ALS or has died of ALS, you will soon.

If I was in a burning building, firemen would try to save me no matter what. If I was in a sinking ship, people would try to throw me a life preserver. If I was buried in an earthquake, people would try to dig me out. We need somebody to try to rescue us, and that's where you come in. I am begging for you to give me — to give us -- a chance. Approve NurOwn. We are dying waiting.

Thank you,
Patricia Manhardt



October 23, 2023

Dear Chairman Casey, Ranking Member Braun, and Honorable Members of the U.S. Senate Special Committee on Aging:

My name is Alex G. Sabo, and I am a father of three adult daughters who have a rare disease called Facioscapulohumeral Muscular Dystrophy, or FSHD.

I have watched the degree of debilitation increase over the years with great sadness and concern. One daughter needs 24/7 care now, as the disease progression has increased over the past 10 years, robbing her, on a physical level, of mobility and dexterity. This disease has also taken a huge psychological toll as it negatively impacts her independence and self-esteem as well as creating anxiety and a fear of the unknown regarding what further muscle deterioration might occur and when. FSHD is also taking a huge toll on her husband who is her primary caregiver, supported by 1 or 2 hired caregivers who are hard to come by and turn over often, requiring repeated training. Her husband's physical and psychological health have also been adversely impacted. In addition, this disease causes a major financial toll, as the costs for caregivers, specialized equipment and medical costs are a huge and constant drain. As an aside, for some reason, this daughter has been denied disability benefits from the US government. Why? Because, after working in the US for a number of years, she moved to another country to work and was in reasonably good health during that time. Her health deteriorated significantly shortly after their return to the US, so she was not able to re-enter the workforce at all. I don't understand why someone in her situation is denied disability benefits in this circumstance.

My second daughter has the visible telltale signs of the disease, but so far physical limitations are mild. The third daughter has had progressive mobility issues since about the age of 12 and has required a wheelchair or scooter for many years. The psychological impacts on this daughter have been huge and she has trouble dealing with the side effects of pain, etc., and has not been able to work.

This is a horrible disease in all its forms. I urge the US Senate Special Committee on Aging to seriously consider authorizing more financial and other support for people suffering with this rare and progressive disease.

Sincerely,

Alex G. Sabo
Lake Oswego, Oregon

CC: U.S. Sen Senate Special Committee on Aging
Sen. Bob Casey
Sen. Mike Braun
Sen. Kirsten Gillibrand
Sen. Richard Blumenthal
Sen. Elizabeth Warren
Sen. Mark Kelly
Sen. Raphael Warnock

Sen. John Fetterman
Sen. Tim Scott
Sen. Marco Rubio
Sen. Rick Scott
Sen. J. D. Vance
Sen. Pete Ricketts

Robert M. | Oregon

Age: 60
Year of Diagnosis: 2018
Type: Bulbar Onset, Sporadic

We Can't Wait

It's a great idea if you live in the city to get fast approvals and access to medicine. Rural communities don't stand a chance.

I'm not sure if I would be interested in something that has a moderate or significant chance of side effects. I guess that it would be what kind of side effects? Death? Worsening of my condition?

Not important at all for the clinical trial process to be complete and the drug to be FDA approved before I try taking it.

ALS had dramatically affected my life! I can no longer enjoy the things that I loved to do. It's too dangerous with high risk of having more falls. I'm pretty much trapped. The people in my life has totally changed, from threats of having me placed in a home because I refused to sell my house and take the money and move to?? I love my home.

How devastating this disease actually is... People have said, Oh have another beer because they think that you're drunk, because of my speech. Very hurtful.

We are still the same person, with the exception that we can no longer walk or have it very difficult to walk without leg braces, other aids, walkers, etc.

Michiel H. | Oregon

Age: 70
Year of Diagnosis: 2014
Type: Limb Onset



We Can't Wait

Extra months is not really what is worth the effort. Early detection with treatment is more important

ONLY AT ONSET OF DISEASE.

In the cases of ALS, promises of one to six months is not worth the effort

Is has ripped our life's apart and the lives of those of the family members to the extent that all joy of life is stripped from us

It has destroyed our way of life and taken away all hope for the future and taken away basically all friends and intra actions with anyone outside the immediate family

They need to understand what a devastating disease that it is and what an impact it has on the lives of those that have been diagnosed and the need for support from extended family. **They will never know what that means the to the person the has the disease and the main caregiver**

They need to understand the disease and what is does to all involved and stop trying to make their fortunes on the backs of the people that have the disease. They need to live day in and day out with those the have the disease so they can get the full impact of the disease. **God forbid they be diagnosed themselves.**

Jan S. | Oregon

Age: 61
Year of Diagnosis: 2014
Type: Sporadic



We Can't Wait

Very important to have access to medicine.

My pALS and I would research these risks and rewards and decide how they would affect my pALS. I am a spouse caregiver.

Not super important to worry about the risks.

He is a quadriplegic, in a wheelchair, 100% dependent on a ventilator. Can still talk. Uses computer with his eyes.

My entire life is consumed with keeping my husband alive.

How much reform is needed in care models. These patients and families need better support that would also help ALL families with devastating diagnoses.

He was respiratory onset and excluded for trials because of low FVC and using BIPAP. Please remove FVC from trial criteria since those don't always correlate to longevity. Diagnosed 2014.



GRACE EKIS

North Huntingdon, PA

In early 2007, our then 4-year-old daughter, Grace Elizabeth Ekis, was diagnosed with DIPG, one of the rarest and most devastating childhood cancers. Although we were grateful to live in proximity and have access to Children's Hospital of Pittsburgh, both my husband and I were shattered to find out that she was given a mere 9-13 months to live. Despite being treated at one of the best children's hospitals in the country, her prognosis was without a treatment plan that could ensure her survival. At the time, the normal course of treatment was one round of radiation to simply extend her life for a few months. There were slim offerings of experimental drugs, and we were told that none of them were specifically targeted to her rare brain cancer. When we questioned why this was the case, we were told that there were simply not enough children affected with this cancer to make it worthwhile for either drug companies or our government to support its research. Left with insurmountable feelings of inadequacy as parents to help our daughter, and no other option, we chose the standard treatment and began to make memories with Grace. On February 14, 2008, 13 months after diagnosis, we were forced to say goodbye to our daughter. Our unfathomable grief and despair have left us with a commitment to begin a journey through the Reflections Of Grace Foundation.

Why the Promising Pathway Act is Important to our Family: The Promising Pathways Act is important to us because it allows children diagnosed with the rarest and most virulent brain cancers options that our daughter was not afforded. It ensures that appropriate drug options and therapies would be available within their lifetime, *without relying on petitioning for compassionate use*. We believe that this Act benefits children and adults with rare diseases by gaining meaningful access to drugs and therapies as they race against time.

Tamara Ekis

Mother of Grace



CAMERON SARUBIN

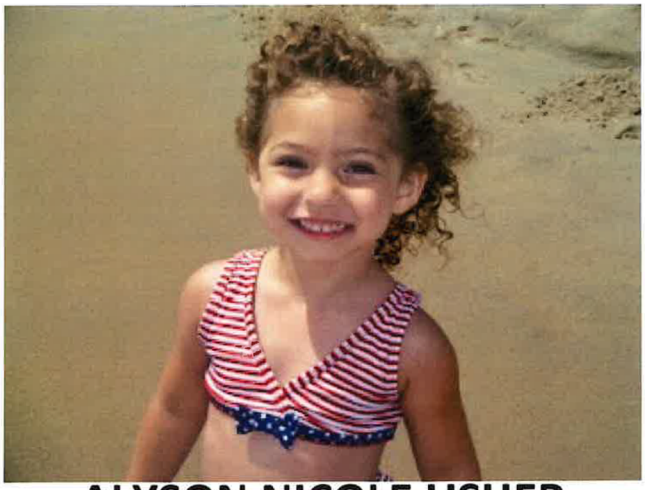
Macungie, PA

Cameron is an energetic, sweet, train-loving boy who adores his little brother, Evan and his Mommy and Daddy — and his whole extended family! Right before Easter of 2023 for four days, Cameron complained of dizziness, was sporadically vomiting and walking with his head tilted. After various MRIs, it was discovered that Cam had a 2.5 cm brain tumor in this 4th ventricle. The doctors at CHOP were able to successfully remove the entire tumor, which was diagnosed as an Anaplastic Ependymoma (PFA) and he started 33 sessions of radiation therapy four weeks after surgery. He has done amazing with recovery and handling the treatments. He hasn't needed any PT or OT which is a miracle in itself. He even walked himself out of the PICU to the car upon discharge, and learned to ride a bike only two hours after a sedated radiation treatment! We fought a hard battle of infertility to bring Cameron into this world and we will be fighting even harder to keep him here, happy, and healthy!

Why the Promising Pathway Act is Important to our Family: Every single day parents are hearing the words "your child has cancer," it's a hopeless, isolating, and earth-shattering thing to hear. We would go to the ends of the earth to save our children, and make sure they are getting every opportunity to live a long, healthy life--the Promising Pathway Act could do just that. With removing the barriers that are taking too much time, which these children do not have, it gives children the hope and opportunity to not leave any stone unturned to healing them. The PPA can speed up the time for revolutionary breakthroughs and finally find the cure that we have been searching for centuries. Please help us save our children and give them the hope to live a long and healthy life that they so desperately deserve.

Cara Sarubin

Mother of Cameron



ALYSON NICOLE USHER

Perryopolis, PA

Alyson Nicole Usher was born in July 2006, she was a very happy and outgoing child, full of life and always wanted to make sure everyone around her was happy. On November 29, 2011 Alyson at the age of 5 was diagnosed with DIPG, a fatal brain cancer with no effective treatment, and was given 6 to 9 months to live. We were told that there was no cure, that treatments were only palliative, and there were no opportunities for participation in clinical studies available. She was given a death sentence with no hope. We were told to take her home, make her as comfortable as we could, and love her. Alyson took her wings in the comfort of her home, tucked into her bed with everyone she loved surrounding her in November 2012. Even though she is no longer with us, her legacy will never be forgotten, and we will continue to work on her behalf until options and treatments become available and a cure is found. The treatments and opportunities to fight for our daughter that were available were simply not enough.

Why the Promising Pathway Act is Important to our Family: The Promising Pathway Act may not provide the cure, but it does open the door for options and gives children like Alyson who face a fatal diagnosis a chance and opens access to trials. The Western Pennsylvania Chapter of The Cure Starts Now was formed in memory of Alyson Usher. The Cure Starts Now (501c3 Federal Non-Profit) is one of the only cancer foundations dedicated to a "homerun" cure for all cancers, starting first with one of the most deadly and difficult cancers: pediatric brain cancer. Many experts believe that the lessons we learn from fighting pediatric cancer may in fact provide us the critical first step in winning the battle against all forms of cancer, both pediatric and adult. Our family and the currently available science and medicine could not find a way to cure our daughter's cancer, but we continue to work so that there are options and treatments for the next child. The Promising Pathway Act is a vital step in the right direction.

Alyssa Hawranko

Nicholas Usher

Parents of Alyson

RAY EWING

Pittsburgh, PA

In March of 2019, as a 42 year old father of four daughters, I was diagnosed with an astrocytoma in my pons. Some have called it a midline glioma, others DIPG. Regardless, I was facing the scary reality (as was my wife) of not living long enough to walk my girls down the aisle on their wedding days. I have been treated using standard of care and have been stable since. But, I get regular scans to monitor my brain.

Why the Promising Pathway Act is Important to our Family: I have many reasons to fight – mainly my wife and 4 kids. When you are facing something like brain cancer, you don't always have time to sit and wait for new approaches to be vetted over many years. The PPA is important to me, so we can more quickly identify potential cures or, at a minimum, slow any growth until there is a cure. If a drug has proven to be a potential answer, I want to be able to get in on it as quickly as I can, if ever needed.

Raymond A Ewing Jr.

Astrocytoma Patient



Good morning Senator Braun and Committee Members:

My name is Paula Smith. My son, Josh Smith, was diagnosed with ALS at just 28 years old. We are writing to share our story that demonstrates the need for the Promising Pathways Act for people with imminently fatal rare diseases.

Imagine if you got a treatment for your 100% fatal disease and it helped you but then you couldn't get more even though you, your family and your world class neurologists KNEW it helped you. And now imagine, you would continue to get worse every day if you didn't receive that treatment. That is what is happening to my son, Josh, and it's why we need your help. Josh participated in the NurOwn Phase 3 trial.and Expanded Access Program It halted his fatal progression and restored some function. As you know as the Co-Chair of the ALS Caucus, this NEVER happens in ALS. But he can't get more and the FDA has refused to approve it under the current regulatory law. **Without NurOwn, my son will die waiting when he knows the drug helped him live.**

We believe the Promising Pathways Act is necessary for people with imminently fatal rare diseases. We have tried, failed and exhausted our efforts to get the FDA to listen to my son's evidence that NurOwn works. We spent 100s of hours on zooms with Congress, including members of both the HELP and Energy & Commerce Committee as well as the specialized committee staffers; we participated in a protest of the FDA in 2019. We've met with the FDA at a PFDD meeting in 2021 with other people in EAP all who shared how NurOwn worked. We've traveled to see multiple doctors, neurologists and pulmonologists to document his every clinical improvement so someone, anyone, would believe us. We've taken our story to the media and local radio. We'e shared our family's private life on social media trying to raise awareness how this drug has given my son a chance to live. Even at NFL football games, we tailgated and advocated to gain attention for Josh's story. We submitted Public Comments for the AdCom and we testified at the FDA's Advisory Committee meeting on September 27th. We've sacrificed quality of life in Josh's precious last few years to get the FDA,to listen to us in the hopes it will give him more time. This takes a horrific toll on Josh, and our entire family every time we have to rehash how NurOwn helped Josh and how he has declined when he couldn't get more access. **No one has listened.** That is why we know we need the Promising Pathways Act to change the way drugs are approved for imminently fatal rare diseases like ALS. **The current regulatory law is allowing my son to die.**

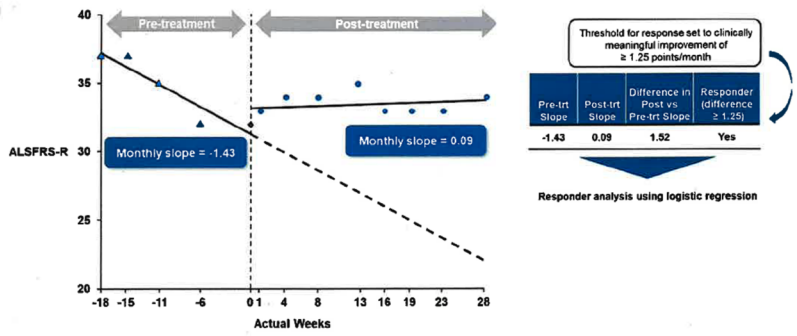
As you know, ALS is also known as Lou Gehrig's Disease. ALS is 100% fatal, but before it kills you, it paralyzes every voluntary muscle in your body. The disease is cruel and relentless. Your body becomes its own coffin. People don't spontaneously get better nor do they halt progression over long periods of time. **But my son Josh has!** The average lifespan is 2-5 years and 50% of the population dies within 18 months of diagnosis. At just 28 years old, my son was diagnosed three decades earlier than normal. Josh had ALS symptom onset in June of 2018 and was diagnosed with ALS in February/March of 2019. Four years ago, Josh was losing 1 point per month of function on the 48-point scale. Joss should not be here today. Instead, he is still walking, talking, eating, breathing and living -- beating the odds of the 2-5 year lifespan. We know that is because of an autologous stem cell therapy called NurOwn.

Josh was in the NurOwn trial in 2019 and 2020, then received 6 additional doses via Expanded Access in 2021 and 2022. Our family and friends know NurOwn works. At the September 27th Advisory Committee before the FDA, Josh and I shared our testimony during the Open Public Hearing. Here is the link to the AdCom Video with our testimony and that of other people in the trial. Our testimony begins at 9:35. In our public speech, I shared:

> **"We believe NurOwn works. My son deserves this promising treatment. I will continue fighting this fight for him to receive it. My son is enough.**
> **He wants to live. Today we ask the committee to grant approval for NurOwn. Josh is living proof that this treatment works. Together we can provide**
> **hope and a chance for a better future for everyone living with ALS."**

Josh was fortunate to get into the NurOwn phase 3 trial shortly after diagnosis. When Josh gets NurOwn, it halts his lethal progression and paralysis. In some ways, he regains function -- something that never happens in ALS. Not only does NurOwn improve how Josh functions, but his symptoms of fasciculations, pain and clonus also decrease. When he gets NurOwn, he gets better. When he doesn't, his ALS gets worse. It's really that simple.

In the trial, the clinical data met clinical meaningfulness and statistical significance for those earlier in disease progression. This was Josh. **This is no different than cancer therapies where those who receive therapy earlier in disease progression have a better prognosis.** The NurOwn trial met its **pre-specified** endpoint for those with scores ≥35 on the 48 point functional scale. In fact, the trial data confirmed that it halted progression for the people with scores ≥ 34. Here is an example of a slide presented at the NurOwn AdCom. It shows that another person with a score above 35 at baseline also halted his progression -- just like Josh! Josh's score at baseline was 40. This slide corroborates our testimony and all of Josh's real world data.



Despite the clinical trial data, real world data and the first-in-class biomarker data in the trial -- and the fact that it met clinical and statistical significance for people in Josh's subgroup -- the trial failed to meet its overall endpoints because NurOwn didn't show efficacy across the disease spectrum for those whose disease was more advanced, Thus, even though there is "substantial evidence" that it works on some, the FDA is approving it for no one. Instead the FDA is requiring the company to do another Phase 3 trial to confirm what our family already knows. NurOwn works. This trial will likely take 5 years to be completed and make it through the regulatory process. **In 5 years, my son will be dead.**

How inhumane is it that Josh knows NurOwn worked on him, and he provided clinical data and video documentation to the FDA that it improved how he "feels functions and survives." Even though this is the legal standard for approval, the **FDA says some evidence is not enough in this 100% fatal disease.** Tragically, NurOwn showed the same "**early evidence of efficacy**" in the Phase 2 trial in 2015 and in the Phase 1/2a trials in Israel in 2011/12. At the AdCom, an Israeli neurologist testified that many people in those Phase 1/2a trials are still alive today -- over a decade later. But this remarkable Phase 1 data was ignored because it was not a placebo-controlled trial. The Phase 2 data was ignored as it wasn't a large enough sample size nor enough doses to meet statistical thresholds. The Phase 3 data has been ignored as it only met statistical significance on those earlier in disease progression, like my son Josh. The EAP data has been ignored as there was no placebo. **This is precisely why we need the Promising Pathways Act as under that proposed law, NurOwn would be approved today and my son would have a chance to live longer.**

Our evidence is not the only evidence that was submitted to prove NurOwn works. Many elite ALS neurologists and researchers also provided testimony and expert opinions that NurOwn works. Not one word of their testimony was discussed at the eight hour Advisory Committee meeting. ALL these neurologists have more experience with ALS than anyone at the FDA. Yet, their clinical observations, real world data, and expert opinions were ignored -- even though they are the only people in the world who had the opportunity to document their patients' improvements on NurOwn.

For example, Josh's neurologist and investigator in the trial was Dr. Robert Brown at UMass. Dr. Brown has been seeing people with ALS for more than 40 years. He is the person who first identified some of the genes that cause ALS, and is one of the world's most pre-eminent ALS experts. Dr. Brown has over 300 peer-reviewed studies. He has an h-index score of 113 and an i-10 index score of 326. This puts him among the world's most elite, published and cited researchers -- in any disease.

Dr. Brown witnessed NurOwn work on Josh. Shortly after the end of the trial, Dr. Brown shared the following opinions. On January 10, 2021, Dr. Brown said there were an: **"EXCEPTIONAL number of folks who have had a VERY DRAMATIC RESPONSE.... I will repeat, I think there is a benefit from the NurOwn stem cell therapy!"** On February 22, 2021, he reiterated his belief that NurOwn works and said publicly, in a press release that **"MANY of us with longstanding experience in ALS therapy development agree that there was EVIDENCE OF BENEFIT from NurOwn."**

Another investigator in the trial who shared his clinical observations and led the presentation at the Advisory Committee meeting was Dr. Anthony Windebank of MAYO Clinic. Like Dr. Brown, Dr. Windebank has been seeing people with ALS and conducting clinical trials for over 40 years. His h-index is 85 and his I-10 index score is 258. This puts him among the most elite, published and cited ALS researchers. In addition to presenting the trial's clinical data and discussing the critical unmet need in ALS, Dr. Windebank offered the following expert opinion that was never discussed by anyone in the eight hour Advisory Committee meeting. **This is evidence of efficacy that would support approval if Promising Pathways were the law.**

> "As someone who treats people with ALS and has been involved in biomedical research & clinical trials for more than 40 years, including as the MAYO principal investigator for the NurOwn phase 2 & phase 3 trials, I would now like to provide my clinical perspective on NurOwn.... Let me summarize why I think this data is compelling & WHY IT SHOULD BE APPROVED.... I believe NurOwn has an acceptable safety profile & have no concerns about treating my patients with this product.... As a clinician investigator, I also look closely on the aggregate basis. While it is clear that not everyone responds to the treatment, **there are CLEARLY A SIGNIFICANT NUMBER WHO DO. I have clearly seen some people STABILIZE in a way that I have NEVER seen IN ANY OTHER TRIAL.** In fact, in the small number of people who participated in EAP & received 6-9 treatments, there were people who STABILIZED while on treatment in the trial. In the interval before they were in the EAP -- which was over a year or more in some cases -- these participants deteriorated... then again STABILIZED in the additional treatment period. There were also **SOME WHO IMPROVED THEIR SCORE FROM BASELINE** ... something that is rarely seen. I should stress that **other investigators who have been working 'hands on' with the participants in the trial have seen similar responses**.... I can tell you that the value of any form of independence or stabilization for these patients is beyond words. For these

reasons, as a physician who cares for patients, I want to see NurOwn made available for people living with ALS. The patients can't wait.

Dr. Windebanks' testimony matches Josh's real world experiences. He testified about the cyclic nature of the stabilization-decline-stabilization-decline-stabilization pattern that happens when people get NurOwn versus when they don't. A summary of Josh's changes in function is attached below. Similarly, Josh's local neurologist -- unaffiliated with the trial -- witnessed the same thing in the years he was treating Josh. In the Public Comment he submitted to the FDA, Dr. Vladimir Klinov said: **"when Joshua was in the Nurown trial, the disease progression significantly slowed down and he even had some improvement, and since the infusions were halted he has declined tremendously. At this point, in my professional opinion, NurOwn trial has given Joshua a quality of life that was unexpected but proved to be giving him more years to enjoy life, especially at such a young age."**

Another one of Josh's neurologists is Danielle Geraldi-Samara. She is a neuromuscular specialist in ALS. Because she sees patients via telehealth and is licensed in multiple states, she has the unique perspective of seeing multiple people in the NurOwn trial. She submitted a Public Comment with her clinical observations that NurOwn works. Her testimony included the following:

> **"What I have not seen, though, is anyone with significant functional improvement from a declining baseline; I have not seen patients rise from plateaus. It does not happen in the natural course of ALS. It did happen with the introduction of NurOwn. The real world evidence could not be more striking.... I have patients with solid plateaus over the course of a year and patients climb up what we have previously known to be unscalable in the disease process, the ALSFRS-r. Some patients slowed their progression from 1 point a month to 1 point every 6-10 months over the ensuing 3-4 years. Some in EAP halted their progression when they received NurOwn and began progressing without it. This pattern was repeated each time they received NurOwn."**

Moreover, Josh is not the only Pennsylanian who was helped by NurOwn. Navy pilot Matt Bellina, also received 7 doses of NurOwn via Right to Try in 2019 and 2020. As a veteran, Matt got ALS from his service for our country. He was the same age as Josh when diagnosed. After getting NurOwn, Matt was able to stand up unassisted out of his wheelchair for the first time in nearly 2 years. He also regained function in his hands and stopped using a bipap to breathe. To this date, he is still not using any assistive devices to breathe. This improvement in breathing function is consistent with what we shared in our Public Comments and testimony, and consistent with the testimony of Dr. Windebank, Dr. Klinov and Dr Geraldi-Samara.

This is a link to Matt's video evidence posted on his facebook page on May 8, 2019 -- where he documented his improvement in real time. Matt and his family have repeatedly shared this video with the FDA, as have other patient advocates in a PFDD meeting in June of 2019. Attached below is a document summarizing Matt's clinical improvement. Unfortunately, Matt's testimony is not in the AdCom hearing as his family wasn't chosen to speak with the FDA's lottery system. But his mother did submit a Public Comment and her link is attached below. Please consider these two points: the Navy entrusted Matt with a $50 million jet, but the FDA won't trust his opinion that a drug improved how he feels and functions. And despite getting ALS from serving our country, our country is now blocking Matt's access to a drug that he proved worked for him.

Attached below are links to the referenced Public Comments submitted to the FDA. Please include these and all other links in this email in the Congressional record for the October 26th hearing of the Special Committee on Aging.

- Josh's Public Comment: https://www.regulations.gov/comment/FDA-2023-N-2608-0060
- Dr. Robert Brown's Public Comment: https://www.regulations.gov/comment/FDA-2023-N-2608-1271
- Dr. Klinov's Public Comment. https://www.regulations.gov/comment/FDA-2023-N-2608-1614
- Dr. Danielle Geraldi Samara's Public Comment. https://www.regulations.gov/comment/FDA-2023-N-2608-1615

- Dr. Terry Heiman-Patterson's (Temple) Public Comment. Josh visited her once when we relocated to Pennsylvania. https://www.regulations.gov/comment/FDA-2023-N-2608-1759
- Dr. Christina Schaff (Temple) Public Comment: https://www.regulations.gov/comment/FDA-2023-N-2608-1827
- Deb Bellina's Public Comment: https://www.regulations.gov/comment/FDA-2023-N-2608-0012
- Joint Public Comment of people in the NurOwn trial: https://www.regulations.gov/comment/FDA-2023-N-2608-0822

Thank you for your time and consideration. Because I am busy taking care of Josh and my husband Randy who just had triple bypass surgery, I have asked another ALS advocate to help me compile the evidence to submit our statement for this hearing before the Senate Special Committee on Aging. But if you have any questions, please feel free to reach out to me.

With hope,

Paula Smith
Carlisle, PA
(732) 232-8621
psmithtigress@yahoo.com



October17, 2023

Dear Senate Committee on Aging,

Those of us who deal every day with ALS know the devastation this disease causes, how ALS takes everything from its victims. For nearly 150 years, ALS has been attacking with no response to slow its progress.

ALS takes away a person's ability to walk, to talk, to swallow, to smile and ultimately to breathe. ALS is not rare and it's actually becoming more prevalent.

We need The Promising Pathway Act to give us some hope. Every day I watch my daughter struggle to care for my son-in-law. I see him in his heroic struggle to help other ALS victims. He and my daughter reach out to others newly diagnosed because they know the hammer hit that diagnosis is.

The Promising Pathway Act will go a long way to helping us find a treatment for ALS. We thought we had NurOwn but the FDA derailed that hope. Help us. ALS is a monster that for unknown reasons is increasing its .ncidence rate. We need the unknown researched to become known. Help us. The monster is already in my family. And ALS, I fear, is coming to a family near you. Help us.

Sincerely,
Cecilia Viti
Mechanicsburg PA

[redacted]

On behalf of the I AM ALS organization, I wish to provide testimony in regard to this pending legislation.

Three months is all that my grandmother lived once she was diagnosed with ALS, or Louis Gehrig's disease. At the time, I was just an eleven year old kid but watching my maternal grandmother not have control of her drooling saliva was an impactful image that sticks with me even today. Little did I know that she would be the FIRST of THREE people involved in my own life who suffered or are now suffering with this excruciating, terminal disease. It rips life out of many Veterans (one in three Veterans are diagnosed with ALS) as well as the general population - mostly those over sixty years young. It has a ripple affect in so many others- all devastating them financially, spiritually, emotionally and socially, to name a few.

These sixty something year olds have daughters, sons, spouses as well as employment roles to attend to. They can no longer do these jobs or any other small tasks like bring home the groceries or manage their homes. Normal living for them completely STOPS. But once ALS hits, they can do nothing of the sort. Their income stops short, they drain their investments and their bank accounts just trying to stay alive long enough to maybe become (or dream about becoming) a grandparent. Many do NOT make it to that juncture in life, as their lives are cut short long before any grandkids are born.

As a private citizen and Veteran who served over 20 years protecting this nation, I urge you to support the Promising Pathway Act (PPA) (H.R.4408/S.1906). This legislation calls for the U.S. Food and Drug Administration (FDA) to establish a rolling, real-time, priority review pathway to grant or deny provisional approval status for drugs intended to treat, prevent, or diagnose serious or life-threatening diseases or conditions like ALS. We did this for COVID; we can do this for the over 6000 Americans who now suffer with this terminal disease. Could we at least provide the ALS patients with a dignified life - what little they may have left? Supporting this bill would send that message from your office onward towards the families who care for the thousands who have or will soon be diagnosed with ALS. Won't you enable them a bit of dignity right when it counts?

Thank you,

Kathy Silvia
Army Veteran

Meg D. | Pennsylvania (1 of 2 pages)

We Can't Wait

Age: 40
Year of Diagnosis: 2020
Type: Limb Onset

Having access to ANY new therapy that offers ANY benefit or chance of improvement for this disease is of utmost importance to my family and me. ALS is one of the only diseases where there is no chance of a cure....it is a death sentence. Chemo may not help or cure a cancer patient, but there is a chance it will. People with ALS don't have that hope. There is not enough time to wait for FDA approval on these new therapies. Let people suffering with this viscous disease make the determination if the risk of a new therapy is worth it to them. It is their only hope! It is barbaric to live with this disease knowing there is nothing you can do but wait until you no longer have use of any part of your body! We need this law to pass now!

As I mentioned above, having access to ANY new therapy that offers ANY benefit or chance of improvement for this disease is of utmost importance to my family and me. ALS is one of the only diseases where there is no chance of a cure....it is a death sentence.. Let people suffering with this viscous disease make the determination if the risk of a new therapy is worth it to them. We would rather try a new therapy and not have success than to sit idle and watch loved ones waste away from this disease with nothing to help them. It is a no lose situation. Let us decide what we can handle.

For diseases like ALS where there is no FDA approved drug/therapy or any drug which helps mitigate the disease, it is not important. The effects of ALS are barbaric....The FDA should absolutely due it's due diligence for any drug or therapy brought to its organization, but for ALS, it should not be the ONLY way to be able to try a therapy when it's a mere life or death situation. So in other words, continue to utilize the FDA as new therapies emerge, but let the ALS patient try therapies as they emerge at their own risk.

It has virtually stopped our life. My dad is no longer able to move or feel his legs, so all he can do is stay home. Our cars can't support his scooter/wheel chair, he can no longer take showers or do ADL's on his own. For now he still has his upper body strength, but that is weakening as well. My parents will need to move or build on to accommodate his lack of ability to move, but struggle with the financial aspects of the disease. My dad was diagnosed the year he retired, so my parents never got to enjoy all the things they had planned. They cannot travel, see their grandchildren play sports, go out to dinner, go to weddings/family functions. Everyone has to come to him. He is morally defeated to know we have to help him with literally everything from going the bathroom, to cutting his hair. The absolute worst part of this is that there is no hope for him. Not one med approved to help him so it's a anxiety ridden waiting game....like what's going to happen next to my body. There is no upside....it's all downhill. We need to be able to try therapies...if it even helps one person, it will be worth it!

Meg D. | Pennsylvania (2 of 2 pages)

We Can't Wait

Age: 40
Year of Diagnosis: 2020
Type: Limb Onset

I have 4 of my own children but my mom cannot care for my dad on her own. They rely on my siblings and I for everything. She is getting too weak to help him...I'm scared at what the future holds. Even the simplest tasks such as outside chores are too much physically for her to do on her own as well as take care of my ailing dad. We visit and help as much as we can, but we miss their visits to our house, vacations, they attendance at kid's games, etc. My children are heartbroken to see their grandfather who was so physically fit and healthy slowly deteriorate.

The despair in knowing there is no hope at the moment. That feeling keeps me awake every single night of my life. My dad needs a chance at life. We can't wait years for therapies to be tested and approved. We need help now!

I did the Ice Bucket Challenge years ago but didn't think too much about it because no one I have known ever had ALS. I never dreamed just a few years later this would be my life. This is not a normal disease. We need hope and we need help! We cannot treat it like a normal disease and we have to get creative in an effort to save lives and bring hope to a ravaging and barbaric disease. Please put yourself in our shoes!

Gary G. | Pennsylvania

We Can't Wait

Age: 67
Year of Diagnosis: 2010
Type: Limb Onset, Genetic

Every discovery is a step in the right direction. Of course, we want to "cure" found yesterday, but each small step builds to finding the cure.

Would not be as eager to promote a therapy with significant side effects, but we have to take the risk to find the cure.

The average life span for an ALS patient is far shorter than the time to take the FDA to approve a new drug. Therefore, we cannot wait for final approval before taking a new drug. We understand the risk, but we also understand we are dying within 2 to 5 years.

My wife lived 3 1/2 years after being diagnosed. About 1 year into her journey, she had to quit working and driving. About 2 1/2 years into her journey , she became bedridden, lost her ability to speak and couldn't eat any longer. Luckily, we were in a position to keep her at home until the last week, so she continued to be around friends and family. That helped immensely.

It was very difficult on us. After she became unable to walk, she was no longer able to take care of herself. At that point, I quit working to take care of her full time. She was most uncomfortable sitting up so being in bed was most comfortable. That meant we spent all our time staying home. Socializing with our friends was difficult.

While it is a debilitating disease, and greatly affects her speech and voice, she was still the same smart person. She sounded like she may have been mentally challenged, but she was not. People also kept asking about her, thinking she had a chance for improvement.

We need to find a way to diagnose ALS much sooner. **Today, by the time a patient is diagnosed, they have already suffered irreversible damage and life with those challenges in no life.** We need to get ahead of the curve, not just find meds that will extend a patients compromised life.

Robert P. | Pennsylvania

Age: 68
Year of Diagnosis: 2019
Type: Limb Onset, Sporadic



We Can't Wait

Very important to have the chance to try something that will help. I would look at the significant side effects and make a determination.

I would assume a risk if the drug has shown positive effects and is not FDA approved. It is a very scary diagnosis, but I try to live day to day.

It has affected my wife the most since she is my caretaker. The devastation of the disease. **Those of us diagnosed with ALS need help quickly.**

Lisa M. | Pennsylvania

Age: 53
Year of Diagnosis: 2021
Type: Sporadic

We Can't Wait

Very Urgent that All ALS patients be provided with ALL options to all and any Trial Medications

As previously stated, the **person living with ALS should have the option to decide** Not the Doctors or the drug companies .As we know each person with ALS can react differently

Very important to be included and complete a clinical trial process.

For me this was life altering . At 53, I am now waiting to see if I will live to see my grandchildren grow up with No understanding of how and why I now have ALS

My children are suffering not knowing what will happen to their mother

That All Person with ALS can progress differently . I would wish that the Neurologist would do more than give a diagnoses then say return in 3-4 months when this is precious time of a patient's life

My life is on my hands ,The drug companies and Neurologist are playing God with our Lives

Scott M. | Pennsylvania

Age: 52
Year of Diagnosis: 2019
Type: Limb Onset; Sporadic

We Can't Wait

It's very important! I for one don't like trying to figure out what's the next thing to stop working and when. It's better than just waiting to die.

If it shows any sort of benefit, I would take it. **I'm not ready to die.**

Too many ways to list here.

How horrible this disease is. It takes your ability to do everything away from you, and you're fully aware of what's happening to you and the FDA sits on their hands while people die.

I'm not ready to die. I think most people with ALS feel the same way.

Get drugs in bodies as soon as possible!

Eudonna L. | Pennsylvania

Age: 63
Year of Diagnosis: 2019
Type: Genetic

We Can't Wait

Very important to have medicine. Any medicine.

There is no hope, only hope is you start trying anything you can!!
Very important to try anything and everything.

It has ruined life for him, 48 years old, you must be kidding

They only have hope to cling to

It's awful effects, A death sentence, you need to start helping!

These questions are an embarrassment, It is sad you would ask these, when you know how bad it is

Lisa M. | Pennsylvania



Age: 71
Year of Diagnosis: 2017
Type: Limb Onset

Give ALS patients ALL ACCESS to all therapy options! VERY IMPORTANT for ALS patients to have HOPE, CHOICES and OPTIONS, even if modest benefit. When my mom had ALS, she was barely even offered any clinical trials for participation!

EACH patient needs to be able to make their OWN CHOICE how they feel about the risk but ALS IS A TERMINAL ILLNESS....Any therapy offering time and hope is important

OF NO IMPORTANCE at ALL to wait on the FDA! The FDA operates at snail speed.....ALS is a terminal illness. Give patients the options to try therapies/and/drugs. **I bet 95 out of 100 ALS patients would agree- SPEED this UP ASAP!** People are literally DYING everyday while someone at the FDA is slowly pushing papers in a clinical process. TIME is of the ESSENCE! Forget the FDA process -- if a COVID Vaccine could be done and available in 6-7mos, the ALS options are possible too!!!

My mom had ALS and she passed in 2018 at the age of 75. She survived just shy of 4 years after diagnosis. **ALS impacted EVERY aspect of our family's life for many, many years.** It was devastating, sad, caused financial hardship and took away my mom's chance to enjoy life, retirement and her 50+ year marriage with my dad. We must find a cure NOW.

My dad, my brother, myself, our spouses, grandchildren and my mom's siblings were all impacted and lost a wonderful person to an awful cruel disease.

ALS takes away your life, your breath, your dignity, your happiness and everything you care about. It is a cruel and awful illness that is not understood by most people. **I implore you to toss the clinical trial process, the FDA "rules" and FIND A CURE NOW!**

This past pandemic year has been especially cruel to ALS patients/families because ALS is SO SO SO SO SO much worse than COVID but no one seems to care in finding a cure. Again, if science can figure out SEVERAL Covid vaccines, Covid infusions, etc. in only 6-7 months time, we can solve the ALS mystery and find a cure!

Kimberly B. | Pennsylvania



Age: 52
Year of Diagnosis: 2018
Type: Bulbar Onset

ALS is a death sentence. All the doctors can do is "manage" the disease and try to outsmart it....and sadly it's an insidious diseases so always has the upper hand.

My brother would have taken the new therapy as ALS is a death sentence.

My brother worked in the pharma industry a good chunk of his life and believed ALS needs to be treated like oncology or infectious disease...when products get signals in Phase 2, it should be open to all ALS patients

My brother passed away March 12, 2021 after a 3.5 year battle with ALS. The last 12 months were awful for him...he was paralyzed, 100% reliant on his wife for care and in great pain as muscles dying cause great pain.

His one son suffers from major depression and has not been able to hold a full college class load of class the last 3 years, **his wife has PTSD from being is full time caregiver,** his 2 other sons also have PTSD from being back up caregivers. Additionally, his wife and 3 sons had to forgo their health for his health.

It's a death sentence, the current rx therapies control symptoms and don't delay progression, and it's very painful disease. In addition to impacting the patient, his family is just as impacted watching the slow, slow decline.

Treat this disease like Oncology or an Infectious disease

Christine S. | Pennsylvania

Age: 70
Year of Diagnosis: 2021
Type: Limb Onset

We Can't Wait

Any drug that will slow down the disease is a blessing.

New drugs give us people suffering from ALS some hope. By the time the FDA approves of a new drug for ALS most of us will be dead.

It has totally impaired my life. I can no longer work or do the normal workload I usually did. My speech is deteriorating, and I am having difficulty breathing. Walking up the stairs has become a chore. Swallowing has also become an issue. I feel somewhat isolated because I can only talk for a few minutes to my friends.

They feel sorry that at the moment there is no cure for ALS My family wants to help me to be comfortable and content.

We need to educate the public about the disease. Most people never heard of ALS. When I told people about my diagnosis, they had to look up the disease. We also need more support from the public. More funds are needed for drug trials.

We need the drugs NOW. If a drug has any type of promise they should let us try it.

Frances P. | Pennsylvania

Age: 67
Year of Diagnosis: Husband: 2020
Type: Limb Onset, Sporadic

We Can't Wait

My husband is willing to try any new therapy.

My husband feels he has nothing to lose by trying new therapies.

That is not important to my husband or me.

I am my husband's caregiver and I take care of him 24/7. It is hard to see him get weaker and less independent. It is hard on our children and grandchildren to see him participate less and less in their lives.

My husband can't participate in my children and grandchildren activities. My grandchildren miss him doing things with them and one always says that he wants his grandfather to be the old way.

I wish people would understand that even though the person with ALS looks different, he is still the same person. They want people to talk to them and not be uncomfortable with them.

Please help ALS patients by letting them make choices on treatment. They don't have time to wait.

John R. | Pennsylvania



Age: 65
Year of Diagnosis: 2013
Type: Limb Onset, Sporadic

Any new therapy that slows the progression of ALS is critical to ultimately solving the 150-year-old riddle of this disease. Meaningful treatments and ultimately a cure will be built upon a foundation of incremental improvements in the now dreary prognosis for patients with ALS.

There isn't much worse in this world then living with ALS. Currently, a patient starts out with a 2-to-5-year prognosis with zero chance of reversal or survival The chance of modest benefit far outweighs the risk associated with participating in a drug trial.

Considering the fact that I have never been eligible for a drug trial because I had symptoms 30 months before diagnosis, and that **there are so few opportunities for ALS patients to get into any trial**, I feel that it is less critical for the process to be complete, and the drug approved by FDA prior to taking it. AMX0035 is the perfect example of a drug I would take prior to the full process being completed.

My wonderful life of movement and doing things I loved to do has not existed for the last 3 years since my diagnosis. Although I am able to function mentally, still eat real food and breathe without assistance, along with the fact that I live comfortably with my wife in a beautiful home and neighborhood, this is not a life I would choose for anyone. Grueling both mentally and physically, **ALS has destroyed what was an incredibly beautiful existence.**

My wife and I have been together for 42 years. we have no children, so she is my primary and currently only caregiver. Her life has changed courses along with mine. it has already taken a mental and physical toll on her. The other most affected person is my 93-year-old mother who still lives on her own. She has endured so much in her long life and watching her child succumb to this disease is heartbreaking. **Our entire family and long list of friends are forever changed by my ALS journey.**

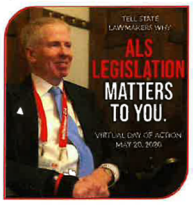
ALS does not discriminate. There is zero chance of survival. Your chance of getting it is the same as multiple sclerosis which has proven to be a long term, livable disease. Anyone living on the planet should be fearful of presenting with ALS.

Personally, I understand that ALS is a very difficult puzzle to solve. **I appreciate the efforts of pharmaceutical companies willing to invest in ALS research.** I also applaud the effort of our FDA to work more closely with industry over the past 5 years. That said, ALS is not like every other disease. The history of failed therapies and the long list of deaths with no chance of survival is ridiculous in this day and age**. I would like all involved to think outside the box with regard to clinical research, clinical trials, and the rules that apply for all drugs that may not be applicable if we really want to solve the mystery of ALS.**

Chip C. | Pennsylvania



Age: 61
Year of Diagnosis: 2008
Type: Limb Onset, Genetic



I think valuable more so to families who want as much time as possible

With great excitement

I am willing to take both if it helps people living with disease or finding cure for future generations
Well, now live in nursing home as my lower legs don't feel or work, and I have feeding tube and cpap
I am not really sure how this has affected my family, **with covid going on I have not seen any of them for almost 2 years**



The more the hear of it and know it's 100 % fatal is always an eye opener

Just that the most drugs and treatments gets us closer to our final goal of a cure

Frederick A. | Pennsylvania



Age: 64
Year of Diagnosis: 2019
Type: Bulbar Onset, Sporadic

Any chance to prolong life is desirable, just to slow down progression of this horrible disease would be welcomed.

If a therapy has no harmful side effects, I see no reason to not try it in hopes it might help in some way.

I am not able to wait the time needed to complete a clinical trial and the red tape associated with them.

Disrupted everything, can no longer work, lost my recreation, can no longer speak or eat, starting to lose mobility. Trying with all my heart not to lose hope. What hurts the most is the fear in my wife's, children and grand children's eyes when the recognize what I can no longer get do.

Terrifies them. My wife had to stop working to care for me, our retirement and are now null and void.

How difficult it us to be isolated in your own body even when you're with people.

Look how quickly everyone pulled together to get covid vaccine out, I do not understand why the same protocol cannot be used wink ALS therapies. ALS us always fatal, 100%, no maybe, would gladly sin a waiver to get a therapy while the experts try to find a cure.

Linda K. | Fillmore



Age: 58
Year of Diagnosis: 2013
Type: Bulbar Onset

Any benefit no matter how small, is vital when faced with a 3–5-year prognosis. Let me try it!

The impact of the side effects on my quality of life would be a factor in my consideration of an exploratory treatment.

I would trust my doctor prior to authorization by the FDA and take it with their recommendation.

I went from being very physically active to basically quadriplegic in four years time and I have had to adapt along the way. My biggest growth was in graciously accepting help as needed.

It has created stress and sacrifice in the lives of my immediate family that they deal with on a daily basis.

ALS is a neuromuscular disease that doesn't affect the minds thinking and processing. Take the time to converse and be patient with alternate forms of communication.

Just keep in mind that small increase in time is important when your time is limited conclusively with ALS.

AVANI DOSHI

Oxford, PA

Born 11/23/2005 Avani was a, fun-loving, and big-hearted little girl. If you were to ask someone what they remembered about her, they would respond with that smile. (She had the best giggle too!) She was the first person to greet a new student and make them feel comfortable in school. Avani loved life playing any kind of sport, she especially loved tennis and played competitively since she was 7. Trying new things intrigued her, she excelled at anything challenging, and she just enjoyed life during her short 11 years. Avani had undiagnosed DIPG. She never showed any obvious symptoms of her cancer. Feb 6, 2017 she became ill, and passed away later that night (Feb 7,2017). It took a few months for us to learn the cause of death – a tumor in her brain that burst. Avani never complained, not even on that night. She was a bright light even in her last moments.

Why the Promising Pathway Act is Important to our Family: Avani never missed a chance to help others. She would even get in trouble herself in order to help someone else. In her short life she accomplished spreading so much hope and joy. If she had the opportunity to help she would never turn it down. When we finally found out it was cancer our first response was why Avani ? She had so much to offer this world, she could have cured cancer.

If there was anyway we could have donated any samples to research tissue, blood, anything we would have done it. It was too late for us but there are millions fighting with no hope. Any chance is a chance. When Covid hit there was so much controversy vaccine/no vaccine. We had a choice well give our children that same choice! Please give a chance of a future to our children! Spread hope! Say Yes!

Sandra Doshi

Mother of Avani



My name is Rosemary Baffa, West Chester, PA, proud mother of Kevin Baffa who has lived with Barth Syndrome for 34 years!

Kevin has survived 9 cardiac arrests. He lives with heart failure, muscle weakness, and the inability to fight infection. What does that mean now?
Kevin works part-time at the Chester County Community Foundation, would LOVE to work full-time, but is physically unable. Kevin cannot drive, would LOVE to have this freedom, but his leg muscles are not strong enough to maneuver the gas pedal/brakes and the steering wheel. Kevin would LOVE to move out of his parent's house, but despite the fact that he has earned his Bachelor's degree (7 years to do so), he does not have the income. We held our breath throughout the COVID time although we all were double, triple, quadruple vaxed. We hold our breath each and every flu season. Despite vaccinations Kevin has gotten the flu twice, once with a horrific heart failure result, the other another cardiac arrest. Life is difficult, but Kevin will never tell you that.

For 34 years we have been fighting symptoms, just trying to stay ahead of the threat of hospitalization and to be blunt, death. Effective therapies could change Kevin's life, and ours as well! More energy could allow him to work full time and receive benefits. More strength would give him the ability to drive and to gain independence. Fighting infection would take the spectre of death away from his psyche. Please help us help Kevin!

Thank you!

[redacted]

Senator Braun,
When my healthy, intelligent, amazing child was about to turn 4 years old, he had 2 "drop" seizures (just fell to the ground) at a birthday party with his friends. At the ER, they decided he had an ear infection - but thought they saw one more seizure. He had 10 more on the way home. Within weeks he could no longer walk, talk, toilet, sit unaided or feed himself. Hundreds of seizures a day ravaged his little body. He did not respond to medications. We were told he would not live to be 6.
Today Billy is a 37 year old man who is intellectually disabled, is diagnosed with Autism, PTSD, anxiety, depression, osteopenia, anemia, mega-colon, IBS, degenerating spine, muscle spasms, kidney stones, and constantly battles infections – including yeast infections that do not respond well to anti-fungals. Even more serious, Billy has a number of seizures a day – many of them requiring medical intervention – and is diagnosed with LGS – Lennox-Gastaut Syndrome. LGS is a rare epilepsy that does not respond well to medications, involves a variety of types of seizures (including seizures that cause broken bones, concussions, stitches, etc) and puts individuals at a high risk of death from SUDEP (Sudden Unexplained Death in Epilepsy).
Billy's brothers and step-brothers grew up in a home where there was no security of "day to day activity". Every day/every night of our lives is impacted by LGS and the co-morbidities that make it so dangerous. Ball games were cancelled, vacations cancelled, events had one parent show up – not two- mom spent as much time at the hospital as she did at home...and it was our "normal"
We fought for insurance, we fought for medications, for therapies, for the right doctors and the right hospital admissions. We fought for services in school and out of school. As a family, we are certainly blessed now, because Billy has a waiver that helps with staffing and supports and I no longer have to stay up all night, work a full-time job, and keep a house.
My parents moved in with me in 2002 when my then husband could no longer take the constant care-taking for our son. They have been a constant in Billy's life and I am grateful – more grateful than I can ever express – but they are now entering a time in their lives when -as octogenarians - they, too, will need care.
I guess the ultimate question is – Who cares for the caregiver? I have CTSD (Continuous Traumatic Stress Disorder) from caring for my son and never knowing if today will be the day that a seizure kills him or maims him again. The constant battles for services, supports, medical help – they wear me and my husband out. There is little/no time for each other and at 63 & 58 – there should be. We both work full-time, intense jobs, pay our taxes, support our loved ones.....but it is never enough. Caregiving is lonely and frustrating. It should never be this difficult to get help or support. Waivers should be better explained, medical care should embrace the whole person, and families should be respected for what they can offer – not questioned and restricted.
Again, I am lucky to live in Pennsylvania with a robust waiver system, to understand it well and to have decent staffing for my son... but it wasn't ways this way. It has been a war that has raged for 34 years and I'm always preparing for the next battle.

Sent from Mail for Windows

October 25, 2023

Dear Senator Braun,

My name is Nancy Small. I am a Huntington's disease (HD) family member, who did not inherit the gene for HD. But that doesn't begin to express the impact HD has had on my own and my family's lives. I have an HD family history genealogy scroll 8 feet wide and 8 generations deep with over 264 names on it that outlines in stark detail the impact this dreaded disease has had on just my family from as far back as we are able to track it. I personally have cared for my mother (who cared for my grandfather), my brother and my niece—3 generations of family who suffered this disease. It has been a major element of my identity from prior to my birth until today at 66 years of age.

For the purpose of this letter, I will focus on my niece, who is 42 years old, and has had HD symptoms since she was 32 years old. Please note her age, as it is a major factor in her unmet medical needs. Before the disease took hold, she was an accomplished teacher, having attained a master's degree from the University of Virginia (UVA) in the top of her class and working as a professional as the reading specialist for her school district. She has been living in a nursing facility for the past 3 years and is now in the advanced stages of the disease. Her twin daughters, ages 10 years old, were conceived using in vitro fertilization and pre-implantation genetic diagnosis to ensure they would be spared from the horrors of being born with the HD gene. Although they do not carry the gene for HD, for which we are grateful, that doesn't mean they've escaped the ravages of this disease for all of their days. Their mom's diagnosis came when they were only a year old. She was already beginning to have uncontrolled movements in her mouth and fingers. Her walking soon became affected. It progressed from there to her ability to speak clearly, sleep soundly, walk, or run with her children, cook their meals, oversee their schoolwork, be alone with them, drive a car, or be a part of their everyday lives. She went through a protracted divorce that alienated her ex-husband from her entire biological family, limiting her children's ability to be loved by anyone other than her ex-husband and his girlfriend. They have suffered right along with their mother. They not only have been witnesses to their mom's degeneration, but they have lived with the impacts of it stealing her from them, piece by piece, day by day as they have suffered the extraneous ravages of a disease so terrible that it savagely tears families apart and leaves children and the ill alone and scarred. They are with their mom about for about 3 hours a week. Their visits consist of lying in bed next to their mom, watching her be fed through a straw, or performing a song or dance or routine in some way to create engagement among them. They love her and they know she loves them, but she has not been able to be their mother for most of their lives. And they will soon grow up without her at all. This is what HD does to children, parents, professionals, marriages, and families.

My niece gave up joint custody of her children when she could not hire enough people to assist in her home to appropriately supervise and care for her children so they could safely live together. The children were forced to go live with their dad and his girlfriend. She moved to a sparkling new Assisted Living (AL) facility that promised her, before she put her home on the market, that she would be able to grow old and die under their care as long as she did not need

nursing interventions such as feeding tubes, permanent IV's, or artificial respiration. She took them at their word. Their care became so sub-par so quickly that the state intervened time and again. She was left in urine-soaked garments, was double diapered, was not provided 3 meals a day, had a call button that would go unanswered for hours at a time, until one night, she was physically assaulted by a staff member. And this wasn't the first incident of abuse and neglect. She had previously had hot coffee spilled on her causing burns, she had been left unattended without the seat belt secure on her wheelchair and had fallen and hit her head so hard that she was profusely bleeding and had a concussion, she had fallen off the toilet and hit her head again while a staff person was supposed to be assisting her with toileting, etc. At the time of the physical assault, she was belatedly taken to the Emergency Department (ED) and an investigation ensued. Because we were able to find another home for her before their Adult Protective Services (APS) investigation timeline ran out, the investigation was dropped. The victimizer continued to work at the facility with no repercussions. In fact, the facility put her on eviction notice. Finding her another home was an ordeal like no other. We investigated 25 Assisted Living and Nursing facilities in the Richmond and Mechanicsville, VA area. All but 2 would not "take" her due to either the disease diagnosis or her age. Any "nice" facility would not take her solely due to rampant age discrimination. They would not even have a discussion with the family, meet her or interview her. The discrimination against her disease was blatant and non-negotiable. For all the awareness building Huntington's Disease Society of America (HDSA) and other advocacy organizations have succeeded in doing, the care facilities have weaponized it against the people with the disease. You mention HD and they say, "Oh, I'm sorry, I must have made a mistake, we don't currently have any rooms available" or they are just more honest and transparent and say, "We don't take anyone with that diagnosis." This should be illegal.

- The unmet medical needs are the lax laws and oversight of care facilities.
- The unmet medical needs are the lax laws around abuse and APS's ability to go after abusers.
- The unmet medical needs are the lack of Primary Care Physicians or Gerontologists who will make in-home visits. As a result, it necessitates the patient go to the ED every time there is any question of an illness or injury. This is not due to lack of insurance or funds. It's solely due to the lack of physicians and medical services who can or will provide in-home care for things such as taking a urine specimen or blood for testing, tending to a burn, or doing a mobile x-ray of a potential limb or body part that might be fractured.
- The unmet medical needs are for transport. My niece has been transported to the ED over a dozen times over the past 3 years without anyone accompanying her or remaining with her while she was left waiting for attention for anywhere from a few hours to overnight while she lay on a narrow cot in a crowded hallway while her body is restrained because of her uncontrollable movements.
- The unmet medical needs are for an appropriate sleep set up. She sleeps on a mattress on the floor because her movements caused the mattress and box spring to separate and catch her between them.

- The unmet medical needs are for an appropriate shower chair that tilts in space, is padded, and conforms to her body and her size.
- The unmet medical needs are for a wheelchair harness that hasn't yet been invented that prevents her from sliding through the tightest seat belts and chest harnesses onto the ground.
- The unmet medical needs are for a scale at her AL home because of the cost and that they don't have the space (also a cost issue) for one that will accommodate her wheelchair. One of the hallmarks of HD is weight loss. We have been struggling to maintain her weight above 100 pounds for over two years now and she can't even be weighed without leaving her facility.
- The unmet medical needs are for consistent and ongoing PT. She "qualifies" for PT and then is no longer qualified because she's not making enough progress. Yet PT is what keeps her walking and keeps her muscles from atrophying any faster than they already do.
- The unmet medical needs are for ongoing and consistent speech therapy. Maintaining her ability to swallow is critical to her life (her two biggest risk factors are aspiration pneumonia and falls) yet she continues to be cut off from speech therapy because the therapy doesn't progress her swallowing or speech.
- The unmet medical needs are for ongoing OT to work with her changing needs for the shower, the scale, an appropriate bed for sleeping, appropriate chairs for sitting up, etc.
- The unmet medical needs are for insurance to cover all the medical equipment she needs when she needs it, such as a specialized bed, chair, wheelchair, walker, or shower chair. Her needs change as the disease progresses and insurance will only cover so much due to prior purchases.
- The unmet medical needs are for social, emotional, and psychological care. Although all facilities are supposed to provide activities and social interaction, a television playing in a group room does not meet those needs. Nor does being placed on a porch outside. Social, emotional, and psychological needs demand human interaction. Someone who has the time or the interest in talking WITH the patient, not at them. Doing something with them such as a craft, or gardening, cooking, or playing music. Someone who has an interest in what they are thinking or what they would like. Neither her neurologist's office nor we have been at all successful in finding a psychologist to come to the AL facility to meet with my niece. The best we have been able to do is to lean heavily on a local church to provide sacrament when they are occasionally able.

So, are there unmet medical needs for my niece? For others like her with HD? And others with rare, progressive, and serious diseases? Yes, there are many. She has been the strongest, most positive, loving person. She has not only endured the indignity of the losses of her marriage, her parents and her siblings, all of whom abandoned her to the disease (except her father who she inherited the disease from and who she personally spent her young adult years caring for), but she has had to live with the terrifying deterioration of her own mind and body and come to terms with her life expectancy being cut short by half. Anything we can do to provide her dignity and the best possible care is what we try to do for her every single day. I do my best as

an out-of-state family member as do the people who care for her where she lives, the private caregiver who supplements the care where she lives, and her children who care for her in their own special ways, but there is more that we as a community of caregivers, medical professionals, and legislators can do for her and others suffering like she does. We can look at these unmet needs and determine where the laws and regulations don't mesh with best practices and quality of care and try to amend them for the better.

I am so very grateful that you provided me with this opportunity to tell you a piece of our story. I hope this is helpful as you and your Senate Special Committee on Aging do your work. And I do hope that other degenerative neurological diseases less known than ALS, Parkinson's, and Alzheimer's, may also get the due they deserve as you consider your tasks going forward. A final thought, although your committee is called a committee on aging, I hope you will be able to make a difference for those who suffer from degeneration before they meet a specific "old" age number. The barriers to care due to being too young to be considered "old" have been especially intractable.

Thank you for listening and for your consideration,

Best wishes, Nancy Small (PA resident) POA and Aunt, on behalf of Christina Houghtaling (VA resident)

Nancy Small
1824 Trails End Lane
Upper Black Eddy, PA 18972
610-390-1786

Christina Houghtaling
7472 Eleanor Drive
Mechanicsville, VA 23111
610-390-1786

CYSTIC FIBROSIS FOUNDATION®

October 26th, 2023

Senate Special Committee on Aging
United States Senate
G16 Dirksen Senate Office Building
Washington, D.C. 20510

Dear Ranking Member Braun and Chair Casey,

On behalf of the Cystic Fibrosis Foundation, we thank the Senate Special Committee on Aging for the opportunity to share the stories of people living with cystic fibrosis (CF). As the committee looks for ways to support patients with rare, progressive, and serious diseases, we ask you to examine the rapidly growing threat of antimicrobial resistant infections to people with CF and other Americans of all ages.

Cystic fibrosis is a rare, genetic disease that affects nearly 40,000 people in the United States and causes the body to produce a thick, sticky mucus that clogs the lungs and digestive system, which can lead to life-threatening infections. As a complex, multi-system condition, CF requires targeted, specialized treatment and medications. When the Cystic Fibrosis Foundation was established in 1955, people born with the disease were not expected to live to attend elementary school. However, the emergence of transformative modulator therapies, which treat the underlying cause of CF, have given many people with CF the opportunity to lead longer, healthier lives. As a result of these new therapies and continuous improvement in disease management, the median life expectancy for people with CF has risen steadily over the last few decades.

Today, people with CF are living into their 30s, 40s, and beyond. According to data from the CF Foundation Patient Registry, half of babies born with CF between 2017 and 2021 are predicted to live beyond 50 years of age.[1] And though we have yet to see the long-term effects of modulator therapies on the age and health of the CF population, the percentage of adults with CF, both younger and older, is significant and ever-growing. As of 2021, over 25% of people with CF were over the age of 30, and approximately 5% of people with CF were over the age of 50. The oldest person with CF in the Patient Registry is over 91 years old. Yet CF remains without a cure, and many suffer from persistent lung infections, a hallmark of life with this rare and complicated disease.

Included in this older CF population is Kirk, a 71-year-old adult living with CF from Arizona, who has seen significant improvements in his health while on modulator therapies. With the help

[1]Cystic Fibrosis Foundation Patient Registry. 2021 Annual Data Report. Bethesda, Maryland. ©2022 Cystic Fibrosis Foundation

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4550 Montgomery Avenue, Suite 1100N, Bethesda, Maryland 20814
301.951.4422 800.FIGHT.CF Fax: 301.951.6378
www.cff.org email: info@cff.org

of these treatments, Kirk goes mountain-biking 50 miles a week and seeks to spread a message of hope to younger people with CF. As a septuagenarian – a milestone previously unreachable for most people living with CF – Kirk reflects on the significant improvements to his well-being thanks to modulator therapies. "I can breathe normally and am not instantly out of breath. I have a normal diet, have a normal weight, and live an active lifestyle thanks to CFTR modulators. I can't tell you how much improved my life is now from that which I was before these drugs came on the market."

Despite significant breakthroughs in CF therapeutics, chronic lung infections remain a hallmark of life for people with CF, who face an increased risk of contracting difficult-to-treat infections for which there are no effective antimicrobial drugs available. In 2021, 30% of people with CF were infected with *Pseudomonas aeruginosa* (*P. aeruginosa*); however, that figure increased to 50% for those over age 35. Kirk lives with a chronic infection of *P. aeruginosa* and requires strong antibiotics to treat his infections. Like many people with CF, he has faced frequent hospitalizations because of it and must remain vigilant. When it comes to preventing infections, Kirk notes, "I am always aware that my health can be precarious and that I need to take precautions."

The existence of antibiotic-resistant strains of *P. aeruginosa* limits treatment options further. Multi-drug resistant *P. aeruginosa* is most common in older adolescents and adults, likely reflecting cumulative exposure to antibiotics. Dustin, a 36-year-old from Indiana, has profound experience with the consequences of antimicrobial resistance; he has a chronic *P. aeruginosa* infection and carries more than four multi-drug resistant strains of the bacteria. Due to this resistance, he has very few antibiotics left to treat his *P. aeruginosa*, some of which have significant side effects. Though Dustin has benefitted from modulator therapies, this chronic infection still poses significant challenges to his health.

"While I am on a modulator,' Dustin says, "it has only done little improvement as far as lung function and lung health goes. With me having lung damage and scarring from years of having recurring lung infections, a modulator can only do so much to help damaged lungs." The constant fear of running out of options to treat his infections is a heavy burdenfor him. "It's hard to live too much into the future, due to having this lack of antibiotics hanging over our heads every single day. Having cystic fibrosis is part of my everyday life, I can't take a day off from fighting it, having to fear that possibly one day I'll have no other antibiotics to help me fight this disease is absolutely terrifying."

Left untreated, infections like *P. aeruginosa* can lead to faster decline in lung function and cause irreversible lung damage for people with CF, leading to respiratory failure and death. A lack of options to treat resistant infections remains one of the top threats to people with CF—both for older adults, like Kirk, and younger adults who want the chance to grow older, like Dustin.

Furthermore, people with CF aren't immune to other health threats. For Anna, a 36-year-old from Pennsylvania, modulator therapies meant new hope for the future. Her health improved, and life with CF became more manageable. "I finally started to believe that I could live a longer healthier life," she shares. However, living longer means an increased risk of diseases associated with aging—including cancer. This is the case for Anna, who faces a newly uncertain future due

Bethesda Office
4550 Montgomery Avenue, Suite 1100N, Bethesda, Maryland 20814
301.951.4422 800.FIGHT.CF Fax: 301.951.6378
www.cff.org email: info@cff.org

to her recent cancer diagnosis. In order to fight her cancer, Anna will be exposed to a different threat: infection is one of the most common complications of cancer and cancer treatment, and infections can be both more serious and harder to treat for people with cancer.[2] Though Anna is particularly vulnerable, as a person with CF, this is also the case for people with cancer more generally.

But even through fear and doubt, Anna pushes forward. "I have seen the power of science and medicine come up with miracles like treatments for my disease," she says. "I know that we need something new and better to treat these bugs. I'm fighting so hard just to see another day, living with CF and colon cancer is hard enough. I'm waiting for science and medicine to catch up so that I can continue to see more tomorrows."

As more people with CF live longer the need to address antimicrobial resistance becomes increasingly urgent. Without an innovative strategy for tackling this crisis, the impact on people with CF and the broader population, particularly as it ages, will continue to worsen. The PASTEUR (Pioneering Antimicrobial Subscriptions to End Upsurging Resistance) Act is designed to address this issue. PASTEUR offers an innovative incentive structure to strengthen the pipeline for antimicrobial products and make novel, FDA-approved antimicrobials available to those in need—like Kirk, Dustin, and Anna—while at the same time providing funding for antimicrobial stewardship programs.

We thank the Senate Special Committee on Aging for your leadership on this important issue. The CF Foundation stands ready to work with you to ensure patients living with chronic conditions, like CF, remain at the forefront of policy discussions and considerations. Tackling the AMR crisis through legislation like the PASTEUR Act will help people with CF; people with other rare, progressive, or serious diseases; and Americans as a whole. We look forward to continuing this dialogue and serving as a resource for the Senate Special Committee on Aging.

For questions or additional information, please contact David Elin, Senior Director, Advocacy & Government Affairs at delin@cff.org.

Sincerely,



Mary Dwight
Senior Vice President
Chief Policy and Advocacy Officer
Cystic Fibrosis Foundation

[2] https://www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts/infections/risk-for-infections.html#:~:text=Risk%20factors%20for%20infection,-Neutropenia.&text=Medications%20such%20as%20steroids%20can,the%20risk%20of%20an%20infection.

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4550 Montgomery Avenue, Suite 1100N, Bethesda, Maryland 20814
301.951.4422 800.FIGHT.CF Fax: 301.951.6378
www.cff.org email: info@cff.org

EUGENE (NEIL) FACHON

East Greenwich, RI

A scholar athlete, Neil entered college at Northeastern University with 36 AP credits, mostly in the sciences, and began to focus on industrial engineering. He was diagnosed with DIPG at age 19, by MGH; given a prognosis of 3 months; and told radiation might extend that time to 6 months. Diffused throughout Neil's brain stem, the tumor had infiltrated an area roughly the size of a golf ball. It was inoperable, due to its extent, nature and location. Shocking news! Neil met with a DIPG expert in Boston; conferred with another in Switzerland; and became immersed in digesting online videos, articles, studies and available DIPG-specific clinical trial protocols, together with his family. He learned that in over fifty years of clinical trial experiments, all were conducted after the standard dose of radiation, *and* those hundreds of experiments resulted in neither a cure nor an extended lease on life.

Through this investigative process, he learned about an experimental treatment and clinical trial *specific to DIPG* – antineoplaston infusion therapy. He spoke with a 29-year-old DIPG patient in Argentina, (1) who underwent conventional treatment, (2) was then deemed incurable by the MD Anderson Cancer Center and (3) went on to try A10/As2-1, become cancer-free and have a family. We combed through numerous peer-reviewed journal articles summarizing the various antineoplaston study results of using the atengental (A10)/astugenal (AS2-1) investigational new drug (IND) combination and were encouraged. We dug beneath a lot of disinformation. At the conclusion of this research, Neil selected A10/AS2-1 as his path forward. It was the one clinical trial not requiring prior radiation, there was no harsh chemical toxicity involved, no *serious* adverse effects, and the most important monitoring would be blood levels of sodium and potassium. In, fact, the prescribed corticosteroid was more toxic than the IND. Neil's choice was deliberate. He opted to bypass radiation and "shoot straight for the moon."

He was the first patient to enroll in the phase 2 FDA-approved A10/AS2-1 clinical trial. He passed all the qualifying tests, had the intravenous catheter installed and was ready to roll when the FDA abruptly moved to suspend the trial, without evidence of legitimate safety concerns. Neil had to take the FDA to court in order to argue his case. The FDA had no sound evidence, their actions were judged "capricious," and, Neil, with his 3-month clock ticking down to 2 weeks, won an injunction to continue forward with the treatment, however, not without having suffered an extremely high degree of emotional duress. The FDA settled by allowing Neil, and only Neil, to continue forward with the A10/AS2-1 IND treatment with the provisions that he drop the case and that he not deviate from the protocol by adding any other drugs, which was limiting, yet he was a willing guinea pig.

Neil survived almost a full year from diagnosis, with a fairly good quality of life for nearly nine of those months, after which he lost his ability to stand, speak and swallow. The primary investigator of his clinical trial maintained highly detailed records, as did we. These records include daily doses of A10 and AS2-1, daily doses of the corticosteroid (dexamethasone), daily up-and-down changes in symptoms, weekly blood tests, bi-monthly MRI scans, and more. After Neil's passing, we submitted these records to the DIPG registry, and there is a lot to be learned from these records. Neil would want that.

Why the Promising Pathway Act is Important to our Family: The Promising Pathway Act is important in that it will take us a couple steps in the right direction, although, with what I know, we have farther to go. The bill states "The Secretary shall establish a priority review system to evaluate applications submitted under this section for provisional approval within 90 days of receipt of a completed application." 90 days would have been inadequate in Neil's case. While the average prognosis for DIPG is 9 months, unfortunately, are unable to afford three months of waiting.

With regards to TRANSPARENCY AND PATIENT MONITORING REQUIREMENTS, the bill states "An observational registry described in subparagraph (A) may be run by a third party, such as a government, for profit, or nonprofit organization, and shall track all patients who use the provisionally approved drug." The registry should be maintained by a third party without conflicts of interest. When one follows the money and revolving door politics, one sees that the government and the drug sponsors have too many conflicts of interest. Unfortunately, our faith in the FDA has been shattered.

Neil entered into the A10/AS2-1 DIPG clinical trial to contribute to science, and we shared Neil's records in good faith, hoping the results would have meaning and might help shine a light on a cancer treatment that is sensible, ethical and humane. Through our ongoing involvement in the DIPG community, we see so many children suffer as guinea pigs, and it is time for us as a nation to move beyond this.

Wendy Nadhermy Fachon

Mother of Eugene

Nancy P. | Rhode Island

Age: 64
Year of Diagnosis: 2018
Type: Limb Onset, Sporadic



We Can't Wait

Extremely important to have a chance.. Presently I am taking the 2 drugs that are available for treatment for ALS. I am also taking Zilucoplan as an open-label drug because I was in the Healy Platform Trial. I have nothing to lose, but so much to gain if my life could be extended by even a few months. It is my hope that these modest gains will buy time. **The additional time May lead to breakthroughs in the treatment for ALS.** I have 2 adult children and a loving husband that I am not and will not be ready to say goodbye to in the near future. Like every parent, I would love to witness the joy of my children getting married and having children of their own. At this stage in my disease, **I am willing to take any risks that may have the slightest chance for slowing the progress of this monstrous disease.** I don't feel that I should be denied access to AMX0035, especially since after phase 2 it is safe, tolerable and hit its targets. I don't understand how the FDA can deny patients with ALS access to this drug. The FDA is not only denying ALS patients and caregivers access to potential treatments, but they are also stripping us of Hope. Please reconsider your decision that a phase 3 trial is necessary for AMX0035. I probably won't be alive by the time the phrase 3 trial ends. How can the FDA do this to me and so many others?

I would choose a new therapy regardless of the side effects or immeasurable benefits. I am looking a horrible death straight in the eye. I will try any new drugs.

It has completely changed my life from one of great independence to complete reliance on my caregivers. I was actively engaged in life and its bounties, now I am an observer in a wheelchair, unable to move.

I was diagnosed 1 year after my retirement. My husband had to retire early to care for me. **We were never able to realize our retirement dreams, my husband' life has changed dramatically.** We have had to move to a more accessible home, leaving a home we loved and many friends behind. My adult son and daughter have lost some of their wanderlust and joie d'vie. Of course, they are very concerned about me and their father. They have put lifelong plans on hold so they can be available to help with the caregiving.

I wish the general public knew how debilitating this disease is. I also wish they understood how swiftly it impacts the lives of those living with ALS and their caregivers. I wish those unaware of the financial burdens could understand these hardships and support legislation that would provide government funding to help the patients and caregivers.

I have never begged for anything in my life before today. I am begging you, on behalf of all of us living with ALS and their caregivers, to give us access to AMX0035 before it is too late.

Robert F. | Rhode Island (1 of 2 pages)

We Can't Wait

Age: 32
Year of Diagnosis: 2014
Type: Limb Onset, Sporadic

"Hello, my name is Julie Sylvestre and I am here to speak on behalf of my partner, Bobby Forster whose voice was stolen by ALS.

Bobby was officially diagnosed with ALS in December 2014 at the age of 25. After his diagnosis he eagerly sought out clinical trials and research studies, anything that might help extend or improve his life. Luckily in 2015 he got into the phase 2b clinical trial for Brainstorm's Nurown.

He created a petition shortly after the trial ended to push for access and accelerated approval in which he detailed his progress after receiving one dose of Nurown. He wrote, **"After two weeks of treatment I went from barely able to stand for more than ten seconds, to being able to walk with a walker, to being able to walk unassisted. I also saw significant improvements in my forced vital capacity (FVC) and speech."**

Other participants yielded great results as well. My improvements continued for a month, then my progression plateaued for a month before I began progressing again. This therapy is one that will require multiple treatments every couple months.

Without accelerated approval thousands of ALS patients could die over the next several years waiting for the traditional process for approval to be completed. This treatment has now been in multiple trials both in the US and Israel. It has been shown to be effective and has no significant side effects.

It is time for all ALS patients to gain access to this groundbreaking treatment." That was five and a half years ago and unfortunately, we have lost thousands of pALS while we waited for a phase 3 trial to be completed.

Robert F. | Rhode Island (2 of 2 pages)

We Can't Wait

Age: 32
Year of Diagnosis: 2014
Type: Limb Onset, Sporadic

Bobby is still waiting for his second dose of Nurown and in the years since the trial, he has lost the ability to eat, breathe, speak and move on his own. In the fall of 2016, less than 2 years after his diagnosis, he was forced to make the life altering decision of getting a trach and becoming dependent on a ventilator to breathe. He was using eye gaze technology to communicate, until about two years ago, when his eye movement deteriorated and he has been unable to use the computer to speak.

Now we communicate with yes/no questions and occasionally can spell words or phrases using what little facial expressions he has left. While we have no idea if Nurown would still work for Bobby in his current condition, I know he would do anything for the chance to try.

He quite literally has nothing left to lose. He continues to fight because he knows that this treatment has the potential to help others and prevent them from suffering the same fate as him and so many others who have come before. Yet it has been stuck in the clinical trial process for over ten years and we are still waiting. Bobby may die waiting. He has said repeatedly, **" I am sick and tired of seeing my friends die from this disease, when I know that a treatment exists that can reverse my symptoms."**

FDA approval or not, he knows there is a treatment that works, and he has not been able to access it. It is inhumane to deny dying people access to promising treatments when there are no other options. Yet that is what you are doing right now to thousands with ALS. You have the power and more importantly the ethical obligation to the ALS community to take action now and help us change this disease from one that is terminal to one that is treatable. "

Carol L. | South Carolina

Age: 64
Year of Diagnosis: 2016
Type: Limb Onset

We Can't Wait

Extreme importance to have every opportunity to get medicine.

Extreme importance to find a cure.

Extremely important to try everything.

Extremely Impacted my life in a negative way

Impacted my life in a negative way

It affects every part of life for me and my loved ones

I am desperate for drugs that will slow progression and pray for a cure in my lifetime

George R. | South Carolina

Age: 66
Year of Diagnosis: 2014
Type: Limb Onset

We Can't Wait

Please. Bring it on. Anything is worth trying.

Trying it if possible

We did not test vaccines for Covid. So, I Would try anything.

Lost my benefits for 33 years of work. Diagnosis was untimely in my case.

People assume Weakness. My opinion is that in my case. I'm tuned in to things more deeply. Very frustrating.

Adaptable vans, lifts, and wheelchairs need to work together. Someone should help. **Please help**.

Karen R. | South Dakota (1 of 2 pages)



Age: 63
Year of Diagnosis: 2017
Type: Limb Onset

I am anxious to have a chance to try any therapy that shows even a modest benefit such as slowing of disease progression or additional survival time, even if it showed such benefit in just a subset of patients. Due to the heterogeneity of the disease, it should not be expected that every therapy will work for all patients. I need to slow or stop my progression NOW to give me more time as we await a definitive cure and give me time to make more memories with my family. What you might think of as a modest benefit, may be of critical importance to me in maintaining my quality of life. For instance, even a 1-point drop on the ALSFRS-R scale in the area of ambulation would mean that I am no longer able to walk at all. A 1-point drop on the scale in the area of dressing myself would mean that I can no longer independently dress myself and would need to rely on the assistance of someone. One more point lost on the handwriting portion will mean my handwriting has gone from slow and sloppy to impossible to perform. **These are huge quality of life issues for me.** I do think a cure for ALS will be found someday and I want the time to live to see that day.

Right now, I know my disease is 100% fatal and I am on the trajectory of becoming more and more disabled. I would gladly accept the risks to try a new therapy - I would be no worse off than I am now and **that chance to TRY SOMETHING** would definitely give me hope. If the therapy has significant side effects, I would be able to weigh at that time whether I can continue the treatment or not. **I JUST WANT SOMETHING TO TRY** as I am dying waiting.

I feel the FDA and manufacturers should allow those of us who do not qualify for the clinical trial to have access to the drug before final approval. That expanded access can continue to provide scientific information about the drug, and I do not have 2 years or more to wait for another trial to be completed. By the time a drug has reached Phase 2 or Phase 3, the safety data should be known enough so that I can feel confident from the safety standpoint at least.

Karen R. | South Dakota (2 of 2 pages)



Age: 63
Year of Diagnosis: 2017
Type: Limb Onset

At the time in my life when I was looking forward to retirement and spending more time with grandchildren, volunteering more, and enjoying life, I find myself grieving loss after loss. Once a very independent person, now I have to rely on my spouse for the most simple of things. **Although I try to remain optimistic and hopeful, it is hard not to be afraid of what is ahead of me.** A future where I am totally paralyzed and a burden to others is very scary. There is also a great financial impact to the disease and care involved, and I worry that once I am gone, my husband will not have enough of our retirement savings left for himself.

I know that this is very hard on my daughter and family but especially hard on my husband. Instead of being partners and teammates, I feel I am becoming more and more of a burden to him, and I know this is very difficult for him but also very hard for him to communicate to anyone else who understands.

I wish everyone understood the urgency of finding treatments and ultimately a cure for ALS. **Many people don't realize that it is 100% fatal** and that not much has really changed since Lou Gehrig's diagnosis. If the resources that were put into the AIDS fight or the coronavirus fight, there would be real progress. In the time that it takes to bring one drug from the lab to patients, the majority of ALS patients will have died.

Please give me a chance to try anything that has been shown to help even 20% of patients in a trial. I want the chance to see if I might be in that subset of patients who is helped. I don't have time to wait for one drug to hit a home run - I just want more time now as I am dying a little more every day.

Christine W. | South Dakota

We Can't Wait

Age: 63
Year of Diagnosis: My husband, Burt diagnosed in 2010
Type: Bulbar Onset

As we were traveling to Burt's Dr. to hear the confirmation of his diagnosis after several tests, he told me he hoped that he would be diagnosed with cancer instead of ALS. At least I will have options for treatment if I have cancer. That was not to be. **If he had had an opportunity to use a new therapy, he would have instantly wanted to try it.**

Burt would have tried it. ALS is a death sentence. He felt he would nothing to lose if a new treatment would have been available.

No importance at all to have a drug approved first.

How did ALS impact his life? Burt was diagnosed with ALS in June of 2010. He was a farmer and the wheat harvest that summer was the last work he was able to do. By Christmas he needed a walker, his ability to eat and talk were increasingly challenging. By April he was wheelchair bound and I needed to feed him. We had to hire help to help him get him our of bed in the morning and dressed and then again in the evening to get him back in bed. Once in bed he did not have the ability to change position. **He was quite claustrophobic, so this was torture for him.** We bought a special bed that was good for protecting against bed sores. We tried a hospital bed, but his voice was so weak that I could not hear if he needed me during the night unless I could lay next to him. **The ALS association provided us with a Hoyer lift so I could get him in and out of his wheelchair. In December of 2011 he passed away almost 18 months to the day of diagnosis.**

Significantly. It was so hard for our family to watch a very independent, hard working, capable man change so quickly to being dependent on everyone for all his needs. **I was asked why I didn't put him in a nursing home. I replied that he had no strength to use a call light when he needed something, and his speech was so affected that only those of us who were with him all the time could understand him.** I would have to live at the nursing home too if he were to go there. Plus, I felt he needed to be home where he had lived all his life. To have that comfort of a familiar place in which to spend his final days. It was the hardest thing I have ever done, and for his children to do.... to watch someone, you love slowly lose the ability to breathe will never leave us.

It is one of the cruelest diseases that exist. It completely destroys the body's ability to do anything, but the intelligence remains intact so essentially you are trapped in a body that will not work. Burt told me he felt like he was in prison.

I appreciate their efforts towards new meds, but I urge them to give those stricken with ALS the chance to decide if they are willing to take the risk of trying a new med that hasn't gone through all the hoops yet to get approved. As I said before, ALS is a death sentence so let them decide what level of risk they are willing to take.

Karen R. | South Dakota

Age: 63
Year of Diagnosis: 2017
Type: Limb Onset

We Can't Wait

I am anxious to have a chance to try any therapy that shows even a modest benefit such as slowing of disease progression or additional survival time, even if it showed such benefit in just a subset of patients. Due to the heterogeneity of the disease, it should not be expected that every therapy will work for all patients. I need to slow or stop my progression NOW to give me more time as we await a definitive cure and give me time to make more memories with my family. What you might think of as a modest benefit, may be of critical importance to me in maintaining my quality of life. For instance, even a 1-point drop on the ALSFRS-R scale in the area of ambulation would mean that I am no longer able to walk at all. A 1-point drop on the scale in the area of dressing myself would mean that I can no longer independently dress myself and would need to rely on the assistance of someone. One more point lost on the handwriting portion will mean my handwriting has gone from slow and sloppy to impossible to perform. These are huge quality of life issues for me. **I do think a cure for ALS will be found someday and I want the time to live to see that day.**

Right now, I know my disease is 100% fatal and I am on the trajectory of becoming more and more disabled. I would gladly accept the risks to try a new therapy - I would be no worse off than I am now and that chance to TRY SOMETHING would definitely give me hope. If the therapy has significant side effects, I would be able to weigh at that time whether I can continue the treatment or not. I JUST WANT SOMETHING TO TRY as I am dying waiting.

I feel the FDA and manufacturers should allow those of us who do not qualify for the clinical trial to have access to the drug before final approval. That **expanded access can continue to provide scientific information about the drug, and I do not have 2 years or more to wait for another trial to be completed.** By the time a drug has reached Phase 2 or Phase 3, the safety data should be known enough so that I can feel confident from the safety standpoint at least.

At the time in my life when I was looking forward to retirement and spending more time with grandchildren, volunteering more, and enjoying life, I find myself grieving loss after loss. Once a very independent person, now I have to rely on my spouse for the most simple of things. Although I try to remain optimistic and hopeful, it is hard not to be afraid of what is ahead of me. A future where I am totally paralyzed and a burden to others is very scary. There is also a great financial impact to the disease and care involved, and I worry that once I am gone, my husband will not have enough of our retirement savings left for himself.

I know that this is very hard on my daughter and family but especially hard on my husband. Instead of being partners and teammates, **I feel I am becoming more and more of a burden** to him and I know this is very difficult for him but also very hard for him to communicate to anyone else who understands.

I wish everyone understood the urgency of finding treatments and ultimately a cure for ALS. Many people don't realize that it is 100% fatal and that not much has really changed since Lou Gehrig's diagnosis. If the resources that were put into the AIDS fight or the coronavirus fight, there would be real progress. **In the time that it takes to bring one drug from the lab to patients, the majority of ALS patients will have died.**

Please give me a chance to try anything that has been shown to help even 20% of patients in a trial. I want the chance to see if I might be in that subset of patients who is helped. **I don't have time to wait for one drug to hit a home run - I just want more time now as I am dying a little more every day.**

Karen R. | South Dakota



Age: 63
Year of Diagnosis: 2017
Type: Limb Onset

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Allie S. | Tennessee



Age: 30
Year of Diagnosis: 2017
Type: Limb Onset, Sporadic

I would happily pay any amount of money that I can afford to just have a chance at receiving a medication that seems promising. ALS is a confusing disease that affects every patient differently. We will never have the chance of knowing if a medication could work for even a small subset of patients if we're never given the chance to try. I would consider taking any medication that could extend my life even for a few months.

I would try any medication as long as it didn't present side effects that would negatively affect my ALS diagnosis, such as respiratory involvement.

Absolutely do not care about FDA approval. I'm dying. I don't have the time to wait.

Everything is different. I can no longer work. It has caused stress and financial strain on our family. I just want the chance to watch my son grow up.

I wish people understood the swiftness of the progression. For many, it's a matter of a few months between recognizing your first symptom and having one of your limbs completely paralyzed. I also wish people realized that this disease isn't THAT rare - 1 in 300 people will be diagnosed with ALS during their lifetime.

Patients and families are willing to pay the money to just have a chance at extending their life. Please make it available to us.

Ress C. | Tennessee

Age: 61
Year of Diagnosis: 2010
Type: Limb Onset

We Can't Wait

Honestly, no one wants to die any earlier than they have to. Yes, I am for it.

With ALS you have nothing to lose.

Not important to me at all to have it preapproved. With ALS you have nothing to lose.

It was a death sentence. No hope!

Totally crushed our family.

Time is limited. Your trapped in your own body. To someone that has ALS please let them try anything you have. They have nothing to lose.

Paul C. | Tennessee

Age: 53
Year of Diagnosis: 2020
Type: Bulbar Onset, Limb Onset,

We Can't Wait

All therapy is important if it can help me maintain quality of life for a little while longer.

All drugs have risks. I should be able to decide for myself if the risks outweigh the benefits or not. I'm the one diagnosed with a terminal disease.

Not important at all. As I said, let me make the decision to assume the risks of the new therapy.

I am dependent on others every day. I've given up activities that I love and struggle with the activities I can still do.

My wife had to become my caregiver along with assume all other activities that I used to do - and work. It is stressing her out. My children have to help me get dressed, get off the toilet and eat - taking a toll on them. They all feel helpless because they can't stop my progression.

That it exists and more people than they can imagine are stricken with this hideous disease.

If you can fast track a vaccine in a matter of months, why can't you do more for us? Our disease has been around for decades. Don't we deserve more than 2 approved drugs that might slow progression?

Mike S. | Tennessee

Age: 78
Year of Diagnosis: 2019
Type: Sporadic

We Can't Wait

It would bring so much hop to have the chance to try a medicine that could help improve my life. I am not worried about the side effects or having FDA approval. I just want a chance.

Reinforced the value of every day and family.

They've circled the wagons and continue to surround me with love and support.

Their support is necessary for the quality of life.

Approve AMXOO35 for widespread use!

Debra O. | Murfreesboro

Age: 69
Year of Diagnosis: 2019
Type: Bulbar Onset, Sporadic

We Can't Wait

I think extremely important to have a chance for medication, because another more effective therapy might follow.

I am willing to take the chance because the only thing certain presently is steady decline.

I think if preliminary trial shows promise, would take without FDA approval. **Every day ALS takes a part of me away.** It is physically and emotionally exhausting because they do so much for me physically, and desperately want to find a solution for me.

ALS is presented as a death sentence; and it is very hard to fight something when hope is being dashed daily.

I know ALS is a small community, but please realize **we deserve the same zeal to find a cure, or at least a slowing of progression, as any other more notable disease.**

[redacted]

My mother and father, both physicians, were affected with two distinct and debilitating diseases: Alzheimer's and Amyotrophic lateral sclerosis (ALS), respectively. My father, a surgeon practicing on Long Island for nearly 40 years, experienced a complicated and confusing journey to his final diagnosis of ALS. The steep descent into a complete shutdown of the body happened over the course of 5 years, in front of my wife and children—we moved back to my childhood home, from Austin, TX, to look after and be closer to family.

The need for private care, initially for my father, and then for my mother grew to 24/7 and often with two aides, one caring for each of my parents. From 2018/19 my father was in home hospice and ultimately succumbed to ALS in mid-2020. We made a series of adjustments to the house, stair lift, hospital bed to creating a first floor master bedroom with easy access to the street and car.

Since mid-2020 my mother's Alzheimer's has progressed at a rapid pace. She has lost all executive motor function and has ceased verbal communication. The private home health aides assist with every basic function and need for mom. Like my father, a skilled surgeon, losing dexterity and bodily autonomy, my mother had a prodigious memory only to have that fade away. Mom has been in home hospice since early 2023 and we are making slow and fast adjustments to ensure has everything she needs to be comfortable.

This experience has been truly eye opening, and however difficult it has been, I am grateful to have been and be present for my parents as they were for me.

--
Ali Madad



BROCK FLEMING

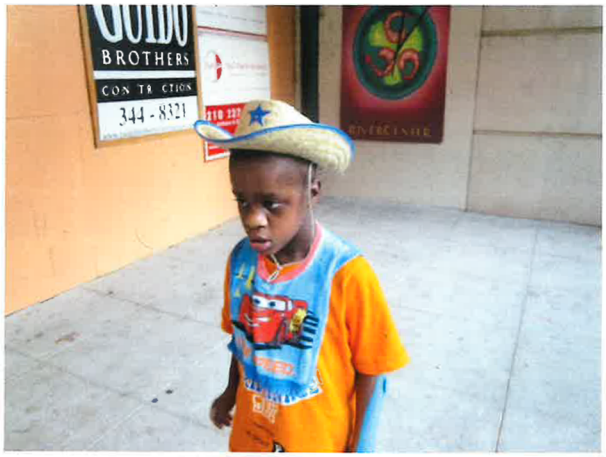
Austin, TX

Brock was a super adorable active 7-year-old. He loved swimming, soccer, and building Legos. His favorite subject was math, and he was the sweetest little Cub Scout you would ever meet. He also loved being a brother to his older sister, Jenna. He was walking his dog with Jenna and his Daddy on May 4, 2016 when he fell and hit his forehead. His parents thought they would be treating him for a concussion and instead were told he had DIPG; an inoperable brain tumor that would leave him with only 9 months to live. Overnight, Brock was not able to walk, drink, or talk. He was determined to get back to running and playing soccer again and did after 6 weeks. He fought courageously for 7 months and did not want to leave his family on December 10, 2016.

During his battle, he didn't understand why his body was doing this to him, why he was the only second grader with cancer in his head, and why the Doctors couldn't fix him. He never complained and wanted to "Kick Cancer in the Nuts!" Melissa, James, Jenna, and Blair are determined to raise money to find a cure and create awareness of this deadly disease. Our kids deserve better!

Melissa Fleming

Mother of Brock



PAUL ALEXANDER COLEMAN III

Fresno, TX

My son Paul was diagnosed with DIPG in May 2011 at the age of 10. Paul was treated at Texas Children's Hospital in Houston, Texas. He received radiation to shrink the tumor. He was prescribed dexamethasone to reduce swelling He also participated in two clinical trials. He battled for 22 months, but his battle came to an end in May 2013, at the age of 12. At the time of Paul's diagnosis radiation therapy was the traditional treatment for DIPG. It has been 12 years since Paul's diagnosis and that is still the standard treatment for DIPG.

Why the Promising Pathway Act is Important to our Family: The Promising Pathway Act is important to me because it offers parents a chance to try additional medications and treatments for cancers like DIPG, which has a less than 1% survival rate. Promising treatments that could help their child survive longer or potentially cure their child is what every parent is searching for because it means there is hope in a hopeless situation. While I live with the reality that there is currently no cure for DIPG, I have never lost hope that a cure may be found. A chance for better access to treatment options brings us a step closer to a cure.

Jacquelyn Coleman

Mother of Paul

Linda R. | Texas



Age: 72
Year of Diagnosis: 2017
Type: Bulbar Onset, Sporadic

I believe it is critical to have access to all new therapy. ALS is terminal therefore the chance to live a few months longer means an opportunity to experience more family and loved one's special occasions; a birth, a graduation, a school event with the grandchildren. Live is now measured in days; one day at a time.

I am willing to risk any side effect in order to have more days. I feel the risk may not only benefit me but may lead to a cure which will benefit all those with ALS.

I have enrolled in every trial I have access to; I do believe the new drug needs to complete the approval process. The alternative is death coming sooner.

ALS has changed the lives of my family, colleagues, friends and myself in countless ways. Having a death notice makes you appreciate every day you have. My life changed in everyday. I am active, independent, had a meaningful career, physically fit and healthy. Now I live with my daughter's family and depend on others.

My family has been impacted by now having to care for me. I never wanted my children to have to care for me. I don't think anyone wants that.

ALS strips you of hope. From the initial diagnosis to every doctors visit you are told of the dismal future.

I don't understand why the FDA would make an ALS patient wait for therapy or treatment. I life expectancy is 3-5 years, there really isn't time to wait. There is urgency in finding a cure and each therapy deserves to have to chance to providing answers.

Melanie F. | Texas

Age: 53
Year of Diagnosis: 2020
Type: Limb Onset

We Can't Wait

If a new medicine will only work for a few months, it's not worth for a few months.

If it offers more than a few months, worth it.

I am a Caregiver for my mom

There is no cure

How can you come up with a vaccine in a matter of months and no treatment for ALS in years.

Philip R. | Texas

Age:
Year of Diagnosis: Wife: 2009
Type: Limb Onset



We Can't Wait

Looking for more than just a few months of additional life

She was not interested in just a few more months of life when offered a treatment known to have significant side effects

If preliminary results are promising, then compassionate use is indicated prior to trial completion and FDA approval

Totally destroyed normal living habits. My family has suffered emotionally and physically. I am also suffering.

The burden on the family is huge !!

Sylvania M. | Texas

Age: 64
Year of Diagnosis: Brother
Type: Bulbar Onset, Limb Onset



We Can't Wait

My brother lost his life after one year and a half of diagnosis. Any chance of an improvement would be priceless for a person losing the normal function as simple as being able to smile, to speak, to the most detrimental lost in the ability take a breath.

It is vital that they are provided with the complete information and given a chance to make that decision for themselves. We already know the outcome of ALS . In the horrifying process of physical function deterioration, one remains mentally aware of what is happening to them.

It many cases it is vital BUT let's take the Covid vaccine as an example. There would have been a greater lost of life if we had waited for the FDA to complete a 6-7 plus year process of approval. Folks with ALS don't have that luxury. Each day is so precious to that person and their family.

With respect, my brother has lost his life due to ALS

On a personal basis as his sister and as a Registered Nurse, I have never felt so helpless in watching my brother, who was physically fit and full of life, loved by his family and friends, quickly but slowly die of this disease. He had made such an impact in so many lives, including saving many lives. The pain that I and my family have words can not describe.

ALS has no discrepancy in who you are. It will ripe every fiber of your love and want of life. It will take your identity of who you are as a human being. The impact of the simple ability such as brushing your teeth will be a fantasy.

I pray to God that this does not happen to you or even worst your love one. Pharmaceutical companies, remember compassion for the patient and the families that struggle to provide the medication that will play a significant potential chance of improvement.

Baker | Texas

Age: 63
Year of Diagnosis: 2017
Type: Limb Onset



We Can't Wait

If the promise is for a few months, I'm really not interested. Again, if the promise is only for a few months, I'm not interested

Not very important to me if it is approved.

My life has been turned upside down because of the debilitating effects of this disease

All have been affected somewhat. My wife has been affected a great deal, particularly with her work.

Constant fatigue along with the embarrassment of extreme help necessary for everyday tasks.

I'm much more interested in pharmaceuticals that give back some of the strength in my extremities rather than extension of longevity for a few months.

Patricia J. | Texas

Age: 71
Year of Diagnosis: Husband – 2017, Death 2019
Type: Limb Onset

We Can't Wait

My husband died 2 yrs. after diagnosis. We went overseas for stem cell treatment which slowed progression for about 6 months. It was 6 months of time where he could at least function and maintain some dignity. We both were so thankful for that short respite. **Why couldn't we take this risk in our own country?** Both of us would've given anything to try any drug that might have helped, no matter how short the time benefit or risk. No hope is as bad as the death sentence already handed down.

What's the difference if there's a risk? ALS is 100% terminal, not even one chance to live or beat it. Side effects are already horrific, so we would've been willing to sign any waiver at all to have a chance at something that might remotely help.

Not important at all! This is a death sentence, so why not clutch at any straw any time?? The alternative is hopelessness every single day. Let the ALS patient incur the risk. I guarantee they will sign every waiver given them if it means some chance at a better life.

My husband wanted to show my children and especially grandchildren that you fight with everything you have. He tried anything at all-going to South Korea, alternative medicine, random drugs that were suggested by almost anyone. ALS robbed him of his very existence, so all he had left was to be a role model fighter for his family.

As his caregiver, I was devastated every day in every part of our lives from emotional day to day living to potential financial ruin. ALS caused both of us so much pain. The repercussions after his death were enormous for me-I can't let go of the pain we suffered. PTSD like flashbacks hit me before I sleep and when I awake every day.

ALS ruins you bit by bit and there's nothing you can do. Lack of dignity, depression and fear are a fact of life EVERY SINGLE DAY.

I am begging you to EXPEDITE ANY AND ALL TREATMENTS-especially revisit the full denials of both AMX0035 and NurOwn. No one should suffer as we have.

Tonya F. | Texas

Age: 49
Year of Diagnosis: 2014
Type: Limb Onset

We Can't Wait

We will take anything. We need HOPE and more time. It is a chance I am willing to take. Give me options.

Took away my ability to work, my family had to relocate from a beautiful place we love, slowed everything down.

They have tremendous support for me as always

The clock is ticking-until this affects your family you have no idea.

The possibility of improving outweighs any risk.

Paul T. | Texas



Age: 66
Year of Diagnosis: 2009
Type: Limb Onset, Sporadic

Rilutek is a drug that fits that description and I take that now. **I am in favor of any drug that will help.** With so many variations of ALS a drug slowing progression may be more beneficial to some than the modest benefit expected

A drug that could work is better than no option. Side effect are more important when weighing whether or not to take a drug. It also depends on where you are in your progression and the rate of your progression

I think the FDA has a role to play but when a drug shows promise there needs to be a fast-track process. With a 2-to-5-year average life expectancy most PALS can't wait for the FDA to run a normal trial. Allow people the opportunity to try. You are allowing people to be in the trial so why not allow people, with the same waivers and sign offs to use the drug.
Allowed me to appreciate each day more and to do things now and not put them off. As my disease progresses, I am becoming more limited in what I can do and what I want to do.

It was rough early on because with a 2-to-5-year life expectancy we didn't know how we would deal with the coming years. As it turns out I am slow in my progression, so we have had time to adjust to my limitations

That there is little to no treatments to really manage the disease and more funding is needed to help improve and extend the quality of life for PALS. People need to know how devastating the disease is on the individual and their family

ALS is not incurable it is under funded. Time is not the friend of PALS so all efforts need to be with a sense of urgency. The way that we attacked COVID-19 was proof that with a concerted effort we can solve the most difficult problems. We have lots of disjointed efforts to find treatments for ALS if we could harness the power of all of them, we could make a difference.

Mary C. | Texas



Age: 61
Year of Diagnosis: Texas
Type: Bulbar Onset

I feel that the therapies used now that only "slow" the progression are useless in most aspects. Some people don't want to suffer longer than necessary when there are therapies that the FDA is sandbagging that actually showed positive results for patients. ALS doesn't affect everyone the same way. So they need to stop searching for one size fits all therapies. All this is doing is letting more and more people die while the FDA & ALSA get to decide if people get these therapies. It shouldn't be up to you. Let the patients decide, They are the ones dying.

The ones now have significant side affects and don't really extend or improve quality of life. What's the difference? You want more drugs that barely help and have side effects?

The FDA hasn't even approved this so called "covid vaccine" and people are getting it. Why not NurOwn? Or other therapies held up in trials? So it's not important to me that the FDA has any day in it. You and they have dropped the ball so far. Let the patients decide if they want to take therapies like NurOwn.

How do you think it has impacted our lives? My mom has a terminal illness and the FEA is holding out on therapies like NurOwn!

It has devastated everyone in my family.

That it's different for everyone. 100% fatal and the FDA is letting people die for profit. Stop looking for one size fits all therapies!

That we all know what you're up to and we're spreading awareness. Things WILL change one day for patients. We don't trust you!

October 25, 2023

Dear Senator Braun,

I am reaching out to you in response to your request for stories on the unmet medical needs faced by people with rare, progressive, and serious diseases for a hearing by the Special Committee on Aging to be held on October 26, 2023.

I am a participant in programs offered by the Huntington's Disease Society of America (HDSA), a leading national organization dedicated to the care and cure of Huntington's disease (HD), a rare and fatal hereditary disorder that manifests as a neurological disease with both physical and psychiatric components. The mission of HDSA is to promote and support research to find a cure for HD; help people and families affected by the disease; and educate the public and healthcare professionals about HD. Currently, there is no clinically available pharmacological, biological, or surgical agent or method that slows or stops the progression of HD.

I am writing this from the perspective of a caregiver. My husband, Jon began showing symptoms of HD around 2008 when he was in his mid-forties. We continued to live our lives and work as long as we were able. Jon and I are pharmacists. In 2014 our oldest son was in a serious relationship and my husband decided to be tested for HD. We both suspected the result would be positive, but we believed Jon would be able to continue working for a few more years. We were told that Jon should no longer drive, stop working and apply for disability. At this time, I was in a corporate pharmacy administration role and carried the health insurance. We would be able to live on my salary alone. After the 6 months waiting period, Jon began receiving disability benefits and after 2 years he became eligible for Medicare.

Jon continued to find a way to be active and involved. He used UBER to get to where he wanted to go. During the pandemic his social activities declined as well as his condition. I continued working until August 2021. At this time, Jon's cognitive decline affected his ability to be independent. Jon was losing weight because he couldn't remember to eat. I was not ready to quit working and have Jon's Social Security be our only monthly income source, I just turned 60. We do have money saved in retirement accounts and are fine for now. If one or both of us need long-term care, these funds will be quickly depleted, and this is a genuine concern as we enter the later stages of the HD journey. I don't know exactly how Jon's condition will progress, but I do know he will be bedbound and I will need assistance with caring for him in the home. I try not to dwell on the what-ifs but losing our safety net is frightening.

Thank you for allowing me to share our story.

Sincerely,

Patricia Huffman
626 Fernglade Dr.
Richmond, Texas 77406

October 24, 2023

Dear Chairman Casey, Ranking Member Braun, and Honorable Mèmbers of the U.S. Senate Special Committee on Aging:

My name is Michael Park, and I am a 51-year-old male living with a disease called Facioscapulohumeral Muscular Dystrophy, or FSHD. Thank you all for the opportunity to tell my story.

I first showed symptoms of FSHD at the age of 19 years old. I was playing basketball at my college gym and noticed my shot was a little off because of a slight difference in movement with my left arm. Long story short after several Dr's visits with orthopedic specialist's and neurologist's: it was suspected that I have FSHD. When explained what FSHD was, I was convinced that the Dr's were wrong. I was strong. In fact, very strong. I was a competitive cyclist who rode 300+ miles per week, a competitive swimmer who often swam 2000-3000 meters a day, an avid outdoorsman and Eagle Scout.

As the FSHD progressed over the years it stole almost everything I seemed to enjoy such as sports, outdoor activities, and the worst: the ability to participate in activities with my family. My disease took a turn for the worse in the winter of 2021. November 2021; I was 6ft 3in tall, 208 lbs. and had the ability to walk without any assistance. January 29th, 2022 (neurologist appointment), I weighed 159pds and cannot walk without the assistance of a cane. FSHD is a very lonely and cruel disease. Until recently, I never met another person with this disease. I was introduced to the FSHD society in 2022 which has been a "God send". Only then did I discover there were possible treatments coming soon. Finally, some HOPE! The problem with FSHD is that time is our worst enemy. I mentioned that this disease is not only very lonely but cruel. Every day I get weaker and lose the ability to do things that I once took for granted like taking a walk with my wife, throwing a baseball with my sons and possibly soon the ability to walk and breathe without assistance if treatment is not available. I often wished that I had cancer or some other terrible disease other than FSHD. I know that is a horrible thing to say but at least with cancer there is some hope of beating the disease through treatment and research. Not with FSHD! Imagine the mental toll on someone facing a disease that slowly takes away your enjoyment of life becoming a burden to your family. Very cruel! Until recently, I was always told by medical professionals that there is no treatment. FSHD not only devastates your body but equally your emotions and mental wellbeing. Only recently have I heard of possible treatments and possibly a cure coming soon. For the first time in over 30 years, I now have HOPE. Not just for me but more so for my three young sons. It breaks my heart to think that my sons may go through the physical and mental devastation that comes with living with FSHD with no treatment. Please do not let that happen.

My name is Michael Park. I am a Husband, Father, Son, Man of Faith, and a tax paying citizen living with FSHD. I pray every day for a cure for this horrible disease. Please do not forget us with rare and progressive diseases when funding research. Please do not take away our HOPE!

Sincerely,

Michael Park

13515 Boudreaux Estates Drive

Tomball, TX 77377

CC: U.S. Sen Senate Special Committee on Aging
Sen. Bob Casey
Sen. Mike Braun
Sen. Kirsten Gillibrand
Sen. Richard Blumenthal
Sen. Elizabeth Warren
Sen. Mark Kelly
Sen. Raphael Warnock
Sen. John Fetterman
Sen. Tim Scott
Sen. Marco Rubio
Sen. Rick Scott
Sen. J. D. Vance
Sen. Pete Ricketts

Katharine Bryan, mother of Judd Bryan
Paris, Texas

Beginning in August, during a vacation with his mom and dad in Taos, New Mexico, our eight year old son, Judd Bryan, began having symptoms of leg weakness and problems going to the bathroom. For two weeks prior to that, he had been waking up in the middle of the night, saying that his back hurt. I had actually taken him to the doctor two different times in the two weeks prior to our trip, and he even had an x-ray the day before we left Paris. Everything checked out fine, and they said to go ahead and go see your family in New Mexico. Honestly, it was pretty immediate when we got into the altitude that he wasn't feeling well, but we attributed it to the elevation. On Friday, August 4, I took him into town in Taos to go to the toy store. When we got back to our condo, Judd came in behind me, and I turned around, and his pants were wet. He didn't know why they were wet, and I realized that he had urinated on himself without realizing it. We quickly called a friend who is a doctor, who told us that it sounded like he might have a tethered spinal cord. He said that it is serious, but he could be okay with surgery and that we needed to get to a childrens hospital for imaging. So we packed everything up and didn't get out of Taos until about 7:30 that evening. Judd has three older siblings who had all stayed back from going on the trip for various reasons. His older two brothers were working, and his sister had just moved into the sorority house for her sophomore year at the University of Mississippi. She actually FaceTimed us to show me her room in the house right around the time when we were leaving Taos, and I didn't tell her where we were going at that time. We made it to Las Vegas that evening, Las Vegas, New Mexico, and decided to spend the night because it was about 10 o'clock. It was really dark, and Judd actually seemed much better. We thought again that maybe it was the altitude. Maybe he just drank too much water and had an accident and didn't want to tell us. So we got to our room and ate a really late dinner and went to bed. Almost by instinct at about 4:45 the next morning my husband and I woke up at the same time, sat up, looked at each other, and said "we should go." When we went to get him out of the bed, he couldn't walk. I tried to get him to go to the bathroom, but he couldn't go. I got him dressed and carried him to the car, and from there drove over 100 miles an hour to Lubbock. Our friends who had helped us the night before had a contact in Lubbock, so they knew that we were on our way. We took him to Covenant Children's Hospital. Almost immediately when we arrived, they took Judd for an MRI. He had to undergo anesthesia, and the study lasted for three hours. They scanned his spine, his neck and his brain. After the MRI, very soon after, a neurosurgeon came to talk to us. He told us that Judd had a tumor in his spinal cord. I got weak immediately and told him I needed to sit somewhere. So we went to a room in the ER and sat down. The doctor explained that because of how the tumor looked on the image that he thought it was benign. We decided with the doctor to be care flighted to Dallas, so that we would be closer to home. We were care flighted to Medical City Dallas at 4am on Sunday, August 6. Very soon that morning after arriving to the hospital ICU unit, a surgeon came in to talk to us. He explained that because of the size and location of the tumor, we needed to be prepared that Judd may be paralyzed from the waist down. He said that he would do everything he could but that it was a very high risk surgery. On Monday, August 7, his big brother's 21st birthday, Judd underwent spinal cord surgery, and the tumor was removed. I'll never forget sitting in the bathroom of his ICU room, crying on the floor at 5 AM before he woke

up. It was an incredibly long day waiting for the surgery, and after what seemed like an eternity, the operation started around 4 PM. The surgery took about 2 1/2 hours. The surgeon explained that it had gone really well and that the tumor had been removed. He said that the first round of pathology that had been conducted in the operating room showed a benign tumor. We were elated, but he was cautionary that we needed to wait on more detailed pathology to come back. He was concerned about how quickly his symptoms had occurred. We spent a week in ICU. I don't really remember much of it. I had left almost all of my stuff in my car in Lubbock, and friends had to bring me everything I needed in the hospital. We were moved to a regular room, Judd began physical therapy and was doing really well. We even had an oncologist come by as a courtesy who told us he didn't think he would be seeing us in the future. Then the pathology came back. We were devastated to find out that the tumor had been found to be an H3K27 Diffused Midline Glioma, DMG. Our surgeon told us he had never seen this variety of cancer in his career in the spinal cord, and at the time we were told that the only treatment for Judd would be proton radiation. We were living in a nightmare. We couldn't get into inpatient rehab in any of the other children's hospitals in Dallas or Fort Worth, because they did not accept affordable care act insurance. I felt like I was having to have a rapid crash course in healthcare and nursing. We were ultimately discharged and rented a condo in Irving Texas, so that Judd could receive 28 treatments of proton radiation. When we were discharged, we still did not even have a neuro oncologist, because there was not one on staff at medical city, and our hospital transfer could not be approved to go to Children's or to Cook Children's. I ended up emailing a doctor at Children's who is a neuro oncologist who was willing to take Judd's case. I also scheduled a meeting with a researcher at the University of Michigan named Dr. Carl Koschmann. I learned from Dr. Koschmann that there is actually a medication called ONC201 that could help keep Judd's cancer from returning, but unfortunately, he did not qualify for any clinical trials, because his cancer had been in his spinal cord and not in his brain. Basically, we would have to wait for it to come back to qualify for a trial. ONC201 specifically targets tumor cells that form from the type of tumor that he had. It seemed backwards to wait for something to come back that could be prevented.

This medication that he needs has actually been in the trial phase for about 10 years, but because the conditions of DMG and DIPG are so rare, it is hard to have a large enough group of participants for the studies. Only about 300 children per year have this diagnosis, most of which are in the brain. But the studies are showing outcomes that are incredibly positive, and compassionate care laws have been passed in France and Germany, so that children can have this medication. Yet in the United States, children are still being forced to participate in clinical trials, where many are receiving a placebo rather than the actual medication. This is a death sentence. In addition, the side effects of ONC 201 are incredibly mild; the most common side effect that has been found to be associated with this drug is fatigue. So considering that this diagnosis does not respond to chemotherapy, this is an amazing option that these children, especially Judd, desperately need.

We are now back home in Paris. Judd completed his proton radiation, 28 treatments to his spine. He goes to school half a day each day, and I go with him in case he needs help going to the bathroom. He goes to physical therapy in the afternoons. We are waiting for our next MRI on Saturday, November 4. We are trusting God to take care of our boy.

[redacted]

October 24.2023

Dear Chairman Casey, Ranking Member Braun, and Honorable Members of the U.S. Senate Special Committee on Aging:

My name is Rachel Sartin. I am a resident of Austin, TX, and I am living with Facioscapulohumeral Muscular Dystrophy (FSHD), a rare progressive genetic disorder that leads to the weakening of skeletal muscles.

My grandmother was a piano teacher. My mother was a piano teacher. I started playing the piano at three years old. I won several state competitions and started teaching students by the time I was 12 years old. But then, at a summer piano symposium, I started having difficulties playing some of the more extreme pieces. That was the beginning of my journey.

My parents took me to doctor after doctor searching for a diagnosis and treatment. Mostly we encountered questionable diagnoses or no diagnosis at all. It was a tumultuous time in my life, and in my family's life. Not knowing the truth. Not knowing where to go. Eventually at the Mayo clinic in Rochester, Minnesota, with various testing, I was diagnosed with FSHD. Unfortunately with this diagnosis, there was no hope - literally nothing. Doctors tell you that you have this disease. You're going to continue to weaken throughout your life. And there is nothing you can do. There is no cure. There is no treatment. There is no help. So I went home to live the best life I could with the reality of this relentless disease. Day after day, month after month, nothing helps. Every day I wake up wondering what is going to get worse today. What could I do yesterday that I can no longer do today? Piano playing is no longer possible. Participation in sports that I used to love is over: swimming, softball, basketball, bicycling. One by one, these activities became difficult, and then impossible. My first year in college I kept falling as I walked across the snow covered campus. I couldn't make it to the next building where the cafeteria was. I couldn't make it to class. I had to leave that college and find another place where I could handle the physical requirements. But my balance and walking got worse and worse until the only way to go to graduate school was start using a wheelchair. This is a fate no 22-year-old young woman wants to ever face, but it was my only option.

And where are we today? Well, I am now 60 years old and that constant relentless progression has affected me significantly. I no longer get out of my wheelchair. I am unable to take a single step. I'm dependent on caregivers to help me move from my wheelchair to bed or bath. Finding good helpers is difficult and expensive. Caregivers are not covered by insurance. In addition, just getting the wheelchair and other medical equipment I need is difficult. There has been ongoing consolidation and other changes in the industry, causing a significant degradation in service. Recently, when my wheelchair broke, it took two months to get an appointment to evaluate it, and then another two months to go through paperwork, insurance, ordering, and eventually installation of the parts. Can you imagine if you broke your leg and it took four months until you were seen? That's literally the equivalent situation for me.

Even finding medical professionals who can treat me is difficult. Because FSHD is a rare disease, many practitioners don't know anything about it. They treat me without understanding the complexities of my condition. I'm constantly having to question treatments for other issues to ensure they are safe for me. Several times I have looked at my medical records, and the medical professional has entered my diagnosis as MS (multiple sclerosis). I have FSHD, which is a form of muscular dystrophy and completely different from MS.

There is some good news. Through ongoing research, the cause of FSHD is known. There is some really good early research going on now. Hoping to find some treatments in the near future. But there are issues. There have been lags and gaps due to funding, clinical trial support issues, personnel, etc. For me, these clinical trials are out of reach. Participants have to be able to walk. And soon I will be too old because they do not accept 65+ year olds.

So what can be done? We need support. We need focus. We need expansion. Rare diseases like FSHD need extra help to enable treatments and cures. We need extra support and funding so that we can replicate the existing clinical trial sites in additional locations. We need to fund and staff all sites adequately so that these trials can be done in a timely fashion. In addition, looking ahead, we need to put in place financial support, so that when treatments come out, patients are able to make use of them. Many rare disease treatments come out and have huge financial costs. That makes them inaccessible to most people. We need a way to get insurance companies and other funding sources to support this population.

I hope you can see that myself, and the other people who are living with FSHD need your help. We need your awareness, your advocacy, and your financial support to help us combat this horrible, relentless disease, I thank you for your consideration and support!

Sincerely,
Rachel Sartin
Austin, Texas

CC: U.S. Sen Senate Special Committee on Aging
Sen. Bob Casey
Sen. Mike Braun
Sen. Kirsten Gillibrand
Sen. Richard Blumenthal
Sen. Elizabeth Warren
Sen. Mark Kelly
Sen. Raphael Warnock
Sen. John Fetterman
Sen. Tim Scott
Sen. Marco Rubio
Sen. Rick Scott
Sen. J. D. Vance
Sen. Pete Ricketts

Jessica P. | Utah



Age: 39
Year of Diagnosis: 2020/2017
Type: Bulbar Onset

I fear ALS is all too often swept under the rug as a rare disease hardly anyone ever gets. An extremely unlikely fate, which affects very few. I believed that for many years until the neurodegenerative condition crept into my life not once, but twice.

In July of 2017, one of my closest friends was diagnosed with military service-related ALS at the age of 48. Brian was an athletic and spirited man. He was a woodworker, artist, mountain biker, and friend to many. We couldn't believe he had received this devastating diagnosis. Over the next three years, our community rallied around Brian while he gradually lost all of his physical abilities but fought hard to maintain his spirit. **Even despite Brian's veteran status, his efforts to participate in a clinical trial or experimental treatment were never fulfilled.** Brian passed away on June 8, 2020.

One month later, on July 9, 2020, my mother visited my husband and me with terrible news. She too had been diagnosed with ALS. At first, I was sickened with the thought that we would have to watch another of our closest loved ones suffer this fatal demise. Quickly, however, my sadness turned to desperation as I tried to contact every research center and neurologist, I could looking for something...anything would be better than the lack of treatments Brian received.

The path was tough with absolutely no guidance or support offered by most including my mother's neurologist. Finally, thanks to the Forbes Norris Center in San Francisco, we became aware of the HEALEY Platform Trial and were able to get my mother accepted in the trial a few months after her diagnosis. This was truly a gift for which we are eternally grateful. Over the last six months of her trial participation, however, we have continued to learn about promising new therapies. **Unfortunately, each of these therapies seems to be blocked by corporate processes and bureaucracy leaving people with ALS hopeless.**

ALS is an always fatal condition that is unrelenting in its progression. It is not waiting for the red tape of our society to be removed. **This is why I request the FDA make every proven safe treatment available to ALS patients.** Doing nothing is not an option. People with ALS and their families are willing to take the risk and deserve to get a chance.

Each patient should be able to decide this for themself. The risk of no benefit or slight side effects would be worth it in my experience.

I have lost one loved one and my mother is currently living with ALS. It is devastating and an overwhelming condition for families to support.

I want the FDA to know that it actually does happen to people.

Please put people before profit.

Gail K. | Utah



Age: 68
Year of Diagnosis: 2020
Type: Bulbar Onset

New Therapy is vital. I read each day about NurOwn, AMX0035 and other very promising new treatments. **Every ALS patient that meets the criteria should be allowed the opportunity to participate**. Every month and year that passes and we are not given this opportunity it feels very cruel. We should be able to sign waivers knowing that we are taking a risk. I am desperate to live each day the best I can, as long as I can. **Please seriously consider what ALS patients are facing. We are desperate for anything that will give us the "Gift of Time"**

When a person has a terminal illness, this should be your Right to make this decision, not the Government.

I realize the FDA serves a purpose in society; however, we are educated people and we should be allowed to make these decisions and accept the consequences.

It is very difficult to know each day that you live in fear of the next day and have nothing to cling to for some sense of hope. It is extremely difficult to read about new medications that are showing promise and not being allowed the opportunity to try.
It is very difficult for all my family and dear friends to know there is nothing that they can do but pray and show support.

People know very little about ALS. People say "Can't you exercise in order to not lose muscle? Speech therapy will help you.

I know that I did not know much myself about ALS before my diagnosis. However, I knew it was a terminal illness. It almost seems as though until recent years ALS was not a disease that was given much research or concern. **I know that now this is not the case, therefore please give ALS patients the dignity and hope we deserve.**



ALEXIS AGIN

Falls Church, VA

On April 10, 2008, my life was forever changed when doctors at Inova Fairfax Hospital pulled me and my then husband into a tiny room and told us that our only child had cancer and was going to die, likely within 9-12 months. Alexis, then just 27 months old, had a CT scan and MRI that revealed a tumor on her brain stem. Diffuse Intrinsic Pontine Glioma, or DIPG, is like grains of sand in a field of grass; it is impossible to pick out every grain, and the tumor is inoperable given its location in the most critical part of the brain. We were told that there was no treatment, other than that she could undergo 30 rounds of radiation that would hopefully cause the tumor to shrink temporarily and give us a "honeymoon" period with Alexis before the tumor started to grow back and eventually would kill her.

As parents, we sprung to action and started looking for second opinions and any possible treatments. But what we quickly learned was that there was no hope; Alexis would die from this tumor. Over the course of the next 33 months, Alexis endured 30 days of radiation, countless MRIs, blood draws, medicines, alternative therapies, and oncologist visits. We stopped using the microwave, switched to all organic food, and started applying essential oils to various pulse points on her body.

Most significantly, Alexis participated in five Phase I clinical trials. You read that correctly-- FIVE. Applying for and getting a coveted spot in each of these trials was a nerve-wracking and seemingly random process that felt like a lottery in which winning meant that our daughter would at least have a chance to try an experimental drug. Because they were Phase I trials, they had limited openings at each dosage level. A few children would be given the drug at one dosage level, and then there would be an undetermined period of time during which the trial investigator would determine if that dosage level was safe before the next dosage level would become available for another few children. Timing was everything. If Alexis failed on one trial, we would have to wait a period of time-- usually at least one

month-- before she was eligible for another trial. And once she was eligible, we would need to see which trials had an open slot. More often than not, trials had no opening, and we were forced to wait or to try another trial that had less promise.

To illustrate, Alexis was on a Phase I trial for an experimental drug called Enzaustaurin for approximately 11 months before her tumor began again to materially grow. We were desperate to find another trial, and learned that there was an opening at Columbia University in New York. We filled out all the paperwork, submitted Alexis to additional blood draws and MRIs to demonstrate her health status, and were told that she could begin the trial. We rode the train to NYC the next day, and subjected Alexis to further tests, including an EKG to make sure her heart was strong enough to try the drug under trial. Late in the day when we had returned to our hotel room, we got a phone call from one of the doctors at Columbia telling us that Alexis didn't qualify. Her MRI results, which had been received by the hospital the day before, revealed that Alexis had a few spots of bleeding on her brain, and they were concerned that this would negatively impact her chances on the drug, and thus jeopardize the clinical trial. Devastated and without options, we planned to head home and wait for the possibility of another trial opening. Miraculously, however, just a few hours later we received a phone call from an investigator at Children's Hospital of Philadelphia (CHOP) telling us that she had been browsing through the trial openings on her computer, and noted that a slot became available on one of their trials, for which we had applied previously. Knowing that Alexis was waiting for a slot (and not knowing that we had in the interim planned to proceed with the trial at Columbia), she immediately "grabbed" that slot and called us to see if we wanted it. Today, it seemed, we had one the trial lottery. Shortly thereafter, we traveled to Philadelphia, and Alexis was enrolled in the trial at CHOP.

Despite the trial at CHOP and a subsequent trial at Sloane Kettering, Alexis passed away in my arms on January 11, 2014. It was two weeks before her fifth birthday. I am forever grateful for the extra time that I had with Alexis, as she survived almost three times longer than was predicted upon diagnosis-- for 33 months. That's longer than she had lived before her diagnosis, more than doubling her life.

Why the Promising Pathway Act is Important to our Family: The Promising Pathway Act (PPA) would eliminate the excruciating clinical trial lottery process for terminally ill children, granting critical access to experimental drugs faster than through current FDA pathways. Today, there are drugs in development that show some potential for efficacy in DIPG. For example, there are now several well-tolerated drugs demonstrating 20-30% response rates or unparallelled success in translational studies. Children with DIPG cannot access these therapies, however, because of the current FDA process and limits by geography and available slots in clinical trials. Under the PPA, such experimental therapies would become available to children with DIPG. Instead of being told to simply take their child home because there are no options, parents would have the option of trying a new therapy. Parents will have access to information about drugs in development and can make informed decisions about whether to try an experimental therapy. Being given that one last chance could be critical for a child, and might even result in a child surviving DIPG. I cannot think of anything more important.

Neely Agin

Mother of Alexis

[redacted]

I want to thank the Senate Aging Committee for allowing the ALS community and others suffering from various severe diseases to provide comments for the congressional record. I also want to thank the Senate Aging Committee for holding a hearing on the Promising Pathway Act, which is very important legislation.

I am 54 years old with a wife and a teenage son and daughter. I was diagnosed with ALS in March 2021. ALS has impacted my life significantly. Like so many others, I have experienced steady and progressive deterioration. I am wheelchair bound without leg function. I am quickly losing arm and hand strength on both sides. My neck and core strength are decreasing, and my lung capacity is declining.

As I increasingly rely on others for care, including for many regular acts of daily living, my role in my family has changed. I am no longer an independent provider. My parenting role for my teenage children, including as a role model, has transformed into one of dependence. My role as a spouse has changed. Caregivers, including family members, devote ever increasing amounts of time, energy and resources to helping me.

Professionally, I was a partner at an international law firm when I received the diagnosis and I have since retired due to ALS. I was no longer able to bring the energy, endurance and commitment needed to maintain a law practice.

Personally, while I strive to stay positive, I have lost the ability to do many of the things I enjoy. A simple family outing now requires major effort and resources to the point they occur infrequently. Up until just a few years ago, I was traveling regularly and playing in a men's ice hockey league. I enjoyed golfing with my son, running and biking. Despite various losses, I do not seek pity or sympathy. I just want the world to know that ALS is extremely debilitating as are other rapidly progressive and terminal diseases. I also want the world to know that diseases like ALS, diffuse intrinsic pontine glioma, glioblastoma and other rapidly progressing terminal diseases can happen to anyone. Therefore, I am submitting this statement in the hopes that legislators and policymakers will prioritize initiatives that can make meaningful change.

I volunteer with I Am ALS and co-chair its Promising Pathway Act (PPA) working group. I truly believe this legislation can make a difference. Some have suggested that those supporting the PPA are self-centered and only concerned about getting drugs approved in the hopes that they will save their own lives, while they believe the PPA would actually harm drug development. This could not be further from the truth. I have no idea whether there is a drug in the pipeline today that would be approved if the PPA were current law. This is about building a foundation for the future, be that in the next few years or decades ahead, that will enable faster access to promising drugs for people with rapidly progressing terminal diseases. I am under no illusion that it will help me in time to affect the course of my progression.

The PPA tackles the important issue of speed to access for drugs that treat certain very serious conditions where there is an unmet need and death will result without effective treatments. Today, existing FDA pathways are not suited for such circumstances. The FDA and others that oppose the PPA suggest the FDA has all the authority it needs to act quickly. They claim existing pathways already serve these illnesses. That is not the case. Drug approvals for serious conditions take many years to wind through various trial phases including in some cases two phase three trials and lengthy negotiations with the FDA prior to filing for approval. The PPA offers the prospect of cutting five or more years off the timeframe for marketing efficacious therapies. That timeframe is enormous for rapidly progressing terminal diseases.

Those that support the status quo point to various FDA pathways and programs that they argue negate the need for the PPA. Those existing pathways are not well-suited for conditions such as ALS. For example, even the FDA's "accelerated approval" pathway is not effective for ALS because it requires evidence that a drug's effect on a biomarker is likely to predict clinical benefit. Ninety-seven percent of ALS cases do not have a scientifically accepted biomarker (a biological measurement separate from direct clinical benefit) to serve as a surrogate endpoint. Even if some scientifically accepted biomarkers emerge for ALS, that does not mean a given promising drug would focus on addressing the mechanisms of the disease associated with the accepted biomarkers. The bottom line is that the current accelerated approval pathway is not a good option for ALS and other rapidly progressing terminal diseases.

Other existing pathways such as expanded access programs or right to try are great, but have significant limitations. For example, subject to some limited exceptions, individuals eligible for clinical trials are generally not eligible for expanded access programs. For diseases like ALS where eighty percent of people live only three to five years and where clinical trial eligibility is frequently for up to three years, the result is a lot of patients are excluded from such programs. Moreover, expanded access programs rely on drug sponsors to offer the drug for the program. While there is some NIH funding for expanded access programs, many such programs are outside of NIH funding.

The PPA does lower the FDA's "substantial evidence" of efficacy standard for drug approval for certain limited serious conditions. This lowering is very intentional. The showing of relevant early evidence of positive therapeutic outcome based on adequate and well-controlled investigations is based in science. The key is that PPA approval is merely provisional. It affords early access to promising drugs to people with extremely serious conditions who are willing to take risks. It allows additional evidence about a drug's efficacy to be collected during the short two-year provisional approval windows. Provisional approval can occur only if a drug has been shown to be safe. Required patient registries enable much broader data collection about a drug's efficacy and safety than can occur in traditional, double-blinded, randomized, placebo-controlled trials, which in the case of ALS, may only involve 100-200 people. In rarer diseases, it can be hard to even find enough people to conduct a meaningful trial.

Importantly, under the PPA, the FDA maintains meaningful authority to collect data and withdraw provisional approval based on safety or efficacy. Moreover, drug sponsors presumably want to obtain full approval of any provisionally approved drug. Other than allowing the use of real-world evidence to supplement an application, the PPA does not alter current FDA standards for full drug approval in any way. In sum, the PPA is common sense legislation with many safeguards that would enable early access to promising drugs for those who have no other options and who otherwise face certain death anyway.

Thank you again for the opportunity to submit these comments.

Regards,

Tim Tobin

Katherine B. | Virginia

Age: 52
Year of Diagnosis: 2020
Type: Limb Onset, Genetic

We Can't Wait

It is imperative that ALS patients be given the opportunity to try new drugs that have been proven safe. Any benefit, including the slightest slowing of progression is beneficial to us. **We should be given the opportunity to work with our physicians to determine if a protocol or drug is appropriate for us to try.**

Any therapy that may be beneficial is worth trying. **Patients, not the FDA, should decide is the risk of any drug is worth the potential benefit.**

The FDA is dragging its feet. There are two drugs that have been proven helpful for some patients. ALS is not a one drug fits all disease. Different patients will benefit from different therapies. The FDA should allow us to make these decisions. Once a drug has been proven safe and shown any potential benefit, such as NurOwn and AMX0078, they should be approved by the FDA for use. The fast progression of this disease does not give us time to wait.

My disease is considered slow progressing, yet it has changed my life, impacted my work and relationships and altered my day-to-day activities. **In the past 6 months I have lost strength in both arms and all fine motor skills in my left.** I cannot type, have difficulty prepping meals and performing some self care functions. I get tired and have experienced cognitive deficits. I pray that does not mean I will end up with frontal lobe dementia which is prevalent in my form of genetic ALS (C9ORF72). **My 16-year-old daughter is now in therapy and is dealing with the mortality of her mom** and mom's inability to do so many of the activities that were a part of our lives just a year ago. **This is affecting decisions that will impact her future** (i.e. she no longer wants to go away for college). I worry about how much longer I can work - I am the primary income in our home.

It has impacted all of my family and close friends.

That our lives are worth fighting for!

Our lives are worth fighting for! We deserve the opportunity to try ANY therapy that may slow or halt this disease. Ever extra day in our lives is a gift that we deserve to claim!

[redacted]

I am a physician and I am a caregiver for my husband jim who has ALS. He is a pediatrician, diagnosed in December 2021. Just two years ago Jim had an active pediatric practice, and was an active academic physician. We were runners, and active in our church. Today, just two years later, Jim is confined to a wheelchair, has no use of his left arm and his right arm is too weak to lift a spoon or touch the keys on a computer. His speech is slurred and communication is very difficult. His thinking is completely intact. He is essentially trapped in his body. As a physician i have seen a lot of suffering, but ALS is in a category of its own. That is why it is THE disease that every physician dreads. ALS is 100% fatal. No one has ever survived. the average life expectancy after diagnosis is 2-5 years. And those years are spent in an agonizing state of constant, rapid decline in motor function. We need treatments. This is a rapidly progressive disease that has not been well served by the current pathways for drug development and approval. It has no reliable biomarker for 90% of those with the disease, so the accelerated approval pathway is not applicable. I implore you to **support the Promising Pathways Act.** This act will enable the many new treatments with good safety profile and promising evidence to move forward with conditional approval. it will give us a fighting chance, and put promising treatments forward.

[redacted]

Hello

My wife was diagnosed for the first time with end stage ALS Dec 30 2022. She is 41 and we have 3 children a 6 year old done and 5 year old boy / girl twins. This disease has devastated our family. Since her diagnosis in dec she has lost function of all of her limbs and almost died of respiratory failure on June 24th. She opted for a ventilator and feeding tube so she can watch our children grow up. I am her sole caregiver and cannot afford to have skilled nursing come in to help because the cost isn't covered by insurance. That is 70 to 75 dollars an hour. I cannot leave her side unless we have some a friend or family come in and watch her. If anything happens she can die of asphyxiation if she doesn't have anyone there to provide suctioning of her lungs when needed. I have to have the kids sit with her while I go take an occasional shower so I can feel like a person. I can just take one because again if she needs something she could die. I constantly hear about helping the middle class but have seen nothing. Caregiver organizations won't help with the suctioning feeding through her feeding tube or medication so I cannot take a break. I myself am an 80% disabled war veteran and cannot continue my therapy for ptsd because we do t have help. (US Army 99-07). I have reached out to every organization that I can find an other then a couple of grants there is no help for actual care. If she was on state Medicaid then we could have help but because I still have full time employment, my company has worked with me and continues too, we do not qualify. This disease doesn't allow me to be a father to my children because I have to be a nurse for their mother which I will gladly do. Everyone says well there's hospice or a facility. Hospice means stopping all life saving medications and allowing her to die and a facility means she and the kids can't be around each other. I feel the system has failed us on all levels. The VA would only provide support for me not a dependent and the state and federal levels don't care about us or what we are going through. I know we are not the only family out there going through this. We need more help not just for a cure but for help providing care for our loved ones. We are watching them die in front of us and have to carry on for our pALS and children so they don't know what we are feeling. This battle is worse then being at war. We are both fighting an enemy that will eventually be able to win. Please I beg you to help with research and care help. I don't know much else to say but am willing to answer any questions you may have. My cell is in my signature block

V/R
Bill Kerner
Sr. BAS Specialist
Chinook Systems inc
1235 South Clark St.
Suite 625
Arlington Va 22202
Mobile: 443.610.5021
Direct: 571.527.0728 ext. 171

[redacted]

Dear Senator Braum and Committee Members,

My name is Kate Vasiloff and I'm a resident of Arlington, VA. My dad, George Vasiloff, was a Marine Corp veteran. He played clarinet in the President's Own and was a prolific and talented musician. When he was diagnosed with ALS at just 65, he knew his days of playing the clarinet were over...and the remaining days of his life were numbered.

Desperate to extend his life as long as possible, my dad enrolled in every possible clinical trial. Unfortunately, his disease was progressing faster than the trial admission process and he was denied over and over again. You can't imagine the devastation when the only glimmer of hope is snatched away because your illness is ravaging your body faster than your government can move.

While people with ALS and their families know cure is likely quite a ways off, they should have full access to any and all potential treatments which may buy them just a little more time together. I would give anything – literally anything – to have had one more month, one more week with my dad. I believe this new drug approval pathway may have given us that.

It's too late for me and my dad, but there are thousands of other daughters out there who want just a little more time with their dads. Please think of them today when you cast your vote in support of the Promising Pathway Act (PPA) (H.R.4408/S.1906).

In peace and with gratitude,

Kate Vasiloff

941-928-6960

katevasiloff@gmail.com

[redacted]

My name is Bruce Truax. I am 74 years old and have been married for over 50 years. I served in the U.S. Navy from 1967 to 1971. I was diagnosed August 2019 with ALS. I initially thought it was arthritis in my hands. Unfortunately, it was ALS. I have been classified as 100% disabled by the VA.

I began taking Riluzole soon after my diagnosis. Six weeks later, I began receiving Radicava. This was administered via IV. The regiment was 5 days of Radicava, 2 days no Radicava, 5 days Radicava. Then 10 days no Radicava. Then repeat. Each procedure took nearly 2 hours to complete. The VA installed a Port in my chest. This enabled the IV procedure to be performed by my wife at home. The Riluzole was taken daily in pill form. Both medications were given in the hope they would slow the progression of ALS. In the firstyar after my diagnosis, the symptom progression was fairly slow but constant. After 2 years on these medications, they were were stopped and the port was removed from my chest. This was done as research had shown them to be ineffective beyond 2 years. Around this time, it was found that my diaphragm muscles were being affected by ALS. My ability to breathe was reduced to about 53% of normal. My Doctor recommended a feeding tube be installed at this time even though I would not need to be fed through the tube in the immediate future. This could not wait till needed due to my breathing. I would be too high a risk should my breathing go below 50% of normal. At this time I began using a Ventilator to assist in breathing.

Fast forward to today. I no longer receive any medications to treat ALS symptoms. Just medications to make me more comfortable. I am not able to dress myself. I am not able to brush my teeth or wash my hands without assistance. I am not able to bathe myself. I am not able to move my legs nor do I have the use of my hands. I also have decreased muscle strength in my arms and torso. The Ventilator is now set to its 100% of its capacity to safely keep me breathing without a high risk of complications. I am now relying on the ventilator 24 hours a day to breathe. I also need assistance eating and going to the bathroom.

For nearly 4 months, I have been in the VA Hospital in Minneapolis, MN. I had several falls in my home. This and due to being unable to safely transfer from my bed to my wheelchair, which required assistance from my wife. For these last 4 months a VA Social Worker has been attempting to find a Nursing Home to which I could transfer. Unfortunately, NONE of the VA contracted care facilities will accept me due to being on the ventilator. I have been denied by a VA Long Term Care facility in St. Cloud, MN. The ventilator is called a Trilogy Ventilator.

Until such a facility is found that will accept me, I remain in the VA Hospital, waiting.

If you need any additional information, please feel free to contact me.

Sincerely,
Bruce Truax
grybrd@hotmail.com
612 402-6952

Mark W. | Ashburn

Age: 59
Year of Diagnosis: 2021
Type: Limb Onset



Having the chance to try medicine is essential.

I would take the chance. Not trying has the side effects of continued deterioration.

I don't believe I necessarily have the time to wait and again side effects are less terrifying to me than the inevitable of the disease

I never felt frail before in my life and psychologically is weighing on me while physically exhausting me.

My family is afraid.

You don't need to pity us. Given the chance we are very strong people and just want a little more time.

There are limits to our ability to make income so pricing the medicines so high is a burden.

[redacted]

Good morning,

My name is Allison Shelton and I live in Midlothian, VA. My husband Brandon and I are parents to an amazing 11 year old son named Declan, who has the rare disease Prader-Willi Syndrome.

When Declan was born almost 12 years ago, how very frightened we were when we learned our tiny newborn struggling to feed had this scary-sounding condition called Prader-Willi Syndrome. What we initially learned about PWS sounded so negative. But through lots of hard work, difficult times and never giving up, we and Declan have persevered through so many challenges, and he is turning into quite the unique and special guy. Things we didn't know at birth if he would accomplish – as basic as walking and talking, learning to eat without a feeding tube, and on to reading and writing, have all come to pass. Declan loves music, game shows, has made special friendships with his classmates and peers, practices tae kwon do, and loves swimming and playing the piano! **But there are still big challenges ahead, as we edge ever closer to adulthood.** He talks about going to college and getting married, and having a job. Our dearest hope for him is that he will be able to do all of this independently, and will not be stymied by the challenges of PWS. So many people with PWS are unable to live independently as adults due to hyperphagia (insatiable appetite), the hallmark symptom of the disorder. This overdriving urge to overeat is so dangerous that it can lead to morbid obesity. We live with worry about the future - what will happen when we are gone, if Declan can't live on his own? We so dearly want him to have a "typical" life - get to go away to college, get that first job, live away from home, be independent! But without treatments for PWS, we fear that will not be possible.

I hope the sharing of our story, and those of so many others, will aid in understanding the unmet medical need for those with rare diseases.

Thank you!
Allison Shelton
--
Allison Frey Shelton
703.867.7620
allison.shelton@gmail.com



SAVAYAH LEWIS

Granite Falls, WA

My daughter was 2 in a half when she was diagnosed with medulloblastoma. She went through chemotherapy for 6 months and had clear scans for only almost 6 months to find out it came back in her spine. She is currently fighting again with a different chemotherapy treatment.

Why the Promising Pathway Act is Important to our Family: Being in the childhood cancer world is a whole new world where you find out how unfair it is to see the limited options these kids truly have. I have seen so many stories that make me incredibly weak and sad for these kids. I probably wouldn't have heard their stories if I wasn't in it myself, which is not okay. That's how much it's neglected. There should be more people that know and care to make a change. When the few options run dry, there isn't much hope. Why not give people the hope to try anything out there that may work? Not everyone understands this hopeless feeling but if there was an option out there that could help treat, extend, improve or better yet cure these kids unfortunate diseases, then why not give them the chance to try? What if making this change makes a big difference in others lives, especially the kids that are left with very few options? Any little (or big) change in the right direction is appreciated when you're dealing with this. You could make that change.

Amy Lewis

Mother of Savayah

Tara B. | Washington

Age: 51
Year of Diagnosis: 2020
Type: Limb Onset



We Can't Wait

This would give a quality and quantity of function and independence that would make a real difference

Not sure but willing to try if recommended by neurologist team

Very important

Fear, anxiety, sadness, insomnia, nausea and anticipating needs of family and response of employer and friends

Fear, anxiety, sadness, insomnia, nausea and anticipating needs of family and **will the wife and very young adult kids be "okay" when my brother is gone**

Its hard, its real and it needs effective treatment options in a timely manner funded by the government

Do not stop development, please...

Gerry E. | Washington

Age: 76
Year of Diagnosis: Neighbor
Type:

We Can't Wait

I view any effort to slow the disease progression is important if a patient is willing to use it.

If it were me, I would feel I have nothing to lose and everything to gain.

If I had ALS (a death sentence) I wouldn't care.

There is a person in that trapped body

Why so slow? ALS is horrible.

[redacted]

My name is Karen Quandt and I live in Washington State. My son Ty had an ultra-rare genetic disease called Niemann-Pick type C (NPC). He died in 2017 at the age of 20. NPC is a fatal neurodegenerative disease that takes away your ability to walk, talk, swallow, eat, read, write, play and breathe. As a parent you watch all of this being taken away from your child as you desperately search for research and medicines to help them. Access to medicines that treat ultra rare diseases is rare. Ninety percent of the 10,000 known rare diseases have no FDA approved treatment. The Niemann-Pick type C community has had 3 different drugs presented to the FDA that were safe and effective treating NPC disease and all 3 were denied approval by the FDA because there is no consistent and reliable pathway to approval for rare disease drugs. All 3 of these drugs are currently being used by NPC patients without FDA approval because they are safe and effective and are helping to improve the quality of life for these NPC patients. One of them is considered the standard of care for NPC disease, even without FDA approval. The current regulatory system is not working for rare disease drugs. The Promising Pathways Act (S.1906) would be a consistent and reliable pathway for rare disease drug approval that would mean access to life saving drugs for many children like my son Ty.

Karen Quandt
253-862-4040
karenrq@hotmail.com

From: Karen Quandt <karenrq@hotmail.com>
Sent: Thursday, October 19, 2023 11:07 AM
To: Karen Quandt <karenrq@hotmail.com>
Subject: Fw: Promising Pathways

Karen Quandt
253-862-4040
karenrq@hotmail.com



To the Committee Members, Senate Committee on Aging;

I would like to share the remarkable journey I have undertaken with my son's rare disease story. My son, Michael, is now 39 years old and received his Syngap1 diagnosis in July 2019 at Oregon Health Science University in Portland, Oregon. It has been nearly four decades filled with diagnoses, misdiagnoses, and encounters with numerous doctors and specialists.

From Michael's infancy, I noticed and diligently journaled his developmental trajectory was significantly distinct from his sister, Mollie, who is 22 months older than her brother. His pediatrician attempted to reassure this concerned mother by explaining that "boys simply develop more slowly than girls." Well, almost 40 years later, I'm still waiting (with intentional sarcasm). Over the years, Michael has accumulated a series of diagnoses, including Developmental Delay, Intellectual Disability, Sensory Processing Disorder, and Behavior Disorder. Then, at the age of three, the seizures began.

Michael's educational journey was as unique as his medical experiences. I initially enrolled him in a parent cooperative Birth to Three program, followed by a three to five program, Kindergarten, and eventually, his neighborhood school. It was the first time my children were attending the same school together. By the age of nine, Michael had already been to six different school buildings. His educational progress was hampered by his aggressive behavior and increased seizures, and he faced challenges due to his inability to communicate effectively. Our home life was challenging to say the least, and often, it was almost unbearable.

When Michael was seven, his father and I divorced, and at the tender age of nine, Mollie took on a parental-caregiver role. Finding childcare was a constant challenge. Mollie attended one childcare provider, while Michael was with another, all before 6:30 am so I could make it to work by 7:00 am and return home in time to greet Michael as he got off the bus at 4:00 pm

Due to the divorce, my children and I had to sell and leave our family home and relocate to a townhouse duplex. Within a month, our landlord issued a warning due to Michael kicking the wall at night. I promptly swapped the bedrooms for Mollie and Michael to prevent him from being in close proximity to the neighbor's bedroom wall. It was a challenging period, and we eventually needed to move to a single-story building as my daughter required orthopedic surgery and couldn't manage the townhouse stairs. So, we moved again. In the span of two years, we found ourselves moving once more to a different house because the rent in our previous residence became too expensive.

During my children's formative years, we relocated on four occasions, had multiple childcare providers, worked with several pediatricians, consulted two pediatric neurologists, engaged with two different pediatric developmental behavioral specialists, collaborated with an orthopedic surgeon, general surgeon, dermatologist, an Ear, Nose, and Throat Specialist, Physical and Occupational Therapists, Speech and Language Pathologists, a Neuropsychiatrist, a pediatric dentist, and several adult dentists, in addition to undergoing Listening Therapy.

Upon reaching the transitional age of 16, I received referrals for Michael to consult with an adult neurologist and an internal medicine physician. This period also involved a multitude of medication trials that put Michael through side effects of anorexia, weight gain, dizziness, enough to make one's head spin, and this was just during his childhood. I'll spare you the intricate details of his transitional school years and the numerous adult specialists and surgeries he had to undergo due to gastrointestinal complications.

During Michael's journey through young adulthood, he developed substantial academic abilities thanks to an experienced and dedicated teacher who not only catered to his communication requirements but also acknowledged his learning capabilities. As his seizures continued to escalate, so did the number of attempts with various medications. Currently, Michael has an implanted vagus nerve stimulator positioned in his upper left chest, connected to his vagus nerve by an electrical probe. He also receives Epidiolex, an FDA-approved prescription CBD medicine, characterized by a thoroughly assessed safety and efficacy profile from clinical trials. Additionally, he takes three other anti-seizure medications.

Faced with a sense of hopelessness due to Michael's intractable seizures, which ranged from 30 to 100 partial complex seizures daily, his neurologist recommended genetic screening. The idea was to explore whether he had a seizure disorder amenable to genetic therapy. It was discovered that he did not have a genetically treatable seizure disorder but did have a genetic disorder known as Syngap1. In 2019, Michael became the oldest

individual diagnosed with Syngap1 (a title he held only briefly) among a global total of fewer than 750 people with a Syngap1 diagnosis. Today, as of the third quarter of 2023, the Syngap Census reports a total of 1,297 individuals (both children and adults).

In our roles as parents and guardians for our cherished family members diagnosed with Syngap1, we grapple with the challenge of establishing an inclusive community life and securing vital community services that we urgently require. At present, services and professionals lack the essential awareness of the needs associated with this rare condition. As part of a compact yet resilient global network of families who provide love, care, and unwavering dedication to our loved ones with this rare condition, my appeal to this committee is for your understanding of our real struggles, financial backing for research and treatment, and a deeper comprehension of the unique path we persistently navigate without any sort of roadmap.

If you need additional testimony, more stories or pictures, I am happy to provide those to all the members of this committee at your request. I look forward to hearing that the Senate Committee on Aging members have prioritized financial resources to help with research, treatment and community based resources we are all desperately in need of.

Best regards,
Monica Meyer
She/her/hers
18201 NE Cedar Drive
Battle Ground, WA 98604
360-904-8938
Mmeyer0801@gmail.com

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[redacted]

Hello,

My name is Katrina Meinen (26yo f) and I live in San Diego, CA. My sister Ashley Meinen (22yo f) lives in Puyallup, WA and has Prader Willi Syndrome.

Prader Willi Syndrome is a genetic disorder that causes obesity, intellectual disability, low muscle tone and shortness in height. Hormonal symptoms include delayed puberty and constant hunger leading to obesity. PWS is a genetic disorder usually caused by deletion of a part of chromosome 15 passed down by the father. There are fewer than 20,000 US cases a year.

Since Ashley was a year old it has always been just us and our mom. She's done everything in her power to give us a good life despite being a single mother raising a daughter with special needs. From my perspective, I've acted as a second caregiver for Ashley since I was young. We didn't have a typical sister/sister relationship but nevertheless we are there for each other. She is not defined by her disability. In fact she is one of the most bright spirited, outgoing, clever and motivated people I know. She's gotten her associate's degree and is on the path to become a teacher...an advocate for others.

I will say it had been hard time to time. She feels constantly hungry...we have to lock up the fridge, pantry and any other source of food (even dog food). In elementary she had a problem stealing other kids lunch boxes. I often found her taking money or snacks from my room if I didn't lock my door. She worked at Walmart for a small while and figured out how to get an advance on get paycheck through the loan center with which she bought so much candy and snacks to eat on her lunch break.

I believe she has remorse for some of if not all of these kinds of decisions though imagine your brain forcing your body to believe you're in a contestant state of hunger. You'd to just about anything to eat. Without proper precautions, there have been various cases of those with PWS eating so much in one go that they perforate the lining of their stomachs to perforate causing death. That is one of our biggest fears especially because of how possible it is for her.

People have never understood how she is 22 but mentally and maturity wise functions as a teenager. Many some she may have autism or possibly a form of down syndrome.

I'd like more people to know of this rare disease, what it means for those affected by it and what our communities can do to support people with PWS.

Thank you for taking the time to read our story.

Roberta M. | Clarksburg



Age: 65
Year of Diagnosis: 2019
Type: Bulbar Onset

I view new therapies as highly important to the ALS community. Anything to give hope, strength and potentially change how ALS is treated is something that we (patients and caregivers) have needed for years.

I believe that any treatment, whether it is effective or not, is one step forward in finding a treatment or cure for ALS.

Not important at all to wait for FDA approval; my mother would have tried anything to treat her ALS, whether approved or not. She HATED the suffering she was facing, to the point she attempted suicide. Her exact thoughts on ALS treatments were that she was already dying from an incurable disease, so nothing worse could happen to her.

My mother went from working fulltime to being disabled within a month of diagnosis. She was miserable, sat in a chair all day watching tv and lost her will to live. She pulled away from family, friends, she lost who she was with her diagnosis. Witnessing this turn around, seeing my mother go from a hard working, funny, vibrant person to an empty shell broke my heart in two and has forever changed me. I was thankful she passed before she became bedridden and immobile, because I knew how miserable she was.

My mother's diagnosis was very hard on our family. She was the rock, the one-person who held what family we have left together and without her we are all lost.

That everyone impacted suffers, not just the patient. I also wish people understood more about the financial difficulties and hardships and that medical companies and insurance providers would change their relationship with hospice care facilities. My mother could not get proper care and equipment due to restraints placed on hospice care.

Stop being greedy, **we need treatments and cures now!** We needed them 100 years ago!! Every second you drag your feet, that is another person you allow to die needlessly!!



IAN LAREW

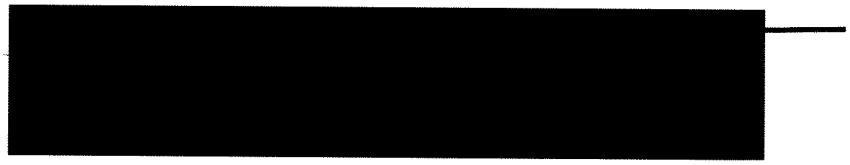
Pewaukee, WI

Ian was diagnosed with anaplastic ependymoma, a rare form of brain cancer, one week before his eighth birthday. Besides surgery and radiation, there are no other current treatment options for him. Ian has two tumor mutations that make him very high risk for a relapse with a very poor prognosis. If he relapsed, clinical trials will be his only hope.

Why the Promising Pathway Act is Important to our Family: These kids are already at a disadvantage due to lack of research and funding for these rare diseases. Any way that our treatment teams can access data to treatments faster will mean children's lives will be spared.

Janel and Robert Larew

Parents of Ian



In August of 2017 I went to Florida for my Grandmother's 90th birthday and to visit with my Uncle who had been diagnosed with ALS.

My Uncle Dave Beck had previously been a Judge in Daytona Beach. He start the Veteran's Court there. Dave had been an athlete and very physically fit all of his life. When I saw what ALS was doing to him I was heart broken. Time was too short from the time he had been diagnosed with ALS to his death Labor Day weekend 2017 for him to try a new drug Radicava that had just been FDA approved in May 2017.

My ALS story does not end there. A few months later I traveled to Wisconsin to visit my mother and step father (he was my step dad for 40 years.) During that visit i went with my step father Bill Benson to his neurologist appointment. Bill was diagnosed to my shock at that appointment.

Bill started Radicava treatments immediately. His desease progression was so rapid that by June of 2018 we were being told that he would probably die before the end of the summer. To our suprise the Radicava treatments must have kicked in. Bill did die but we had 2 more years with him. When he died it was Covid May 2020. He died alone of the worst disease a person could have.

Fast forward to today. Now I am on the cusp of an ALS diagnosis. I say that I am on the cusp because everything else appears to have been ruled out in all of the testing that i have been doing through the VA in Minneapolis.

The VA system has been amazing for me. My appointments are timely and my doctors appear to be very qualified. The only reason i do not have the formal diagnosis today is that it takes time to prove that my symptoms are getting worse.

When I go to my next EMG and appointment with my Neuroligist at the end of November, most likely I will have my diagnosis.

I am already looking into options for new treatments and hoping I can live long enough for a cure.

My daughter and grandkids live in Colorado and VA has an ALS clinic there as well. So i am pretty sure I will choose to move back to Colorado.

I have the option if I move back to Colorado for assisted suicide but I wont have the option to try any and every possible treatment to save my life. It sounds so crazy to me that my government will allow me to kill myself but not try to save myself.

After losing my uncle Dave and Bill, my family will be devistated to lose another to the same cruel disease. I am not blood related to either my uncle or step father.

Please consider funding ALS reaserch and relaxing FDA rules for treatments that might extend or save lives. There are no known preventive steps to take to prevent ALS. This diagnosis is a death penelty and I dont think it is as rare as we all think. 5.5 - 9.9 in every 100,000 Americans will get ALS according to your website NIH.gov

Thank you for your consideration

Lisa Jenkins
Altoona, WI

Attached are photos of me with my step dad Bill in 2019 and with my uncle dave in 2017.




#EndALS
CURE ALS
ALICE'S QUEST

[redacted]

Hi my name is Amy Wald. I am here today on behalf of my son, Levi. I live in district #5, in Wisconsin. Levi was born on March 30th, 2012 in Menomonee Falls, Wisconsin. It was a great day. My husband was so proud he had a boy! Everything seemed great until we woke up the next morning thinking we were going home. It was just the opposite, we were sent to Children's Hospital of Wisconsin NICU instead. He was a patient at Children's Hospital for over a month until they could figure out the diagnosis of Barth Syndrome. They too had never really diagnosed this disease before at that time and had to concur with their counterparts in many states to reach this final diagnosis. Imagine what we were going through and how scared we were for our new precious baby, who had just been diagnosed with a disease nobody heard of before. I did everything right during my pregnancy, I never skipped a prenatal vitamin, exercised, ate right and did everything I was supposed to do with my first pregnancy, but all that didn't matter. We were dealt something we had no control over.

To date, we have had excellent care at Children's Hospital of Wisconsin and at John Hopkins Hospital. Our son was put on 4 medications the first month of his life and continues taking them. These are the only medications right now helping his heart function and intact at this time but unfortunately, he has to wear pull ups at night because he always wets the bed because of taking these medications. He is now 12 and this situation doesn't work very well for sleepovers with his friends. They make fun of him. In the mornings, I have to peel him out of bed because he's so tired and has wet the bed because he doesn't wake up in the middle of the night to go because he's wiped from the day.

Levi loves sports! He was voted MVP of the baseball team last year. He excels at the only position he can really play on the team, pitcher. When he hits the ball, he has a very hard time running to the bases with his low muscle tone and weakness. His feet turn inward due to this weakness and trips a lot when he walks, and causes him to run very slow and labored. He feels bad that he can't help the team score a run. Levi, of course, also likes basketball. The coaches allow him to make the team. He just wears his jersey and sits on the bench. He can't take the running in this sport either, but he feels part of the team. It keeps him going. He was fortunate enough to spend an afternoon with his hero, JJ Watt, through Make A Wish Foundation. They played some football and spent time together at Camp Randall stadium. We had to carry him the whole way, because it was too much walking for him to handle. He still talks about the time he spent with JJ, and the items he gave him to remember the day.

Levi has a brother and sister who love him very much. He compares himself to them all the time. "Why do I have to take medication every day and they don't." "I want to be normal!" He breaks our hearts, but we support him every day and love him endlessly. We constantly fear that any day, he could just fall over with his heart condition with no symptoms prior, or no time to save him. We are very thankful and continue to pray for our son and every other boy that has this terrible disease.

I thank you today for taking the time to hear about my amazing son, Levi. He's loved and supported by his entire family, grandparents, friends, and the community. We would do anything to make sure my son and his counterparts with Barth Syndrome receive every effort to treat and cure this terrible disease. I understand when you look at this disease, only one person with this disease is in your represented area in Wisconsin, but congress has authorized the FDA to use flexibility in these cases where there are so few patients who can participate in trials. There have been 17 boys affected with Barth Syndrome that have passed away since starting this process. What if this drug Elamipretide could have saved their lives. They could still be here.

We made a visit to John Hopkins and I met a researcher connected to the Barth Syndrome Foundation, he believes treatment of Barth Syndrome is just as important as any other disease. If we can find a proven medication and/or treatment plan, a cure for this disease can hopefully be obtained. We are asking for a fair, equitable and appropriate review of elamipretide in Barth Syndrome by the FDA before we lose access to this drug, the only medicine currently in development for our life threatening, ultra rare disease. Elamipretide could be the answer we have been waiting for to save our boys. This medication could then be considered the answer for other diseases that have some of the same symptoms as Barth Syndrome, such as MS and many others. Supporting the approval of this fair and equitable review of our application for our disease, Barth Syndrome, but other diseases too. Imagine a cure for some of these terrible and rare diseases could possibly start here. I thank you for anything you can do for your constituents back in Wisconsin. A great state that thanks you for your voice in Washington D.C.

Please sign the letter drafted by Senator Braun on our behalf. On behalf of Levi and his Barth Syndrome brothers and families.

Thank you,

Amy Wald

Hartford, Wisconsin

Craig P. | Wisconsin

Age: 63
Year of Diagnosis: 2020
Type: Limb Onset

We Can't Wait

Extremely Important, I wake up every day hoping that this is the day I get a phone call that a new drug is ready, and I can start immediately.

Score of 1-10 this is a 10 all day long, I don't have months or years to wait its now or never I need HOPE! any drug or the promise of a new drug gives me that HOPE.

If a trial for a new drug is showing to be safe with few side effects like AMX0035 has shown to have promising benefits, then it should be available immediately. **As a person living with ALS, I do not want to wait for stage 5-6-7 trials time is most important!!!**

I wish everyone at the FDA could live for One month with ALS or sit at there kitchen table and look at their spouse who has ALS and tell them there is a new drug that's showing great results but I'm sorry honey we have to run more trials it should be approved in 3-5 years. After a lifetime of sports A love of the outdoors, a cabin in the north woods of Wisconsin I'm left with a window to look out of a TV remote and a lot of books to read that's how ALS has impacted my LIFE !!

Devastating, to watch a loved one die slowly before there eyes, To try and keep their spirits up let them know that there is hope for new drugs and maybe to slow the progression down, its sometimes harder to give loved ones hope then yourself.

That time is critical !! This does not go away when you turn your back, we need to speed the process of making new drugs available ASAP. Please give us HOPE !

Think for one minute how different a person living with ALS is compared to someone working for the FDA or a pharmaceutical company. when Friday night comes and you go home for the weekend you make plans with your family camping trips, zoo, swimming, you shut down your work with ALS. A person living with ALS doesn't know the difference from Friday night to any other night we can't shut down and start back on Monday with our symptoms. You have the luxury to wait till next week or next month or a year to make decision for approving the use of new drugs, **Guess what we don't have that luxury we can't wait !!! We don't care if the new drug makes us glow in the dark as long as it slows down the progression, we are all in PLEASE !!**

Edwin B. | Wisconsin

Age: 59
Year of Diagnosis: 2019
Type: Limb Onset

We Can't Wait

Extremely important to have the chance to take any medicine that will help.

Highly important to have any opportunity, when no chance exists doesn't make a difference

If it shows potential their decisions are meaningless

In every way it is important to find a cure.

They are my caretakers 24/7. It seems no gives a shit.

Big Pharma has one Concern $$$ People with ALS are statistically moved from moral equity to nothing profitable and forgotten. The FDA problem 1 first word.

Lynn M. | Wisconsin

Age: 70
Year of Diagnosis: 2017
Type: Limb Onset

We Can't Wait

I think that all new therapy is promising. While not curative, new therapy provides hope to those who have ALS. In my husband's case, **he was very interested in starting therapy that only slowed disease progression and continues to take Rilutek even though he is currently in the end stage of his disease.**

All new therapies are relatively untested in the general population and for each person, their response to the therapy, whether new or still in clinical trials, is unique. The responses to therapies under study can range from no benefit in some people to a significant benefit in others. Side effects are to be expected. **If a person has significant side effects, they and their doctors can decide - on a case-by-case basis - whether it is worth stopping the new therapy.**

It is not important at all for me, although I have been a cancer research coordinator in my career. It is very important for my husband that the FDA has weighed in on the new therapy. He is not interested in therapies in clinical trials (he is the patient) so we have not pursued any of these.

Our entire life has been impacted. Currently my husband, who moved to Colorado to hike in the mountains, is totally unable to move at all, and needs total assistance with all of his ADLs, including turning in bed at night. He uses a ventilator (without a trach) as assist breathing sporadically during the day and all night long. We have moved to Wisconsin now to be close to family, although he never wanted to move back to Wisconsin.

I am his caregiver. Although I am an RN with 43 years of experience and am very able to deal with all of his ADLs and therapies, I am with him 24/7 and have to get up with him several times during the night to turn and use the urinal (which I have to place). **This is the hardest thing I've ever done in my life.** Currently, my grown children are helping with his care. My adult son has basically moved in to help and works from here on his computer. My daughter in law comes at least 2 days a week to help with cares although she works full time and has 2 teenagers at home. My husband's sister who lives in Florida is very upset that he is doing so poorly.

That it is worse than cancer. No effective therapy and no cure. More research is needed desperately to develop effective therapies and a cure. **ALS is a death sentence.**

This disease needs more funding and new therapies need to be approved quickly. If you get ALS, currently, it always ends in death and pain for the family.

Sara S. | Wisconsin

Age: 44
Year of Diagnosis: 2020
Type: Genetic

We Can't Wait

Having the chance to try a new medicine that may or may not help, It's better than nothing.

Incredible. Hopeful. Gives pals a fighting chance. We're dying- how is this not understood? Let us try.

We're dying. We're volunteering to be the test subjects. Give us the option.

It's a freight train that has destroyed it.

It's destroyed them. There's no hope. All they can do is watch us waste away.

You die a little inside, and outside, everyday. From the neurologists that misdiagnosis due to inferior education, or pure hubris, to the crippling onslaught of debilitating symptoms. Every day you die another small death. Let us fight. It's all we ask.

"You're playing games with our lives. You've given us nothing. Then snatch away even the smallest opportunities. If this, were you, or a loved one: What would you give for a small chance of hope? The answer is Anything."

Lisa B. | Wisconsin

Age: 55
Year of Diagnosis: Dad: 2002
Type: Bulbar Onset, Limb Onset

We Can't Wait

I've known several people who have been diagnosed with ALS since my dad was diagnosed. The one thing they share in common is they wanted more time with their loved ones. More time being able to feed themselves. More time with being able to walk or talk. **Any chance of slowing the disease opens them up to more quality time with their families.**

I don't view having no benefit as a risk. It may be a disappointment, but it's worth trying. We would have been wiling try just about anything to help my dad. These people are living with a death sentence. As far as side effects, that's for those who are living with ALS to decide personally. As with any drug, you weigh the side effects with the benefit. Again, the mere chance that something would help outweighs the risk. **The clinical trial process is too long. I am not advocating that any drug brought to trail be widely available.** There still has to be guardrails. But as I said before, people with ALS are living with a death sentence. They are trapped in their own bodies. Any promising drug should be made available.

My dad was diagnosed at the age of 60. He died 27 months later. It was heartbreaking to watch him slowly lose the ability to use his hands, then walk, then talk. He was diagnosed in 2002 and the technology available today wasn't there. **The next time you feed yourself, think about not being able to do that. The next time you have an itch, nope can't scratch it.** Want to turn over in bed to get more comfortable - sorry, no can do. Have to go to the bathroom, hold on, someone will help you shortly. These once independent people are now relying on others to provide 24/7 care for them. My father had to allow his daughters and son to help him in the bathroom and shower him. Any modesty needs to go right out the window. Don't get me wrong, **it was an honor to be able to assist my dad, but it also was very taxing and stressful.**

Our family was lucky. Our community rallied around my dad and us. We had a caregiver come and get dad up during the week to shower and feed him. His 3 children rotated putting him to bed every night and getting him up and showered during the weekends. He needed care going to that bathroom and feeding. **It's absolutely heartbreaking to see someone trapped in their own body.** To go from being active, to not being able to move. During dad's illness, we were the master of schedules. Making sure there was always someone there with him, someone who could feed him and take him to the bathroom. In addition, we were always researching new therapies and got our hopes up every time we heard of a new one. The stress put on the families of ALS patients is extremely high.

In my opinion, there is no worse diagnosis. Almost every other disease has a potential cure, or the hope to prolong life and hold the disease at bay. ALS is a death sentence where you are trapped in your own body. Slowly you lose function. Slowly you lose the ability to do things for yourself you never thought twice about. You rely entirely on others to do EVERYTHING for you. When my dad was diagnosed, I never knew someone with the disease. We participated in the first ALS walk in Appleton, WI and I think there were about 20 people there. Fast forward to today and there are thousands of people. It is so sad to see how many people in our area are affected by ALS. This disease is not "someone else's" disease. It's affecting your coworkers, your family and your friends.

Please continue to work tirelessly on a cure. Don't give up, because we're not giving up hope. Please make new therapies available as soon as they show promise. Folks with ALS know they are going to die without new therapies. They are willing to try anything for a shot at slowing down the disease in the hopes of spending more time with their families and an eventual cure.

David W. | Wisconsin

Age: 68
Year of Diagnosis: 2015
Type: Bulbar Onset



We Can't Wait

Very important to have the opportunity to try medicine that could help me. It depends on the side effects. It is not important to me that it is FDA approved.

It took my life away. Has taken from my family's life as well. ALS and how it effects every aspect of your life - it's awful.

"We need to look beyond the box"

[redacted]

Dear Mr. Chairman,

My name is John Linnell and I was diagnosed with COPD in 2005. Since then, I have had to leave the workforce and go on SSDI. This has totally changed my life. Rather than just sitting at home with an oxygen cannula in my nose, I decided to become involved and am a strong advocate for the 14 - 16 million Americans living with COPD. Please understand, there are another 14 - 16 million Americans with COPD that are undiagnosed. So, certainly not a rare disease, but most definitely a progressive disease and it has no cure.
I would like to address a few of the unmet needs regarding COPD:

- Oxygen Reform - Those needing high flow oxygen that needs to be delivered with liquid oxygen is unavailable to most all of us due to CMS Competitive Bidding. While Competitive Bidding may have been good for some areas, it failed when it came to liquid oxygen. The suppliers of liquid oxygen wound up losing money and stopped supplying it. This makes those needing liquid oxygen homebound. American citizens unable to leave their homes and enjoy any Quality of Life because our government has been unable to remove oxygen from competitive bidding. This is a travesty. Over 25 patient groups are supporting a yet unwritten bill for oxygen reform. I am in hopes your committee will support this once it is brought to the floor.

- Funding for Research and Education - COPD is the third leading killing disease in the US. It is also about 167th in funding. The 3rd leading killing disease yet 167th in government funding!! We need funds allocated to the CDC for the states to initiate awareness and education plans that can help with earlier diagnosis. We also need funds allocated to the NIH specifically earmarked for COPD research. I would also encourage Congress when deciding on CDMRP allocations (Congressional Directed Medical Research Program) to make COPD a uniquely funded Topic Area rather than just tossing it in the mix with others. COPD deserves to be a Topic Area.

- New Medications - Along with the above request for research, we need new medication research. The "newer" medications for COPD coming out are simply blending of current families of medications ie triple therapy inhalers which, while effective, are just putting three existing medications together in one inhaler. We need more research done in this area.

I have struggled with COPD for 18 years. Being a progressive disease, I am now on oxygen almost 24/7. Travel is becoming more difficult. I find myself often not leaving my house for days. When I travel to speak on behalf of COPD I now need my wife to travel with me. It is frightening to think that the day may come when I simply cannot travel and advocate for all of us living with COPD, whether to a conference, meeting with one of the many non-profit panels I am on, or to travel to 'The Hill' and meet with elected officials such as yourself.
I used to be so independent, yet now I have to rely on my wife and others to help me. Thankfully, I can certainly write letters such as this and share this journey that so many millions of us are going through. We need and want your support. I thank you for your time in reading this. I am happy to respond to any questions or to virtually meet with you and any committee members.

Best Regards,
John Linnell
740 E. Decker St.

Viroqua, WI 54665
freeborn1956@gmail.com

My Scleroderma Story

By Demeshia (Demi) Montgomery

My name Demeshia Montgomery and I'm a 23 year scleroderma survivor. I would like to share my story with you. I had twins, a boy and a girl at 19 years old. They were 1 pound babies and had truncus - they were 27 weeks early. My daughter made it to 6 months old, had one operation on her heart and three months later had been hospitalized for three weeks before being sent home on oxygen. She passed the same day she was sent home. My son went on to have 3 total heart surgeries. He passed away during the last surgery. I was truly devastated.

Exactly one month later I began having really extreme pain in my fingers. I also had a black mark on my arm (which I thought was a bruise). This pain in my hands went on for a while till I just couldn't take it anymore and went to a dermatologist. While I was there she did a skin graph and told me we would get the results in a few days. The results came in and she informed me I had morphea (which is a lesser version of scleroderma). She then referred me to a rheumatologist. I was scared and didn't visit the rheumatologist for another 5 months. By the time I did my hand had gotten so stiff I could barely make a fist. It reminded me of a claw and I had several sores on it. Needless to say I was scared out of my mind.

At my appointment with the rheumatologist I learned I had Scleroderma with Raynaud's Syndrome. I was warned that "I better get ready to feel some of the worst pain ever". There was no treatment, just preventive care. I left there feeling terrified. I then started my journey to find out exactly what scleroderma was. I found a local support group and met Penny Davis who was getting a proclamation from her city every year and encouraged me to do the same. So I began getting proclamations annually from my city about 3 years later. For the next ten years my hands contracted more and more until my left hand was locked in a claw position. The ulcers kept coming, eating more and more of my finger tips. At about 29 years old I got pregnant again. When I was about 4 months old I felt horrible and went to the emergency room. There I learned the baby had died and they would have to

induce labor. The hospital then informed me the baby had Dandy Walkers Syndrome.

By this time I had been attending scleroderma support group meetings for about 10 years. I truly felt no one understood, my family either acted like nothing was wrong with me or they shamed me by saying I had AIDS. By this time my skin was a black color with light blotches spread all over. I felt ugly and isolated. Then I began having ulcers that would get infected. My left thumb was first and got gangrene in the tip and had to be removed. This also happened to 4 more of my fingers and a toe. My elbows also tightened and ate themselves off to the bone. Leaving one of my arms unbendable. My knees and buttocks began getting calcium rocks. Some so big I had to get them surgically removed.

I had really begun getting heavily involved with advocacy for scleroderma. This helped me to cope with the continuous pain and calcium rocks that seemed to be covering my whole body. I was now getting proclamations from 2 cities annually and had begun training to be a support group leader for the Arthritis Foundation. After losing several scleroderma friends to the disease I decided more awareness was needed. That's when I found a co-sponsor (Senator Bill Beagle) to declare June Scleroderma Awareness for the whole state of Ohio. Bill 133 was passed into legislation in 2016 and made Ohio the first state to have a bill for scleroderma awareness month.

During this time my foot began showing signs of lack of blood flow. Which ended with me losing my pinky toe.In 2019 a proclamation guide was created with a team of scleroderma advocates. They all believed in my dream and were active in their own state to bring awareness. At the beginning of 2020 we began looking for more scleroderma advocates to cover all 50 states. The hopes are in June of 2020 we will have Scleroderma Awareness Day proclamations in all 50 states. More recently I have begun leading a national grassroots effort to get proclamations and building lighting from cities throughout the US on top of the state proclamation project. I then went on to write a BIPOC program and create a team to include equality and diversity programming. I have since left that organization and have started working on building a company that provides networking opportunities and resources to all disabled communities called The Waiting Room Entertainment.

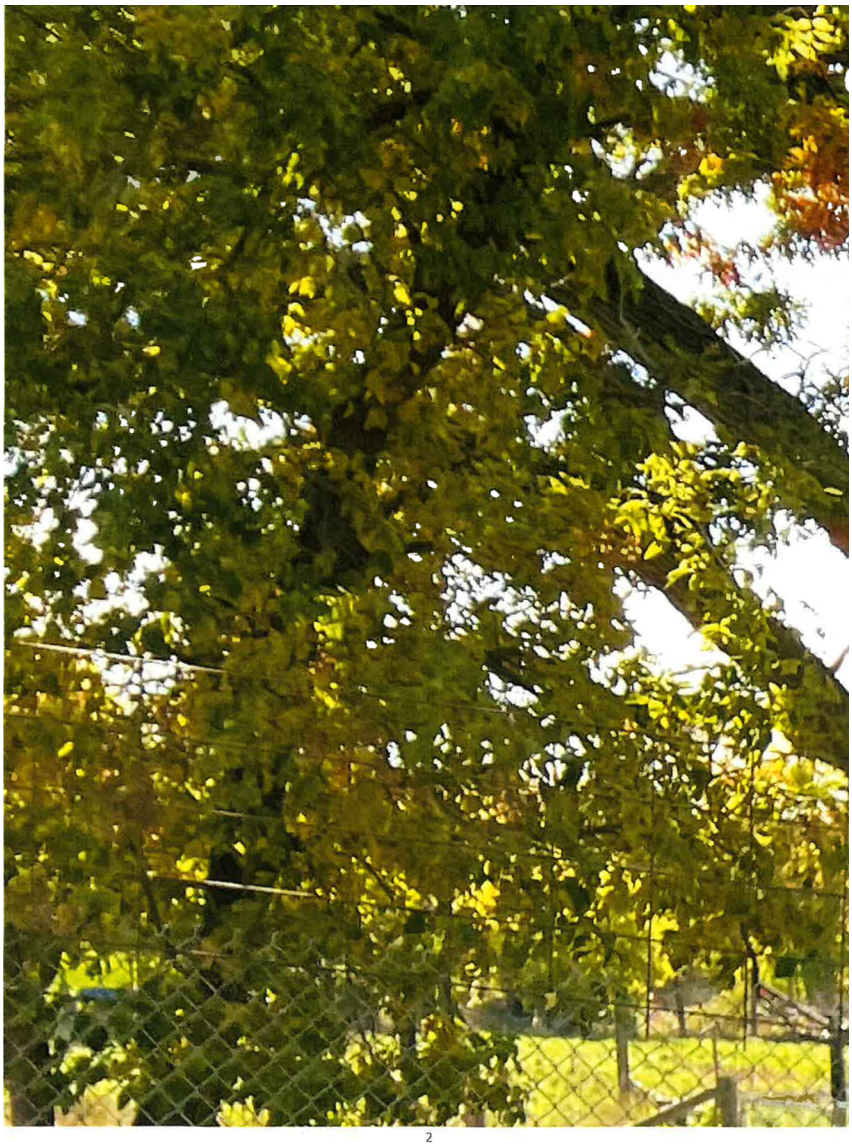
With a team of 4 founders. I tell you this story to share how a disease so horrible can be a gift at the same time. Over the years I learned to turn my grief, frustrations and fear into motivation. Now at age 42 and newly diagnosed with Pulmonary Fibrosis I'm determined to help bring awareness and I advocate for research funding for rare diseases. I pray that the patients being newly diagnosed will have more information, treatments and knowledge available to them then I did. If sharing my story comforts even one person, then all the pain was worth it. I would like others to know it's not a death sentence but an opportunity to experience life in a different way. If you believe you can succeed!!! Hopefully the information you receive today will stay with you throughout your career and you will be able to understand and appreciate the vital role you have in a patient's health care journey!

My motivation is my husband and stepdaughter. They both have sacrificed so much for me to be able to live a normal, comfortable life. I feel that it is my duty to be strong and put up a good fight! They inspire me to be the best at what I can still do and to continue to learn more ways to advocate for myself and others that suffer from disabilities. Their love for me gives me the strength to smile and push forward and to continue to Dream!

[redacted]

Good evening,

My name is Jessica Sheldon. I live in Muskego, Wisconsin.



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I have three children, one of which has Prader-Willi Syndrome.

When Audric was born, something was wrong. We didn't know what. We didn't know why. But there were a few characteristics leading us to attend a plethora of appointments ending at dead ends until our pediatrician said "okay, let's look at seeing a genetics specialist."

At the initial appointment, I vividly remember asking the geneticist, "do you think he has Prader-Willi Syndrome?" Before I could finish my statement he replied. "No, no way. He isn't floppy. He isn't failure to thrive. There is something going on, but I don't think it's that, let's run the tests." - we waited a month to get our results. And those results confirmed our son had Prader-Willi syndrome.

Prader-Willi syndrome is a rare genetic disorder effecting 1 in 18,000 individuals. It's equally prevalent across all genders and races. It's equally complex and complicated across each individual and their families.

Since receiving Audric's diagnosis I have firmly believed in "hope for the best. Prepare for the worst." Since receiving Audric's diagnosis, I tell myself this almost daily. There are many debilitating components to PWS. Ranging from cognitive and developmental delays, to gross motor and fine motor delays, medical diets and restrictions. When, as a parent, you are given news of such, it is life changing. It is devastating quite frankly. But then, knowing my husband and I wanted to do absolutely everything and anything we could to help our child live a socially significant life, we were going to.

One of the first pamphlets my husband read upon getting Audric's diagnosis stated my son would never ride a bike. On top of not being able to read a bike, we were told early intervention would be key for his future. Audric would make wonderful gains and live a socially significant life if we started therapy ASAP.

Audric has been participating in physical therapy, speech therapy, and occupational therapy since he was 4 months old. Audric has been participating in hippotherapy since he was 18 months old.

Audric attends school full time and is integrated into a regular Ed classroom with support. Audric LOVES sports, Audric is extremely social.

Audric is routine oriented. Audric's conversations are quite rigid. Audric experiences anxious behaviors and is easily distracted.

PWS is a spectrum, there are common traits most individuals experience, in some way shape or form. The key characteristic we've recently started exhibiting is hyperphagia.

For the first time, two months ago, I caught my son drinking creamer from our fridge at 2am. I caught my son the following night reaching for half and half, at about 4am. The night after that I caught him going into the bathroom looking for toothpaste to eat.

My son had started demonstrating the key characteristic of PWS which we don't have a cure for. Hyperphagia. In a nutshell, hyperphagia is the sensation of never feeling full. Ever. Period. Starving. All of the time.

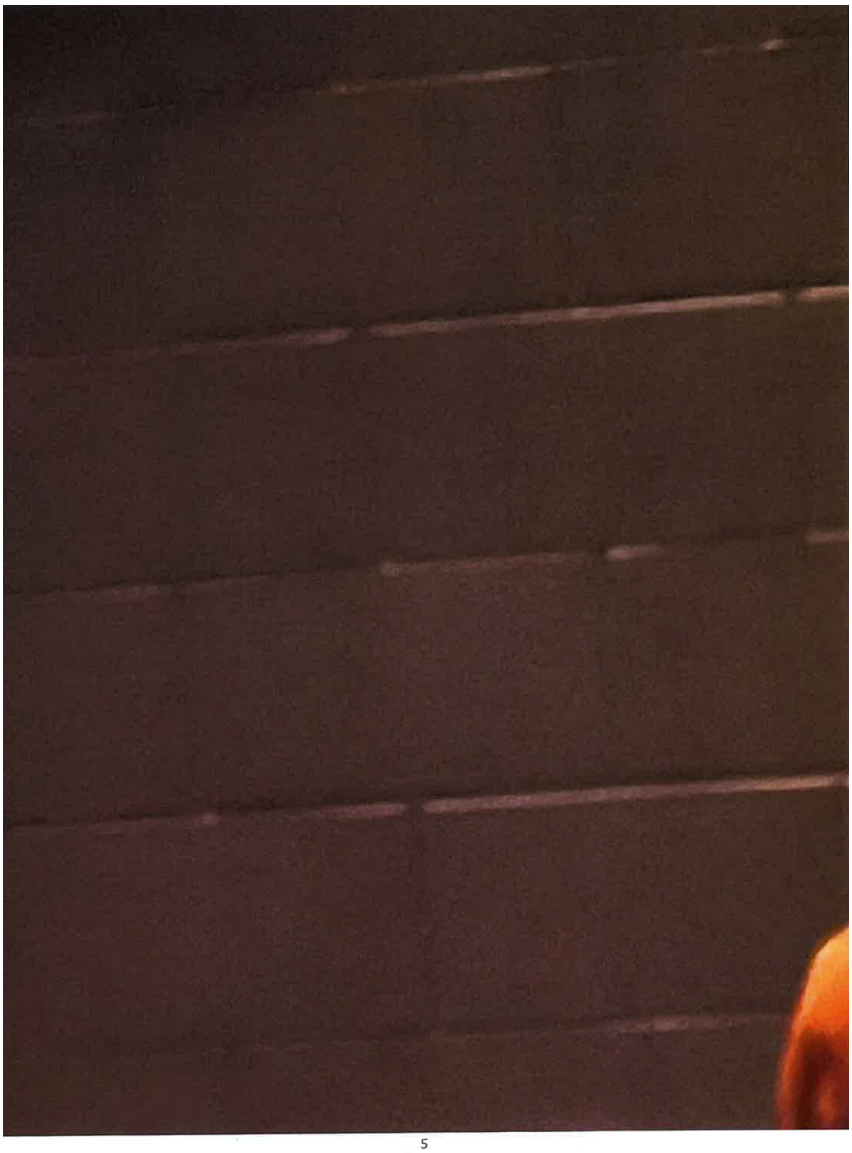
And it's terrifying knowing and hearing the history of PWS' impact on other patients and families. It's even more terrifying knowing there is not a cure, or a solution to hyperphagia.

Audric has said he wants to be a doctor when he grows up. He has said he wants to be a fire fighter. He has said he wants to be a baseball player. Without a solution to hyperphagia and it's life threatening affects, none of these dreams are remotely possible for him.

There is treatment, right now, demonstrating statistical significance for individuals with PWS. DCCR is a once-a-day tablet, supported by Soleno Therapeutics that has been and is continuing to collaborate and fight for changing PWS's natural history with DCCR.

The FDA has never approved an orphan drug. Not only would the FDA be opening a possibility for our community, but it would be opening a pathway for all rare diseases a fair a true opportunity for change and hope.

Thank you for taking the time to read my story. If you have any questions please do not hesitate to reach out.



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Warm regards,
Jessica Sheldon, mom of Audric - age 7

[redacted]

Ania Bey – PWS Avenger

When I became pregnant with my fourth child, I was most looking forward to the older children experiencing the wonders of baby in utero – the crazy movement of baby. My pregnancy in 2015 was, however, not typical in hindsight. You see, the little lady growing inside did not move nearly as much as her siblings did, and what I most looked forward to (the kids marveling at how my belly moved) was seldom witnessed. This was the first sign that something was different.

In July of that year, we welcomed our little Ania who looked remarkably perfect – like a little porcelain doll with painted lips. All were instantly in love. Within 10 hours, however, my instinct told me something was very wrong. You see, Ania didn't cry, she didn't open her eyes, she wouldn't nurse. She was much like a floppy, silent doll. We had to fight hospital staff to pay attention, to provide a nursing pump, to help me feed this infant with the tiniest syringe I had ever seen. We had to fight not to be discharged and instead to request a consultation from the NICU because something was so incredibly not right.

When the NICU specialist held our daughter on his hand, her head, arms and legs literally fell and dangled. He looked up at his colleagues and simply said, "Her tone." Then at the end of his assessment, he looked to my husband and I and commented that he had only ever seen one other child born with a rare genetic condition called Prader-Willi Syndrome, but he thought he may have it. Researching from our phones, we were sickened and devastated. PWS instantly appears to be horrifying and incredibly challenging. Our sweet, perfect baby was going to have a life of unbelievable challenges.

Yes, Ania faces many challenges – most unseen from the casual observer because, besides wearing glasses, she looks like your typical 8 year old girl. But then she moves, or talks, or you hold her ice-cold hands (because poor muscle tone affects circulation) .... Then you begin to notice that somethings are definitely different. Perhaps you see her lunchbox with extremely healthy choices or you send a treat to school for your child's birthday that Ania politely refuses because "it's not good for her belly." Then you may notice that something is different.

Ania's life is very different ... loaded with medical specialists, weekly appointments with a variety of therapists and practitioners, daily growth hormone injections, very restrictive diet, poor speech articulation, limits on how long she can be outside in warm or cold weather, no sugar – ever, limited carbs of the healthy variety, quick exhaustion, anxiety and emotional dysregulation, lengthy illnesses or hospitalizations, and the list can go on and on and on. But the part that has us most anxious through it all is the impending dreaded hyperphasia – incessant hunger. No full cure because this is a genetic deletion. She is a fighter, your average, everyday PWS Avenger.

You see, ALL PEOPLE living with Prader-Willi syndrome will, at some point in their lives, cease to feel satiated. Their brain and stomach will no longer speak to each other, so the PWS individual feels constant hunger. Hunger as if they haven't eaten in days. Hunger that is so intense that those living

with PWS often refer to it as their monster. Hunger that can lead to overeating, eating uncooked foods, eating from the trash or things not typically considered edible, eating, eating, eating. All with the potential to lead to additional health concerns or death.

Our beautiful, sweet, kind, silly Ania. Oh it's heartbreaking to consider what her life entails. All the work she puts in to achieve simple tasks, to accomplish what most deem natural. Our loving little angel. Her life is already hard, and we know the hunger is on the horizon. Our hearts break for her, and we live in a constant state of "when."

Most children ask mom or dad for a snack, and we readily provide the Goldfish crackers. Someone says they want more for dinner, and we put it on their plate. A child says they are hungry again, and we giggle because they must be growing. These normal moments put me into a panic. I always question, "is it starting?" You see, Ania can't have the typical snacks of her peers – only very limited healthy options proportioned correctly and only once a day. She can't have more during a meal – only what we proportioned that meets her dietary requirements as outlined by her specialists. If she tells me she wants another snack because she is hungry again, I can't offer it because her daily caloric intake is limited for her health, safety, and body type. But already her world revolves around food. Everything is about food.

About three years ago, Ania developed this intense interest in food. She would constantly watch others eat, would walk into the kitchen if she heard a cabinet open, she would be asking for more, etc. Ania is not even finished eating dinner, and she is asking about what lunch is for tomorrow! Her endocrinologist prescribed Diazoxide to try and stabilize her blood sugars to hopefully help lessen this interest and intensity ... and to hopefully forestall hyperphasia. This twice daily liquid has been beneficial, but as each day progresses, I see it becoming less and less effective. I see her emotions more and more dysregulated with sudden inconsolable outbursts for minor things that push her anxiety. I see her eyes wander toward the foods others are eating. I see her peaking around the corner wall of the kitchen. I know it's coming – the hunger – sooner than later.

I'm unbelievably afraid. I'm nervous and anxious myself.

How will I keep her safe from food? What modifications to our home will be needed – locks on cabinets; walls built around the kitchen with a special entry door; what about the garbage cans, freezers, pantries??? Oh, my list of questions rises.

How will hyperphasia change this little lady? How will the monster increase her anxiety, affect her emotions, change her physical self? How do we help her cope? How do we keep her safe? Will she need a care facility? Who will keep an eye on her when I'm gone? How long is her life expectancy? How will she fight the monster?

The individuals living with Prader-Willi syndrome, and the families and caregivers of, NEED to have help. DCCR is a medication that is proving to help many fight their hunger. We need congressional support for people living with rare-genetic conditions to support medical research and potential pharmacological interventions that may help. Our family encourages you to support our efforts to help our families.

Sincerely,
Mrs. Katie Bey
Mother of Ania
195 Cavil Way
De Pere, WI 54115

[redacted]

I am Brianna Vander Zanden. I live in Appleton, WI (in the 8th Congressional District). I am a mom of 4 boys ages 6, 4, 2 and 5 months. I am an Advancer Practice Nurse Prescriber. I am a wife. I am struggling.

May 26, 2021 is when we welcomed my son Grant into this world. I had a normal pregnancy. I had a normal delivery. I had what I thought was going to be a memorable day filled with love, tears of happiness, elation if you will. What I had was nothing like that. What I experienced was trauma. One of the definitions of trauma is a deeply distressing or disturbing experience. This is not something you want to associate with your child's birth date. Now imagine (and please try to personally imagine) the OB provider handing you your baby for the first time. You are holding this true miracle of life for the very first time. And for the very first time you feel utter fear. You feel your baby and your intuition tells you something is not right with your child. You feel a limp, loose innocent baby in your arms. You feel your heart race and your stomach tighten because you know something is not right with your child. You are reassured nothing is wrong until a new provider steps in and pulls up a chair next to the bed and looks at you with a straight face. A look that would be concerning considering this was supposed to be a day of happiness welcoming a healthy baby boy into this world. 20 minutes after my son was born my husband and I were told we could not put the gender on the birth certificate because his testicles were undescended and we could not technically say if he was a boy or girl. That is something most parents don't expect to hear and mind you most parents do not want to hear shortly after delivery. Next, the nurses tell me they are concerned with his muscle tone. Valid point as I, a nurse practitioner, was also concerned. MULTIPLE providers offered reassurance that his muscle tone seemed fine, but when my baby would not awaken to nurse- they decided to run some labs. My baby did not cry. He did not flinch. He did not move. He had multiple IV sticks, in his tiny arms, in his scalp, even arterial punctures and he did not move. Have you even received an arterial puncture? It is not comfortable. It is painful. It hurts. Immediately my fears of something is not right with my child- came to fruition. I spent the next 48 hours try to feed my baby. Syringing milk and formula into his mouth. Hand expressing milk on to a spoon and gently guiding it into his mouth, but he just couldn't swallow. It felt like I was watching my baby slowly decline in front of my eyes. I knew we couldn't go home like this. I had two other boys to take care of and a household as well. I hadn't slept in 48 hours- how could I continue like this? I asked to be transferred to another unit to find out what was going on. The walk down the labor and delivery hall with our new born in his car seat to a final destination of HOME didn't happen. Instead, I pushed my baby in a cart in tears to the peds unit.

It was there he had a nasogastric tube placed. It was there he had an MRI because they were concerned he had a stroke. It was there he had a lumbar puncture because they were concerned with his floppiness and high pain tolerance. It was there that a physical therapist told me she was "very concerned" about my son. It was there that I watched my baby's vital signs start to decline- poor temperature regulation, lower oxygen saturation and increased lethargy. It was there that I started searching what could possibly be wrong with my child.

After a few more days and a restless night of hemodynamic instability he was transferred to NICU. At this point genetics was consulted and labs were in process to ensure there was no syndrome causing his symptoms. Even as a health care provider I wasn't quite sure what that meant. "what do you a mean a syndrome?" NICU is where he spent 2 weeks hooked up to IV antibiotics, oxygen and IV fluids. It was there I was told he had sepsis from a UTI and that he was going to get better. His muscle tone would get better. HE was going to get better. My husband and I hugged each other and cried in the halls that day. That day we thought we were going to be able to bring home our baby and live the life we had pictured. THAT day never came. Instead my son didn't get better after IV antibiotics. He didn't gain weight despite feedings through his nasogastric tube. His muscle tone didn't get better with time. Once again we were transferred, this time to Children's Hospital Milwaukee. Transferred via ambulance. I always thought I'd get pictures of my new baby strapped into his car seat preparing for his first car ride home. Instead I saw my tiny sweet baby being strapped in a

portable incubator with IV lines, oxygen tubes and telemetry straps to his chest for his first ride in an ambulance. This is an image and experience I don't wish upon any new mother or father.

My son spent another 2 weeks in the NICU in Milwaukee as we awaited further genetic testing. Something that I was told would take 10 days, but instead it took another 4-6 weeks. This is an eternity while you spend every waking hour in a hospital away from your family all while trying to heal from labor, pump breast milk every 3 hours around the clock and try to recover from the sleep deprivation you endured so far. I wanted to go home. I wanted to be with my family and hug my boys. I was mentally and emotionally drowning and in order to get Grant home he needed to show he could gain weight. He underwent his first surgery at only 21 days old. He had a gastrostomy tube placed for tube feedings. We left the NICU after 1 month. We left with a baby who had failure to thrive and NO ANSWERS as to why.

July 12, 2022. This was D day. Diagnosis day or Dooms day when you become the unexpected parent of a special needs child. This day I was told my son had Prader Willi Syndrome. Prader Willi Syndrome or PWS which is a genetic disorder causing behavior problems, intellectual disability, short stature, delayed puberty and constant hunger leading to life threating obesity. How could this be? My son can't gain weight and wants nothing to do with eating. How could he have Prader Willi Syndrome? Why does he have Prader Willi Syndrome? Why is this happening to us? Why him? All I could do was sob and keep shouting "WHY!" This day my worst of the worst nightmares came true. This day my life changed forever. A change that will impact not only myself, but my entire family as well.

I spent the next week deciding on whether or not we could even care for him. I asked myself many more questions. Not questions a normal new mom of 3 should be thinking. Instead of worrying about nap times and wake windows I was asking myself "how is this going to impact the life of my other two boys?" "Is bringing one life into this world now going to negatively impact the rest of the 4 lives that were here before him?" How am I going to continue to work in a busy general surgery practice, care for my family and now become a caregiver to a special needs child?" "How can we survive on only one household income if I can't work?" "How are we going to pay for all of this?" "How am I going to mentally recover and still be the mom, wife, nurse practitioner I was?".

I spent the next year figuring out finances, health insurance and how to build Grant's care team. I was unable to manage our lives and had to significantly reduce my hours at work. I lost our health insurance as my husband had just opened his own LLC the month Grant was born. Even with our life slowly crumbling I continued to search for the best PWS specialists, therapists and surgeons. When I still had insurance through my employer we were able to seek care outside of the state and establish a team. I will say I never comprehended how challenging and frustrating it could be to apply for state insurance, waivers, titles and enroll in specialty pharmacies. I never imagined as a Nurse Practitioner I would be on the "other side". I was used to PROVIDING patient care and not the other way around. Let me tell you this journey has NOT been easy to navigate. If I, a health care provider, struggled then who else out there is struggling more? This is another topic for a different day.

Today, Grant has the basis of his care team. He has a phenomenal endocrinologist, Dr. Jennifer Miller, who advocates for him and his future needs. He has an orthopedic surgeon whom he sees every two months for EDF casting under general anesthesia for treatment of scoliosis and to monitor his hip dysplasia. He has physical, occupational and speech therapists who see him 2 times a week to ensure he can hang with his busy brothers someday. Today, Grant is thriving more than I could have ever imagined.

Today I am asking you really hear our story. I'm asking you to try and understand what it is like to be a parent of a child with a rare disease and to help where you can. My goal for us and for Grant is to be able to live a fairly "normal life". I want to see my son frost Christmas cookies with his brothers, to enjoy a Thanksgiving dinner with our family or simply go to the grocery store without crying and signing that he's hungry. I want him to go to a homecoming dinner UNSUPERVISED with his friends. I want him to live a life where he doesn't feel the twisting pain of hunger every moment he's awake. My son is a warrior. He has fought so hard and continues to fight daily. But because of the ugly disease that PWS is, his fight will only get harder. With PWS the very thing a human being needs to survive (food) is the VERY thing that can kill him. (Pause) Just think about that for a moment.

Bradley P. | Wyoming

Age: 56
Year of Diagnosis: 2020
Type: Sporadic



We Can't Wait

How will I know the difference of a few months? What will my well being be at that time

Not interested in side effects. This disease has provided plenty of those.

Completely, but not as quick as Covid approval, that is a mess

How would you think? I am deteriorating and becoming dependent. With a smile ?

People are a lot worse than me; a cure needs to be found. **Hurry up, gather funding and develop a cure**

Andrea | Sonora, Mexico

Age: 35
Year of Diagnosis:
Type: Bulbar Onset

We Can't Wait

I prefer a longer life with better quality.

I would like a new therapy that offers the chance of a modest benefit even if it has significant side effects.

It is important that the FDA approve the drug before I take it.

Everything has changed, I am not independent, I feel trapped in a body.

My family has changed their lifestyle because of my illness, which makes me very sad.

ALS is a more common disease than is believed and that there is no cure.

We are waiting for a new hope to be able to live with a better quality.

Evgeny E. | Russia



Age: 42
Year of Diagnosis: 2019
Type: Bulbar Onset, Limb Onset, Sporadic

It is necessary that people have access to medicine.

I will try anything; it doesn't matter what the consequences are.

Everything around me has faded and my family is very tired.

No one is protected from this.

I would like to receive any effective medicine I can.

Mariano A. | Argentina



Age: 39
Year of Diagnosis: 2021
Type: Limb Onset

Time is life, every minute count, all trials is hope"

With ALS only Want time until the cure be available

I am filled with...

Depression.

Sadness and depression.

The important time to find a cure. Every minute is life.

All patients of ALS in the world needs gift us time for enjoy our family.

Gudjon | Reykjavik, Iceland

Age: 61
Year of Diagnosis: 2004
Type: Sporadic

Click Here to Play Video



Hope is all we live for; hope is so important.

I don't mind trying a drug that is not approved by the FDA yet. **I am waiting and dying. I'd much rather die trying.**



Safe is the only thing that matters. Please do whatever it takes to get us a drug in every way.

My family is affected, I am affected, and our social life and health are too as a family. **It is killing most of us very fast. 100% deadly.**

We choose life but do not have the time to live. But we do our best with help from our friends and family.

Please watch my video. Please help me have more days like those I experienced. Please don't make it my last.

Aqeel A. | Dubai

Age: 38
Year of Diagnosis: 2020
Type: Limb Onset

We Can't Wait

1% improvement is good enough to try new drugs, I have nothing to lose.

If drug shows benefits, then no need to wait for lengthy approval

Every month I lose a function, feels like will be bed bound in next 6 months

Life has gone upside down

Approve any drug that shows 5% improvement.
Approve NurOwn asap.

Alok R. | Assam, India

Age: 56
Year of Diagnosis: 2020
Type: Limb Onset

We Can't Wait

No, we don't need a therapy, all we need is a cure, a permanent cure. For the end of ALS.

Please do something FAST! PLEASE? THE CURE IS NEEDED VERY VERY URGENTLY.

The situation is very bad up here. I can literally see my family tearing apart and I can't Help. Please please find a cure for ALS. PLEASE, AND FAST!

I will do whatever it takes. Can you please make the process of finding the cure faster. **It's really very urgent!**

Esteban B. | Ciudad de Buenos Aires

Age: 51
Year of Diagnosis: 2021
Type: Bulbar Onset

We Can't Wait

I find it really important even if it implies a modest benefit

The fact that there isn't any cure makes you want to try new things, even thought that may bring no benefits at all.

For me it is essential to have the FDA approve something I would try. It makes me feel secure and positive.

At first I was devastated. I am a very active person and ALS meant the end of everything. But then I felt in peace. I am a catholic person and believe that God never asks you to carry a cross heavier than you can bare. I believe that from my public role I could help not only myself but others. And that's what I'll do. My family is my central support.

I was afraid to tell people around me that I was diagnosed with ALS because I felt they wouldn't understand that I wanted to keep on working, being active and not treated as a diminished man. I received exactly the opposite reaction. People around me went extra supportive and we immediately started working together, investigating all treatments available, and speaking to other diagnosed people. We've made a very good network and still pushing forward.

More awareness

To keep on developing this trials and medicines that gives ALS patients hope and strength to keep on going on.

Testimony of Gabi Conecker, MPH
Co-Founder and Executive Director, Decoding Developmental Epilepsies

Epilepsies Action Network

for the

Senate Special Committee on Aging

October 25, 2023

Senator Braun, I am sharing testimony today on behalf of the Epilepsies Action Network and the millions upon millions of people touched by epilepsy.

I am Co-Founder of Decoding Developmental Epilepsies, which includes both disease-specific and broad-based epilepsy organizations (the International SCN8A Alliance and DEE-P Connections), serve on the leadership team for the Epilepsies Action Network, and work as an advocate for systemic change to improve epilepsy patient outcomes. But most importantly, I am a mom of a child with a rare and catastrophic epilepsy.

First, I thank you for your past support of research, public health, and health care programs that help increase understanding and treatment of the epilepsies as well as support for people with the epilepsies. I would like to share information on the vast impact of this neurological disease and my son's journey in order to illuminate the challenges for the committee and the public. I hope this will encourage you to enhance your efforts to increase funding and programmatic support within the Department of Health and Human Services for the epilepsies.

To start, I'd like to share my and family's story, and then I will address the larger epilepsy challenges and opportunities for Congress to consider.

Elliott, my first, was born in late 2012. Within days, we noticed that he was making strange movements, which turned out to be a very severe type of seizure but were dismissed by the pediatrician for months before we received a referral. Our diagnostic odyssey, with a dozen doctors along the way, lasted a year and half. During that time, Elliott had hundreds of seizures and was hospitalized many times, never receiving care that was in line with his diagnosis. In 2014, Elliott was finally diagnosed as a result of genetic testing. At the time, little was known about this disorder as it was newly discovered. Nearly 10 years later, despite knowing that there are many more people living with SCN8A, it falls upon small, caregiver-led groups like the one I started with other SCN8A caregivers—the International SCN8A Alliance—to find, track and monitor those living with this disorder. In addition to caring for loved ones who require 24 hour a day care, caregivers are also left to lead organizations in order to provide support, education and resources to families all while asking their families, friends and neighbors to help finance—on bake sales and lemonade stands—the search for a cure.

are living with epilepsy, of which 470,000 are children or teenagers.[1] Of the more than 500 neurological conditions and disorders, epilepsy is among the top three. Neurological disorders are the leading cause of disability and the second leading cause of death worldwide.[2]

Just like cancer, there are hundreds and hundreds of epilepsies, which are disorders of the brain characterized by abnormal nerve cell signaling that leads to seizures (uncontrolled bursts of electrical activity) and often impact behavior, awareness, and muscle movements. With the rise of genetic testing, the epilepsies are increasingly comprised of an ever-growing number of rare genetic epilepsies. Beyond seizures, those with epilepsy can also experience cognitive, behavioral, and psychiatric mood disorders, as well as mobility, gastrointestinal, and respiratory issues.[3] Epilepsy can also be fatal. Sudden Unexpected Death in Epilepsy (SUDEP) can occur at any time in one's life, even among youth who are otherwise healthy. Every year, 1 in 1,000 people with epilepsy die from SUDEP and this number increases drastically to 1 in 150 for people whose seizures are not controlled by treatment.[4] Alarmingly, the mortality rate increased 47% from 2005 to 2014 overall and this increase was about twice as high among the non-Hispanic Black population.[5]

While some have thrived with epilepsy, such as singer Prince, Olympian Florence Griffith Joyner, singer Elton John, President Teddy Roosevelt, and NFL legend Alan Faneca, others have not, requiring 24/7 care or suddenly dying from SUDEP. Sadly, the cause of the disease is unknown in roughly 50% of cases and over 30% of adults and 20-25% of children do not respond to treatment — this is even higher for patients with rare, genetic epilepsies.[6] There are no biomarkers for the vast majority of the epilepsies, and there are only a few often isolated studies systematically learning from the experiences of patients living with epilepsy. Moreover, epilepsy and/or seizures impose an annual economic healthcare burden of at least $54 billion.[7]

Despite the vast number of Americans impacted by epilepsy there is so much that is still unknown and many that go untreated. Only .5% of NIH's $42 billion spent annually on medical

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[redacted]

Good morning,

Here are a few things I have experienced as a person living with a progressive rare disease in America:

-- Afraid to leave a terribly stressful job because my health care is tied to my workplace, and the very expensive injections I get twice a month were tied to my health care plan at that job. Not to mention MOST jobs in America have a 90-day waiting period to get health insurance.

-- Having to battle with insurance companies to get coverage for the drug I take for my rare disease, despite that drug being the ONLY option

-- Seeing my father and other older family members struggling with hearing loss, dental issues, bone pain, body parts stiffening and a range of other issues knowing that taking the medication that I am on now (FDA approved in 2018) is my only hope that I may not get THAT bad.

My rare disease is x-linked hypophosphatemia, or XLH, and I have hope that one day America will make things easier for us rare disease patients.

Emily Helm
Mississippi



We are the Ivan family - Matthew, Stephanie, and Leo. We live in Appleton, Wisconsin where Matthew and Stephanie both teach and Leo is enrolled in 4K.

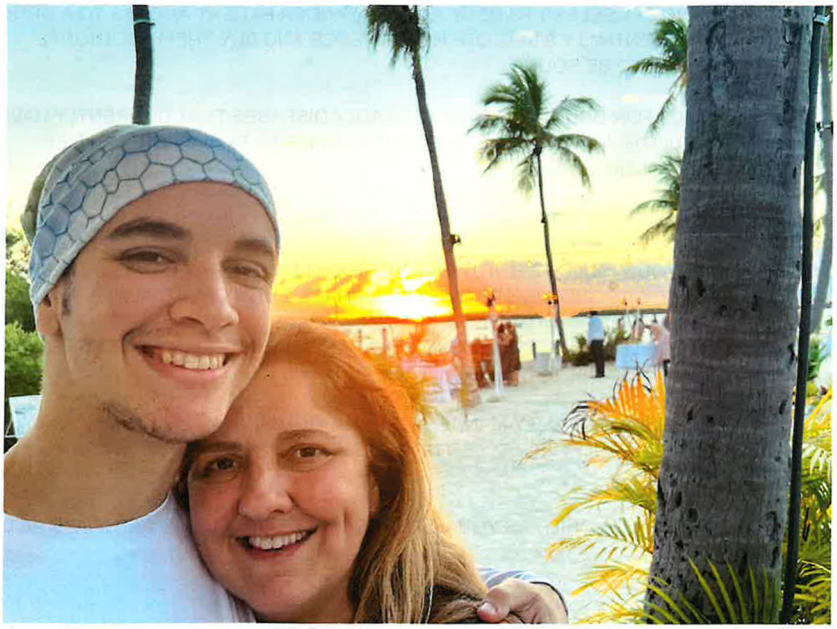
If we could meet you today you would see a little boy who is absolutely thriving. He is learning so much at school, making progress in speech and communication, and getting so strong. Leo has recently started making jokes, he loves anything vehicle related (especially button start engines) and is always up for a cuddle.

While Leo does have challenges related to PWS, our days are not currently overtaken by them. We can be in the community, celebrate holidays with our family, and attend events at our church and school. All that could change any day now. The next phase of PWS - hyperphagia - has an average onset between ages 4-8. Leo will turn 5 this coming February. Any day our sweet boy's attention could turn from cars, bus rides, and friends to his insatiable hunger - a primal need for food that will never leave him.

As of right now, there is absolutely nothing any of us can do about it. We give nightly growth hormone shots and stick to a strict sugar free diet, hoping and praying these will make a difference. And while they do make a difference in many ways, they have little effect on the most debilitating aspects of PWS.



As I'm sure you are well aware at this point, there are currently no approved treatments that will stop PWS from taking over a person's life. We ask that you please do everything in your power to change this! We know there are treatments that have proven to be safe and effective. Please help us ensure the FDA will give Leo and countless others the chance to live full, meaningful lives!



HI I'M DEXTER RABIN. I'M 22 YEARS OLD. IN APRIL 2022 I WAS AT UNIVERSITY OF FLORIDA HAVING THE TIME OF MY LIFE. I HAD JUST TURNED 21 AND I WAS IN THE BEST SHAPE OF MY LIFE.

THEN SUDDENLY WHILE PLAYING BASKETBALL WITH MY FRIENDS I HAD WHAT I THOUGHT WAS A STROKE. IT TURNED OUT TO BE A SEIZURE CAUSED BY A TUMOR IN MY BRAIN. I HAD BRAIN SURGERY TO REMOVE THE TUMOR AND SOON AFTER I LEARNED THAT IT WAS A CANCEROUS TUMOR. NOT A GBM, BUT A GRADE 3 ASTROCYTOMA.

BEING TOLD YOU HAVE BRAIN CANCER AT 21 YEARS OF AGE IS A SHOCK TO THE SYSTEM THAT FEW PEOPLE CAN IMAGINE. NOT JUST TO ME, BUT TO MY PARENTS, FAMILY AND FRIENDS.

I SUPPORT THE PROMISING PATHWAYS ACT BECAUSE I BELIEVE THAT PEOPLE WHO ARE DIAGNOSED WITH DISEASES LIKE BRAIN CANCER SHOULD BE ALLOWED TO QUICKLY HAVE ACCESS TO MEDICATIONS THAT SHOW BOTH BENEFIT AND SAFETY IN EARLY CLINICAL TRIALS.

[redacted]

Can you imagine being a 39 or 59 year old person who has been diagnosed with a life limiting diagnosis and not having options to access emerging treatments due to your age or some other factor? Can you imagine your child was diagnosed with a life limiting disease where your child is given a time frame of a year or less to live and then does not have access to emerging treatments. DIPG and DMG is a rare pediatric brain cancer which can affect young children up to rare diagnosis for adults. Doctors May throw up their hands and say they just do not have treatment options. Meanwhile there are organizations like The Cure Starts Now which is funding research for the hope of emerging treatment that may help a child live longer or an adult can live to see their daughter give birth to their first Grandchild. the Cure Starts Now is also helping patients trying to obtain emerging treatments such as Onc201 but only the lucky few can qualify for a trial while others desperate for any chance to live ends up buying from another country at costs near $10,000 every other month. Does that seem right? We can do better! We can make a pathway which would allow reasonable accommodation and access to emerging treatments when there are no other options. Please consider supporting this and giving people a chance to have more time with their loved ones by allowing access to these hard to obtain treatments.

Lisa Kirkbride

[redacted]

Hello,

My name is Kathryn McGhee and I am the mother of Hannah McGhee who is 22 years old and living with Prader-Willi syndrome. She was in a clinical trial that changed our lives, but did not get approved.

Below is my speech to FDA Advisory board.

I am asking for your approval of carbetocin as a treatment for PWS.

My daughter Hannah has been in the Care-PWS trial for 33 glorious months, and by glorious, I do mean glorious if I compare it to our life prior to carbetocin.

Hannah experienced zero side effects and she has never missed one single dose. It is far too important so she would never allow us to forget.

Hannah is 20, the youngest of our four children and she was diagnosed with PWS at 12 days. She has exhibited food-seeking behaviors since she was only 2.

The first time we caught Hannah eating from the kitchen trash, we were shocked. We learned to lock the trash in the pantry and throw food away in the disposal.

Her every thought no longer revolves around food leaving her more relaxed and less anxious. She has more self control and independence. She can transition better, adapt easier to change and is really able to enjoy SO MUCH MORE of life, family and friends.

The " old Hannah" would EAT each and every chip she ever found in her brothers room.

The "New Hannah" brings us the chips uneaten. She wants a PICTURE , holding the bag, with a huge smile on her face, so we can shame that brother for leaving food
out.

I used to worry about her future ALL the time.

But now?

Yes, I still worry, BUT I no longer have the constant, debilitating and terrifying fear that my daughter might "eat herself to death." Another big plus is we no longer have to supervise our daughter 24*7.

It's hard to describe, as a mother, what a relief and a blessing this has been.

Hannah's anxiety has gone down several levels and our whole family is in a much happier place. It has lessened the burden and made all our lives better. It is not perfect, but the improvements have been LIFE CHANGING.

It would be devastating to Hannah and our family if Carbetocin is not approved. The new and improved version of Hannah is infinitely better.

Before carbetocin, we struggled to keep Hannah at a healthy weig thinking about ways she could get more food. She would even for It ran her life, and ours.





Hannah has been on carbetocin for 32 months. She has stopp The photo taken on October 27th was shortly after beginning C weight loss in the photo taken September 11th wearing the san







SHEPHERD

Prepared by: David Hysong, Founder & Chairman of the Board, SHEPHERD Foundation

Prepared for the Senate Special Committee on Aging

October 25, 2023

Thank you for the opportunity to submit this testimony in support of increasing funding for rare cancer research, clarifying the definition of rare cancer, encouraging more training of clinicians in genetic testing, and advancing molecular diagnostics in cancer care. These issues are deeply personal for me. While undergoing Navy SEAL selection training at age 27, I collapsed, and upon subsequent examination, was diagnosed with a rare cancer called adenoid cystic carcinoma (ACC). I quickly discovered that the options I had for treatment were extremely limited. While I was able to get my tumor surgically removed, my disease is very likely to return. I will have no choices for treatment beyond more surgery, radiation, chemotherapy that is ineffective in treating ACC, and other treatments which have not been proven to work for this cancer.

I found that I was not alone in facing this dire situation – the lack of treatment options is the unfortunate reality for most rare cancer patients. Frustrated at these shortcomings in "modern" medicine, I started a rare-cancer focused biotech company called SHEPHERD Therapeutics and an associated nonprofit. We may be the only pan rare-cancer focused organization in the world. I am extremely proud of the work our team has accomplished. SHEPHERD is comprised of patients and caregivers, those who have lost loved ones to rare cancers, and those who are still fighting. Our mission centers on ensuring that cancer patients have the treatments and diagnostics they need to survive. To achieve this mission, funding for



200,000 new rare cancer patients faced their diagnosis without a modern treatment. Part of the challenge is the lack of development due to insufficient financial incentives to develop rare cancer therapies. This is in part is due to a dearth of clinical trials that include rare cancer patients. SHEPHERD's analysis of all cancer clinical trials between 2012 and 2016 showed that approximately 75 percent of all trials did not include even one rare cancer by name. Only 13 percent of all rare cancers were specifically named as a focus of a phase III clinical trial in those five years. More than four times as much money in that time frame was spent on non-rare cancer trials than on trials which included a rare cancer. Clinical trials are expensive to run, and pharmaceutical companies are unlikely to choose to run a clinical trial in a small indication with few patients when a drug will work for a large population, even if that population already has dozens of drugs available for use, and even if that drug is a "me too" therapy which provides little benefit over the current standard of care. Most companies decide that the cost of drug development cannot be justified by the potential market for a rare cancer like mine, ACC, which has around 1,200 new patients a year.

Fortunately, in the last few years, the FDA has encouraged new trial designs that allow trials to be run that target the molecular drivers of a cancer, allowing all patients whose tumors exhibit that genomic trait to potentially be included in the trial, regardless of their specific diagnosis. More good news: This approach can reach hundreds of thousands of additional patients right now via the utilization of molecular diagnostics. These tests can identify the presence of specific genomic alterations in a tumor that can be treated with an FDA-approved therapy *today*. Unfortunately, most patients are never even offered the option to receive these tests. Though broad spectrum molecular diagnostics cost less than a single round of chemotherapy, they are not reimbursed by CMS until the cancer has metastasized or reoccurred.



SHEPHERD

an FDA approved targeted therapy. Additionally, these changes must strive to greatly increase the utilization of molecular diagnostics at both diagnosis and reoccurrence to ensure that patients are receiving appropriate therapies. Synergistic efforts to close the rare cancer equity gap would also encompass the following: 1) CMS and private insurance coverage of molecular diagnostics for all cancer patients at the time of diagnosis and when the cancer reoccurs 2) Education on the use and interpretation of molecular diagnostics for oncology care providers, and 3) Establishment of more clinical trials that specifically include rare cancers, either as an indication or via mutational target inclusion criteria.

Behind the statistics there are over half a million Americans who at this moment do not know that during the course of this year they will be diagnosed with a cancer for which there is frequently no treatment beyond what their parents or even their grandparents would have been offered. Science sees no second-class citizens, only patients in need of help. We ask Congress to do the same and take the necessary steps to make cancer a thing of the past. Thank you.



To the members of the Senate Special Committee on Aging,

My daughter, Peyton, was born with a rare genetic condition, Prader-Willi Syndrome (PWS). PWS affects approximately 1 in 15,000 births. People with PWS are missing a piece of their 15th chromosome and this affects hormones, muscle strength, behavior, cognition and learning, temperature regulation, pain tolerance, sleep patterns, and appetite. One of the most challenging symptoms of PWS is hyperphagia, or an insatiable hunger. People with PWS feel hungry all the time regardless of how much they eat. They also struggle from a slow metabolism and must keep on a very strict diet in order to avoid life threatening weight gain. Without continuous supervision, they are constantly at risk of overeating to the point of stomach rupture.

When our daughter was diagnosed with PWS, we were devastated. We lacked hope for her and for her future. We have since discovered the Foundation for Prader-Willi Research (FPWR) and it is through the foundation, and the research that is being done, that we have found hope for our daughter and for her future. A great deal of research is being done, and clinical trials are showing great potential. My daughter was part of a clinical trial for Carbetocin. It was life-changing for her. The medication helped control her hunger, eased her anxiety, and made her behaviors manageable. Everytime I met with our trial site, I informed them of the incredible benefits we were seeing and asked for my commentary to be logged. I wanted to capture the incredible changes that we were seeing in my daughter and the improvement in her quality of life as well as ours. Unfortunately, after being on the medication for 3 years, it was not approved by the FDA and we lost access. This was a devastating loss for us. The company was unable to fund an additional study and had to close. Thankfully, another company bought the rights to Carbetocin and another study will be underway by the end of this year, but we have been without this medication for a year and a half. It is difficult to put into words what it feels like knowing that there is a medication that is life-changing for my child and yet we cannot have access to it. The sleepless nights, the tears, the questions from my daughter, it has been devastating.

There has been another medication, DCCR, that showed promising results and went to the FDA only to be denied approval. Fortunately, the FDA moved forward with a double blind withdrawal study as opposed to recommending an entirely new study. Still a devastating experience for those that lost access during that trial.

As we all know, clinical trials are very expensive, and in a rare population it is difficult to raise the funds necessary to fund these studies.

I worry for my daughter's future. I am her primary caregiver and I want better care for her, and for her future. There are medications that will change her life and we are unable to access them.

I appreciate your time and your efforts. I hope that with your help, changes can be made to ease the approval process and/or access to these life changing treatments through the Promising Pathway Act.

Best regards,
Renee Snyder



These three photos weren't even twelve hours apart. Your life changes so drastically when cancer strikes. We went from living a relatively normal life struggling with migraines to she has a mass to it's brain cancer so quickly. Nothing prepares you for it when it happens. Everyone tells me, "I couldn't even imagine" and it used to make me so angry hearing it because no you couldn't possibly. Even though I was guilty for saying the same thing before all this. Seeing everyone post their perfectly healthy kids playing and going about their lives on social media made me burst into tears, sometimes it still does. We were robbed of that. My daughter struggled to do basic life needs, I've been away from my husband and two other kids for months. Rinoa was diagnosed with posterior fossa syndrome after her brain surgery. Her surgeon was amazing and got 95% of her tumor removed but it's such a tricky spot that PFS is always a possibility. The tumor was so large it filled her entire fourth ventricle and indented her brain stem. She lost her ability to talk and move. The recovery of her surgery with the PFS diagnosis made every day a real struggle. I'm grateful to have had my husband and sister-in-law help me along the way. We had to help her do every little thing. She progressed fairly quickly her doctors told me. She got to the point where she could walk with assistance and say a few words. Mostly; yes, no, brownie and bathroom. She loved her brownies! Another side effect of brain surgery was when her mind was at rest, like at night trying to sleep, it would tell her she needed to go to the bathroom. So we had weeks of her asking to go to the bathroom literally every 30 seconds. Neither of us got much sleep. Eventually she had to be on three different sleep meds so that we could both sleep but even then it didn't last long. I tried to put the cancer diagnosis in the back of my head and focus on her being able to be her again. For a whole month I was a mess and constantly crying in secret. I never wanted to cry in front of Rinoa, trying to stay strong for her but it was a real struggle. I broke down in front of her finally on her 10th birthday which was also the day of her official diagnosis of #Medulloblastoma. The biopsy confirmation took weeks and Google was not my friend. The worst weeks of my life. My brain kept going to worse case scenarios, like #DIPG and other terminal brain cancers. When we finally learned it was Medulloblastoma, I worried it was subtype group 3 which has an awful prognosis. But when we were told it was subtype WNT which is only 10% of Medulloblastoma cases, I felt like I could take a breath again. WNT has the best prognosis but hers had also spread to her spine so I was still on edge. A few days ago we got the news that her spine showed no evidence of disease and it was that day that I felt like we could actually beat this. That my baby girl was going to make it. My mind has settled from the months of darkness and I'm ready to fight by her side until we kill this fucking cancer. Therapy has been amazing, she has almost become her old self only struggling with walking and balance now. She is talking non stop again. Her spirit is contagious and will make the whole room burst into smiles. The positivity coming from her is infectious, I can't help but smile every time she laughs. She is the strongest person I know and that's a fact. I'm tired of cancer looming over us and glad to be with her in this moment getting the best treatments from St. Jude's. She finished her treatment at St. Jude and is currently no evidence of disease but will receive scans every three months to see if she stays that way. We just take every day one by one and make memories. Childhood cancer is said to be rare yet thousands of families are going through this. Medical professionals think it's rare to the point they kept brushing off all the warning signs for years, misdiagnosing my daughter over and over again. We shouldn't have to fight and fight for proper health care and being told that is rare over and over again. My heart goes out to all the families and children going through this #morethan4



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October 25, 2023

Senate Special Committee on Aging
Senator Mike Braun, Ranking Member
RE: Unmet medical need faced by people with rare, progressive and serious diseases

Dear Honorable Senator Braun and the Senate Special Committee on Aging:

We are the PF Warriors patient and caregiver support organization representing thousands of Americans suffering from debilitating and life-threatening respiratory scarring, also known as pulmonary fibrosis (PF). Thank you for your invitation to share our story and the plight of our patients who have no disease halting or life-saving therapy.

Pulmonary Fibrosis is considered a rare disease that afflicts 200,000 people in the U.S. By its definition, the disease is scarring of the lungs. The scarring inhibits normal breathing and ultimately destroys the lungs, a process that is progressive, irreversible, and almost invariably deadly. The median survival ranges between 2-5 years. The average age of our patients is
65 for sporadic cases and 10 years younger for genetic ones.

Drugs, devices and innovative options are desperately needed and yet research dollars are sorely lacking given the increasing incidence and prevalence and the desperation and the excruciating nature of the disease that ultimately causes suffocation and death.

Our patients are from all walks of American life. And at least one of our patients was a member of Congress. Rep. Charlie Norwood from Augusta, GA introduced the first legislation for PF before he died. Our patients are veterans of our military who were exposed to Agent Orange, burn pits and particulate matter in various parts of the world. They are 9/11 first responders, coal miners, construction workers, pilots, and firefighters among other professions. The largest increases in cases appear to be in severe COVID and long COVID patients.

Most of our patients are forced to give up their careers, livelihoods, favorite activities, family time, past times and dreams. Breathing is difficult and it worsens with activity. Over the past 15 years, not only have more people been diagnosed than ever, the amount of benefits our patients receive from Medicare continues to decline including lack of access to oxygen and related equipment as well as pulmonary rehabilitation. So, not only can our patients not catch their breath, they can't catch a break, either.

Shelly Mathis is the interim director of the PF Warriors and the wife of PF patient, Scott Calhoun. Shelly discovered the PF Warriors organization when her husband was diagnosed and soon joined the team of the organization. Both volunteers, Scott also helps the organization that provides support services for patients and their caregivers.

Traveling is difficult for Shelly and Scott because Scott needs a significant amount of oxygen 24-hours-a-day. Like most respiratory patients in America, he struggles to get the oxygen supplies he needs to be able to remain active since the more he moves, the more oxygen his body needs and the more supplemental oxygen supply he requires. They noticed on a trip outside of the country that gaining access to oxygen supplies was significantly easier, more accessible and the tools for oxygen use were much improved.

Scott participated in a pulmonary rehabilitation program not long after being diagnosed. He was able to learn how to live and breathe better and more efficiently. Because of Medicare cuts to pulmonary rehab for PF and some other respiratory patients, though Scott has a doctor's order for more rehab, he will have a difficult time accessing it because of lack of reimbursement for providers along with vast increases in patients requiring oxygen support and suffering from respiratory issues since the pandemic driving increased demand.

For a lucky approximately 2,000 patients in the U.S. suffering from life-threatening respiratory disease and damage, including PF, lung transplantation is an option. For Scott, who is 74, the odds are stacked against him and even for younger PF patients. Recent changes to the lung transplant organ distribution system appear to seemingly discriminate against people over 65 who now may have decreased access to the only life-saving option since the new system went into effect in March of this year. Arbitrary estimations of how long a patient will live post-transplant are applied to individual patients – to their detriment.

One additional example of issues regarding Medicare support for respiratory patients is the not-so-recent letter issued by FDA warning about inconsistent pulse oximeter readings from non-FDA approved devices. And yet Medicare has taken no action to provide these higher-priced and hard-to-find approved devices to patients requiring oxygen, thus subjecting them to damage in other organ systems as well as further damage in the lungs due to hypoxemia.

PF patients are not just struggling to breathe, they are struggling against a broken system. The tools they need are difficult to get and harder to maintain due to unreliable oxygen equipment systems that are damaged because of deep cuts by Medicare. They are struggling because there are no therapies available that can improve their lungs or save them from this nightmare of a disease. The only two drugs that have ever been approved for the disease were approved almost a decade ago. Though modestly effective at stalling progression, most PF patients are not on them – due to lack of tolerability of side effects and the six-figure price tags. There have been more than 25 failed drug trials for PF here in the U.S. alone and still we have no life-improving therapies

PF Warriors appreciates the opportunity to share Shelly and Scott's stories that reflect a dimming reality for our patients.

Please Congress, help move legislation that can increase innovation in the respiratory space, especially in pulmonary fibrosis. Please ask Medicare to stop the cuts and improve the access for our patients to life sustaining oxygen and oxygen equipment. And please consider a funding option such as a common fund request to ARPA-H / NIH for a desperately needed focus on fibrosis and respiratory failure.

Sincerely,

Teresa Barnes, Chief Executive Warrior, PF Warriors (teresabarnes@pfwarrior.com); 303-521-4080
Dolly Kervitsky, RCP, CCRC, CNP, President, PF Warriors (dolly@pfwarrior.com)
Shelly Mathis, Interim Director, PF Warriors and Scott Calhoun (shelly@pfwarrior.com)

CC: PF Warriors Staff, Patients and Caregivers

MY JOURNEY

was born with an abnormal heart valve. We vere told a couple of years ago that I would ieed a replacement. Two weeks before my *irst surgery* February 12, 2009, I experienced hortness of breath, I knew something didn't eel right. I made an appointment with the loctor, a test was ordered, surgery date was cheduled, I contacted my family and friends, nd begin to pray and focus on what was :etting ready to take place in my life. A dockage occurred after the first surgery, then received a pacemaker, during my *second urgery*, February 16th, 2009. On June 23rd, .010), after a regular check-up, including a acemaker reading, at the doctor's office, my *hird surgery*, pacemaker revision (outpatient rocedure), took place the following day. *'ourth surgery* (outpatient procedure)took dace, December 21st, 2015: I received new atteries in my pace maker.

Before *my first surgery*, I contacted my family nembers, Pastor and Church Family, mployer, co-workers, friends, neighbors, etc. My strong support system provided prayers, hone calls, flowers, books, beautiful cards, ospital visits, home visits, meals, etc. It was mportant to have support for my husband and hildren. While we discussed the surgical rocedure with our children, it was necessary o continue providing a secure and stable nvironment. The door is always open nytime for the kids to come to us with any uestions or concerns. The valve replacement irgery was successful, then I developed the lockage. The doctors notified my husband that I would need a pacemaker to help my heart function. It was unplanned, but necessary. The second procedure took place four days after the first procedure. We prayed with the Chaplain before the heart valve procedure. I also received visits from the Chaplains, at my request, throughout the time I was hospitalized: a total of eleven days.

My Faith in God, support from my husband, family, Pastor and Church Family, medical staff, friends, neighbors, Radical Love Family, co-workers, employer, etc... continues to play a major role in my healing process. I know that God loves me and promised never to leave me alone. He helped me get through this time of testing. Jeremiah 30:17: "For I will restore health unto thee, and I will heal thee of thy wounds, saith the Lord, because they called thee an Outcast saying, 'This is Zion, who no man seeketh after.'"

Acceptance is also crucial during the recovery stage. Not living in denial, but accepting the daily challenges occurring inside my body, coping with breathing issues on a daily basis, living with a pacemaker, taking coumadin for the rest of my life, dealing with the discomfort in my chest, etc., empowered me to move forward. Where does my help come from? Believing and trusting God with my life. I know without a doubt that He is a healer. God is also loyal and faithful. Psalm 107: 1 "O Give Thanks unto the Lord for he is good: for his mercy endureth for ever." My relationship with my husband is even stronger. We were married in 1993 and promised to love each other unconditionally. He continues to provide emotional, physical, mental and spiritual support. While I was recovering he helped the kids with their homework, made daily trips to the grocery store, ironed the kid's clothes, worked hard every day and spent quality time with me. I thank God for my soul mate.

When I returned home from the hospital: February 23rd, 2009: my 10 year old son quietly walked in my bedroom and prayed by my side every night. It was very important for him to thank God for healing his mother. When my 7 year old daughter saw the scar on my chest, which was the incision from heart surgery, it made her very uncomfortable. She thought I was in pain. I spoke to the school counselor about the issue. My daughter touched the scar and saw that I wasn't in pain. I'm happy to say, my daughter is now comfortable with the scar. After my surgery, our children asked about the limitations, when I would be able to drive again, how did I feel overall etc. We continue to keep the lines of communication open in our home. It's very important for our children to express their feelings. I continue to pray for my husband and children. We are determined to face any obstacles "together" with God's guidance.

Through FAITH, FAMILY, and FRIENDS, I'm able to face each day and know within my heart that God continues to bless me and my family. Everyday is a GIFT from God.

Mrs. Kimberly A. Goodloe

kagoodloe@comcast.net
http://4wedobelieve.wordpress.com/
(health blog)



Our youngest daughter, Ayden Jane, suffers from Prader-Willi Syndrome (PWS). Honestly, suffers almost doesn't fit Ayden Jane as she counts her blessings, rather than her limitations. That's impressive for any teenager, but even more so for one who works harder at everything. I'd say, Ayden Jane is on a life mission to conquer PWS. As a part of this she sticks to a very strict diet. Incorporates exercise into every day. Works hard in every way, all day, every day. Zero vacation days are possible when you are fighting against your own rare disease. She manages scoliosis bracing, narcolepsy/cateplexy, impaired immune system, medical diet, anemia, global dyspraxia, language deficits, wacky temperature regulation, the list goes on.

Ayden Jane is now 16 years old. She has poured her efforts into life and is proud of her high academic achievement. She is smart, earns A's and B's in honors classes in high school. Excels in math and science and loves to learn. It takes her longer, but she puts in the added hours; and I mean hours. She runs on the cross country team because she wants to be a part. It takes her longer and she is one of the last finishers every race. Ask her though, and she will tell you about her improvements and how running keeps her healthy. Handwriting... a challenge. Fine motor anything? A challenge... Notice challenge is the word I chose. For Ayden Jane excuses are not an option. She gives her every ounce of energy, focus, attention, strength, every day to be able to somewhat keep up with typical peers.

Those are the incredible qualities of my daughter. I am so proud of her and we do anything and everything we can to support her drive. Sadly, however, the truth is with all she can do, the limitations of PWS will not allow her live independently. She has worked hard and wants to go to college, get a job, and give back to the community. Academically she can, however, she will not be able to maintain the strict diet and manage all the "bonus features" of PWS. She is unique for PWS teens in that she has a large part of control over what she eats. We are trying to teach her and allow her to learn while she is still within our home. What she learned last month, however, is that the sleeping monster of insatiable hunger - like an addict's drive for drugs - can be triggered by small forays from the strict dietary rules. She even scared herself as she realized she was spiraling out of control and couldn't stop grabbing any food within reach. She asked me if she would ever be safe if on her own. She is worried that she will not be able to grow into adulthood like her siblings. That she will always need our family to fill in the gaps and be her constant back up.

I call Ayden Jane a gap kid. She is not a typical kid. Her body does not work well enough to keep up with typical kids no matter how hard she tries. However, she also does not fit with special needs students. She does not fit into their programs or supports. Her dreams are gigantic. Her heart for others is just as big. Her life, however, is lonely because she doesn't really belong anywhere.

PWS is such a complicated genetic syndrome, but researchers have learned so much in AJ's lifetime. We took the approach when she was diagnosed to do all we could to support her to live to her full potential - whatever that was going to be. I stayed home and our family struggled financially. Our other 3 children have grown into amazing, compassionate adults who had to learn what is really important in life quite young. We decided we would live each day, growing AydenJane's brain, helping her to be as healthy as possible, giving her as many opportunities as we could. Encouraging her to dream big. Now I fear we have succeeded in raising a daughter who believes in herself. Believes the researchers who are unraveling the mysteries of PWS. Believes the help she needs to live the independent life she so desperately wants to will be there in time to set her free.

Pathways to Possibilities could provide my daughter and so many others like her with the opportunity to have the scientific research come to life by creating ways for these incredible warriors to be set free. It is such a long slow process to watch small communities with massive burdens attempt to navigate a system that was not designed to take into account the life-threatening and quality of life barriers that our children live with daily. Keeping them safe and alive just isn't enough. In fact, that's actually the bare minimum. Thank you for taking a moment to listen to a piece of my daughter's story. and hopefully grasp how close we know we are to easing her burdens.... we just need a little help.

[redacted]

Senator Braun & Congress Members-

My name is Sally Conroy & I have a great-niece with Prader-Willi Syndrome (PWS). This rare disease includes motor delays, language impairment, hypotonia, central sleep apnea, hyperphagia, severe anxiety and more.

It can be almost impossible for PWS families to navigate the medical system to meet the needs of their children. Often numerous phone calls & emails have to be sent to get a service or device approved (speech therapy, physical therapy, psychology support, endocrinologist, sleep doctor, access to a wheelchair, etc). It can take many hours to fill out applications, send paperwork & access life saving assistance.

Children with PWS have to have their food & fluid intake monitored at all times. They need help with sensory and obsessive-compulsive issues. One of the most challenging obsessions is skin picking which can be life threatening.

Most children with PWS require assistance in the bathroom and with daily grooming skills. And, many of them use of a CPAP machine.

In addition, their hyperphagia means that they have to be very closely monitored for ingestion of non-edible substances. They are at a high-risk for choking and/or aspirating.

It is difficult for these families to find competent respite providers. Parents often have to leave work and help with school issues. Some of these familes have been harrassed/bullied when parking in a disabled spot or requesting accommodations for their children.

Children with rare diseases require (and deserve) more support than they are getting. These familes are struggling!

Thank you for taking the time to learn about this issue.



Hello - I'd like to submit the following for the congressional record.

My name is Kristin White. I live in Washington, DC with my family. I am the mother of three sons that I love more than anything in this world, my second son was diagnosed at birth with Prader-Willi Syndrome (PWS). Like most people I hadn't heard of PWS before a doctor in the NICU told us that was his diagnosis. Today there is no cure or treatment for the primary symptoms of PWS.

Rafa is 7 years old now and is in first grade. He is good at math, he loves Power Rangers, and he is a great brother and friend. Rafa is magic, he lights up any room he is in.

But Rafa's diagnosis means that he is robbed of the carefree childhood he should be enjoying. He has spent thousands of hours in occupational, physical, and speech therapy, he receives an injection every night of medication, the anxiety and behavioral issues that accompany his diagnosis make school and social interactions harder for him, and worst of all we live in fear of the day he will experience the never-ending hunger that is the hallmark of PWS. This hunger could rob him of his future independence and make every day a battle for him and for his family. Nobody wants this for their child.

I know that research and science can provide therapies and drugs that will help Rafa have a better quality of life. This will also allow me, his dad, and his brothers to have a better quality of life. We are a family, and we are in this together.

I ask that Congress recognize the challenges faced by families living with rare disease, and the challenges faced by the clinicians that are trying to treat them. I ask that Congress increase pathways for rare disease research and drug development and ask the FDA to use all the flexibility allowed when considering drugs and therapies that could help people living with these diseases. We are not waiting for perfect, we are waiting for anything that will help our loved ones.

Kristin White

[redacted]

What DPIG did to my baby girl (4) is absolutely heart breaking. Something needs to change NOW

Her story:

Breelynn was born on October 31st, 2017 🎃 👻. From the moment she was born she decided to do things how she wanted. She loved her big brothers, Beau and Chase, and had no problem keeping up with them. Breelynn loved to dance, sing, swim and cook the list goes on and on. 💃 ♥ ✨

Breelynn was a healthy 4 year old with no prior health issues. Her mom noticed that her eye had begun to turn inward. After seeing an ophthalmologist they were then referred to Valley Children's Hospital for an urgent MRI. That is when they discovered the unfortunate news that Breelynn had Diffuse Intrinsic Pontine Glioma. A tumor on the brain stem and it was inoperable. Breelynn immediately began treatment and had a picc line put in, a shunt placement surgery, as well as 13 sessions of radiation..

Breelynn will always be remembered as a child who cherished life and had a zest for adventure that took her on many journeys. She was fearless and never shied away from trying new things, and was curious to explore and discover new wonders. Her strength and determination were an inspiration to all of us, and her fight against DIPG was truly remarkable. She never lost her spirit, her hope, or her courage, even when facing the most difficult challenges.

Breelynn's family misses her dearly and send all their love to Heaven everyday, knowing that she is now cancer-free dancing, singing and playing. 💃 ♥ ✨

A parent should never have to wittness the nightmare of DPIG and what it takes from their child. It is crucial that more awareness, funding and reseach continues

[redacted]

Hi! Sharing our Kai's story for your consideration. We are an open book and will do anything to help our child and children like him, future kids.

Keepfightingforkai.com
IG: keepfightingforkai
https://linktr.ee/Keepfightingforkai

Kai was diagnosed at 7 months old. He's endured many surgeries, chemotherapy, and radiation. He just relapsed for the second time and we are back at it with less options. His little body can only take so much.

There are a few trial options but they take months to get in. We don't have months. ATRT is too aggressive and won't "wait" for the red tape to clear.

We are desperate to help him continue to fight for as long as he can.

Please let us know how we can future support your efforts.

Melissa Atwood (mom) 714-732-3799
Chasen De Leon (dad) 480-758-9710

MELINA MICHELLE EDENFIELD

As a mental health counselor, daily I am discussing the discomfort with change. I talk about the need for growth. And how complacency creates its own set of issues, it keep us stuck. Unfortunately where our buerocracy stands today represents complacency and sadly I did not know that until it affected my life. As a mother of three beautiful girls I never thought I would be in a place where I had no options to save my youngest daughter's life. When my four year old was diagnosed with a terminal brain tumor I was told I had a chance at maybe six months. I had 32 days with my Melina before she was gone. A perfectly healthy child who was gone in 32 days. I vowed to my child that I would spend the rest of my life fighting for answers so that no other family had to live with the pain that we do daily. It was then that I became aware, through our foundations involvement with funding research, that there were options of possible hope. I was held helpless as a mother by complacency. I was stuck and couldn't fight in the way that my child deserved. So now I am strongly asking you to consider the Promising Pathways Act. I am asking you to help us fight for the children and families that deserve more. Every child deserves hope. Today I ask for change.

Michelle Edenfield

Mother of Melina

Heather G.

We Can't Wait

Age:
Year of Diagnosis:
Type:

I think this is important, especially for younger people diagnosed with ALS. **What would be wonderful is adding years of additional life or significantly slowing the progression of the disease rather than just modest benefits.** However, we must walk before we can run, and if modest benefits lead to breakthroughs that provide significant benefits, then let's do what we can. **Too may people's lives are being cut short and too many families are being robbed of time with loved ones because of the cruel, quick-moving disease.**

For most people diagnosed with ALS, it is unexpected and completely alters the course of their lives and the lives of their loved ones. Without advances in treatment that give people more time, that means more lives cut short. That means weddings and graduations not attended. The milestones of children and grandchildren missed. It means never hearing that person's voice again or giving them a hug. All this being said - when you are given a death sentence, which, to be clear, ALS is a death sentence, you will do whatever you can to have more moments with loved ones. Give people a choice and let them weigh the risks/benefits with their medical team and their loved ones about what makes sense for them.

People with ALS do NOT have the time to wait for the normal clinical trial process to proceed. Let them make the decision, along with their doctor and families, about what makes sense for them. Clinical trials, rightly so, have rigid parameters. But, because of the relentless progression of this disease many people are often ineligible for studies because they are too far along in their disease and/or access to trial sites is challenging. All trials that have passed Phase 1 for safety should be opened for compassionate use to ALS patients.

Both of my parents had ALS. No family history on either side, it was completely sporadic in both cases. They went from being healthy active people to dead in a matter of months.

How devastating the disease is on the people who have it and their families. And, how limited the treatment options are.

People with ALS do NOT have the time to wait for the normal clinical trial process to proceed. Let them make the decision, along with their doctor and families, about what makes sense for them. All trials that have passed Phase 1 for safety should have an option to be opened for compassionate use to ALS patients.

Greta L.

Age: 59
Year of Diagnosis: 0
Type: 0

We Can't Wait

Extremely important

100% worth it and necessary.

ALS patients have NO other hope, it is a death sentence.

Not at all important to risk everything – it will be worth it.

MC C.

Age:
Year of Diagnosis:
Type:

We Can't Wait

My comments to the FDA –

https://www.statnews.com/2021/04/30/als-groups-wont-be-played-again-fda-drug-sponsors/

ALS groups to the FDA and drug sponsors: 'We won't be played again'

By Mary Catherine Collet April 30, 2021 Reprints



Matt Scozzari holds his girlfriend Sabrina Parker's hand during a friendship ceremony in Jacksonville, N.C., in November 2010 to pledge their commitment to each other. Sabrina passed away days later from ALS, which also killed her mother and grandmother.
GERRY BROOME/AP

[redacted]

Dear Senate Aging Committee Members,

My name is Kate Peters and I have ALS. I am a 40-year-old mother of two boys, 3 and 5, and the wife of an amazing husband. I am also a veteran of both the Marine Corps and the Navy, and a combat veteran of Operation Iraqi Freedom. While the cause of ALS is unknown, we know veterans are two to ten times more likely to be diagnosed with ALS than civilians. A recent study revealed that among deployed post-9/11 veterans the prevalence of ALS is 19.7 per 100,000 returned veterans – this is more than 3.7 times the prevalence of ALS in the U.S. population over a similar time period. Sadly, almost no veterans with ALS are told of clinical trials and have very few treatments available. The treatments that are available have very limited effects, which is why we urgently need more drugs to be approved to combat this awful disease.

ALS is a 100% fatal disease but I am not without hope. The treatments that are currently in clinical trials have given me hope that I might be here for the future I thought had been taken away when I was given my diagnosis 3 years ago. Seeing the results of trial drugs has made me realize that I might have a chance to see that happy future my husband and I envisioned when we were married and started our family.

I was diagnosed with ALS a few weeks after my second son was born and my older son had just turned two. We were all, of course, devastated by the diagnosis and the way the future we had dreamed of had changed so drastically in an instant. There is a critically unmet need for therapies that can slow down the relentless progression of ALS and that was devastating to learn. There is currently nothing that can save us, but the regulatory flexibility the FDA has to approve drugs for 100% fatal diseases like ALS gives me hope that drugs that are currently showing promise in clinical trials will be approved quickly and give me a chance at a future with my family. A new pathway to approve drugs quickly would give so much more time and other quality of life for me to spend with my family.

Naturally, as a mother, I desperately want to be there for all of the happy milestones that come with beautiful, wonderful, ordinary life. I want to be there for band recitals, soccer games, birthdays, Christmas mornings, Easter egg hunts, graduations, first jobs, weddings, and grandchildren. More importantly though, I want to be there for the challenges and difficulties my boys will face. I want to be there for the skinned knees, the times they're picked last for a team, the breakups, the college rejection letters, the tough decisions, and all of the other disappointments in life. I am their mother and I want to be there to provide the comfort, love, hugs, and kisses they need when they are at their lowest. I want to lend an ear when they need someone to talk to, be a shoulder to cry on when they are upset, and give them advice when they need it. Most importantly, I want them to really know the unconditional love I have for them and to be their safe harbor.

I'm a mother, a mama, a mommy, a mom, and I want to be here to experience this amazing life; all of it. The good moments, the bad moments, the running hugs at school pickup moments and the "Ugh, Mom, drop me off a block away" moments. I want to be here to share knowing glances with my husband when our sons tell us they already know everything. I want to see my husband holding our first grandchild and remember how he looked when he held our first child so many years ago.
All of it. I want to be here for all of it. You can give me that chance. Rapid approval of trial drugs could give me the opportunity to slow my disease progression and possibly even give me back some functionality to live life to the fullest with my family.

608

[redacted]

Good Morning!

My name is Michelle Federico, and I was diagnosed with ALS just after my 51st birthday on November 29, 2021. After receiving this devastating news and trying to recover from the shock of being diagnosed with a fatal and terminal disease, I immediately set out to learn as much as I could about this disease and registered to be considered for any clinical trial where I could meet the qualification criteria to participate. It didn't take long at all to receive a call in March 2022 to participate in a Phase 3 clinical trial called COURAGE-ALS for the drug Reldesemtiv.

Reldesemtiv, a fast skeletal muscle troponin activator that slows the rate of calcium release from the regulatory troponin complex of fast skeletal muscle fibers and leads to an increase in skeletal muscle contractility. COURAGE-ALS enrolled 460 patients (out of a target of 555 total) and 200 patients completed 24 weeks of placebo-controlled treatment. For all patients enrolled, the double-blind period was followed by an additional 24 weeks of open-label treatment with 300mg Reldesemtiv.

I completed the 48-week trial and was allowed to continue taking the drug for an additional 3 months. Then on March 31, 2023, I was notified that the sponsor discontinued the COURAGE-ALS study due to futility, which means that the study could not meet its primary endpoint even if enrollment was continued and all patients completed the study. And, that I had to stop taking the drug immediately.

As disheartening as that was, it was even more disheartening to learn on September 30, 2023, that I was included in the "placebo" group during the first 24 weeks of the trial. It truly felt like I had been punched in the gut when I received this news because I couldn't help but wonder if I "had" been given the Reldesemtiv the whole trial period, would it have made a difference? And if I "had" been allowed to continue taking the drug, would it have slowed my progression anymore?

On November 29th of this year, it will be 2 years that I have been living with ALS. I am currently taking 3 FDA approved drugs intended to slow the rate of progression, that I like to call the Triple R drugs – Rilutek, Radicava, and Relyvrio. Last year I could walk with the assistance of a rollator, could drive, feed myself, dress myself, and take care of my dog. This year, I can no longer walk, talk, control my neck and body, or move my right arm and hand. I have a feeding tube where I receive all my nutrition and medication, receive 24/7 care round the clock, and can only be moved using a hoyer lift. In short, my life revolves around this dreaded disease, and I am completely reliant on my caregivers for everything. Which, if anyone who knows me will agree, is the exact opposite of the fiercely independent person that I have been since the age of 16 and goes against every fiber of my being.

In addition to this, having to live with the knowledge that -- there is no current cure and only one inevitable outcome - death -- is an excruciating weight to bear day in and day out while still trying to live as normal of a life as possible. Each day I pray for a cure and wish that there was something out there that could slow down or stop the disease progression.

It's this thought that leads me to the purpose of this hearing. If I had access to other clinical trial drugs for ALS, regardless of whether they are approved or not, I could potentially extend my life even more. If my ultimate fate is death, shouldn't I be allowed to try **any** ALS drug that shows promising results? If there is a chance for the drug to work, we (the ALS Community) should be allowed to have a choice.



I am writing to you today to express the urgency and importance of approving a drug for galactosemia, a rare metabolic disorder that affects my daughter, Lousha, and many others like her. As a concerned parent and a dedicated teacher, I have witnessed the impact of this condition on my child's life and the lives of families in similar situations.

To help you understand the gravity of this issue, I would like to share a personal story. As a teacher, I often conduct creative activities with my students to encourage self-expression. One assignment I give to my students is for them to create 6-word memoirs for me to get to know them a little better. Before giving this activity to my students, I decided to test the activity with my daughter, Lousha. After some brainstorming, she composed the poignant memoir, "Young girl yearning for a cure." This simple yet powerful expression encapsulates the daily struggles and aspirations of my daughter who lives with galactosemia.

Although my daughter participated in a clinical trial years ago, the memories of that experience still linger, symbolizing the hope that someday she might lead a more typical life, unhindered by the constraints of her condition. The approval of this drug is not just a matter of medical significance but also an avenue for granting individuals like my daughter the possibility of a more regular and fulfilling adulthood.

I implore you to take immediate action in supporting the approval process for this critical drug. Every passing day without this medication means further challenges and limitations for individuals suffering from galactosemia, hindering their ability to lead healthy and productive lives.

I trust in your commitment to the welfare of our community and sincerely hope that you will champion this cause in the legislature. Your support in ensuring the swift approval of this drug will make a world of difference to my daughter and all those affected by this debilitating condition.

Thank you for your time and consideration.

Sincerely,
Have a fabulous day,
Michelle

Enjoy the little things in life because one day you'll look back and realize they were the big things. —
Kurt Vonnegut Jr.

[redacted]

To The Senate Aging Committee,

My mom was diagnosed with ALS less than a year ago. She is a 72-year-old grandmother, who should be enjoying her golden years with her husband and grandchildren. Instead, she can no longer speak, she can no longer go to the bathroom independently, she can no longer swallow solid foods, she can no longer dress herself, she can no longer write her name, and she can no longer walk up or down stairs (to name a few). She has lost her indepence of doing the most basic and foundational tasks of daily living. She relies completely on my father, who is himself aging. My mom loved to cook, take walks on the beach, play with her grandchildren, and travel. She can no longer do the things she loves. She is a shell of the person she used to be. Not only has this had a physical impact on her life, but also an emotional impact. My mom no longer has light in her eyes. She is depressed and has lost all hope of living, as her body is rapidly deteriorating.

Not only has this horrendous disease robbed my mom of the things she loves and the way she used to live life, but it has also had a drastic negative impact on our family. My father is the prime caregiver for my mom. The majority of his time is spent caring for her, scheduling doctor appointments, and dealing with a flawed health insurance system. I have a family of my own, with two young children. I split my time between my own family and helping my mom and dad, as they try to cope with the struggles of this disease. The emotional burden of watching your loved one suffer and die a slow death, is enormously painful.

ALS is a 100% fatal disease. People who have ALS do not have time to wait for drugs through a slow moving regulatory process. ALS is a progressive neurodegenerative disease that quickly ravishes the body. The time needed to force a second AdComm caused almost a year to be lost and access delayed for Relyvrio. This had a negative impact on so many people living with ALS - their progression continued, capacity was lost and lives were lost. People with ALS do not have the luxury of time.

Please consider the Promising Pathway Act, we beg of you.

Best,
Karen Peters

--
Karen Peters, M.S., CCC-SLP, TSSLD
Speech-Language Pathologist

[redacted]

Thank you for the opportunity to share. I wonder what each of you would say when you are trying to put in writing what it feels like to slowly watch the love of your life lose his strength to the point where he can't button his pants or eat well and know that things are only going to get worse.

I'm going to lose my husband. Shane, Annie and Jennifer are going to lose their dad. Hunter, Ivy, Niah, Aubrey, Jude, Blaze, Teagan and Sonny are going to lose Grandpa. Will Sonny remember him? We can only pray. Friends will also lose the guy who could always be counted on to visit those in the nursing home or home bound. Gary and Mike will lose a great friend. Rod and Brad will lose their big brother. There is no cure.

My husband began having neurological symptoms about 3 years ago. We were told many times that we didn't need the specialists he was seeing at the ALS clinic. Then symptoms progressed and he began to show some atrophy. On June 6 in Room 36, our world changed with confirmation that he does indeed have ALS. We believe he is now beyond the 3 year time frame for clinical trials but are waiting for confirmation.

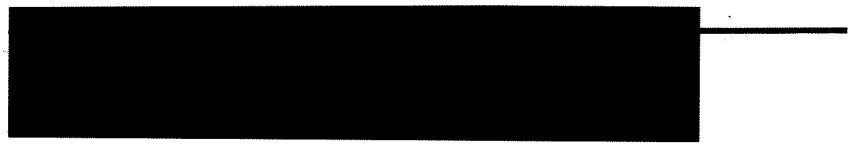
The realization of what lies ahead is slow and gut wrenching. Trying to put it in words is hard.

Two of the medications he is now taking to prolong his life by 6 months are around $40,000 a month before insurance. We have had to ask for help for the first time in our lives.

Please consider this when looking at the Promising Pathways Act.

I hope no one who reads this is ever touched by this hideous disease.

Sent from my iPad



To the Senate Aging Committee,

My name is Laura. I am a sister, daughter, and lover of animals and plants. I have a zest for life and adventure, and I especially enjoy being outdoors.

I lost my father to ALS disease in 2019. The family didn't know much about the disease, and we were told that it wasn't genetic.

My story starts as noticing something funny with my foot soon after my father's passing. A mild symptom which I dismissed as something strange, but it would have an easy fix. However, it soon progressed to drop foot. I was able to do most things, but the quest for an explanation continued: X-rays, MRI's, blood work and numerous other tests and theories were provided, but no clear diagnosis. The lingering thought of ALS started to creep up in the back of my mind, but I felt I should exhaust all possibilities before going down that road. All the while getting around progressively became more difficult, as well as everyday pleasures such as walking the dog, and getting around the nursery at work.

A friend encouraged me to get a second opinion. They ran tests and determined that ALS was a 60% possibility. I was devastated and my world was turned upside down. I was not ready for this diagnosis as a possibility so I pursued any and every other potential explanation for my symptoms. I received regular acupuncture, and I underwent neck surgery as there was a chance that the nerve damage could be affecting my lower limbs.

As time went on, and my symptoms were not improving, I decided to undergo genetic testing. The month-long wait was agonizing as my mind weighed all of the possible outcomes, and knowing what my future would look like.

When I received the news that I carried the C9 gene mutation, I could no longer avoid the realities of what I would be facing. I now confirmed that my father most

[redacted]

Elampratide is vital for the well being and growing health in the Barth Community. This is of testimony of importantance that this wonder medicine could do. The mere 75mcgs that was administered 6 days a week was a specal in the wonders it brung myself. I gained weight faster than ever before, not including the strength and close to 25 pounds.! Plus stamina growth. This medication took me from the bottom of the energy spectrum and ignited the smoldering stove we originally had burning. I could walk blocks without tripping over my inverted feet or gasping for air or energy. Elampretide was the key to opening the doors to normality for all mito patients. I had the will and want to go out and make friends and do activities that I thought wasn't possible. I sadly had to be removed from it do to medical complications but that doesn't shun my hope for the rest of my brothers. I myself can't change the minds of others but maybe all of us together can! So please help join us in the fight for our battle. I would love the opportunity to try this wonder drug again!

Thank y'all for your time.!!

[redacted]

First of all, I would like to thank you all for bringing this legislation back up in order to get it passed.
I can see from reading the descriptions that have been put forward and quotes from the members that you understand the desperation and urgency from people with ALS.
Having been diagnosed in 2017 at the age of 61, female, with no prior health issues whatsoever, I can attest to the fact that this condition can occur to anyone at any time with no warning whatsoever. Everyone dies. But not everyone has to live their lives in a continual decline of muscle function. You are asking fewer and fewer muscles to do the work of the muscles which have atrophied and that ratio declines daily. It's not weakness of the muscles that exist. It is simply a decline in the number of muscles performing the same function. This is a horrific way to die.
Promising Pathways Act will cut through the red tape for companies of all sizes to get their medical therapies into the bodies of those who may benefit. To expedite the approval process for those therapies shown be beneficial and reasonably safe would give real hope to the hopeless,
Thank you all,
Caroline Boggs
Sent from Proton Mail for iOS

[redacted]

Thank you Senators for taking the time to support the bi-partisan bill (Promising Pathways Act).

I am including a video that was recently made for awareness. It includes my son Alec and myself.
https://youtu.be/8plJXTUEQA?si=g06G8mvSMk3ybd5q

Our SWEET Hayley was diagnosed in 2011, 12 years ago today. Our journey advocating for Ultra Rare Diseases began that day too. We were devastated again a few months later when my son was diagnosed after we were all tested. We have been receiving a life saving drug for 10 years this December and have run into many roadblocks with the FDA. IT WORKS and we need you to help us keep the supply to all patients with NPC (my son is an adult now).

For individuals with life-threatening, serious diseases, timely access to treatment is an essential element in the fight for life. Drug approval pathways used by the FDA must be continually rethought and redesigned to promote efficient access to effective treatments for patients with progressive diseases that, if left untreated, will continue to diminish their functioning or lead to an early death. The Promising Pathway Act would grant patients with rare, progressive, and similar serious diseases earlier access to safe and promising therapies.

I hope & pray you will share your voice with Congress to help move this important bill and change the way FDA approaches rare disease treatments.

Help us support our community, Keep our HOPE & FAMILIES ALIVE

[redacted]

Dear Senators of the Senate Committee on Aging

I believe you all understand that ALS is a 100% fatal disease. But I think that generally a person who has not lived with the disease or lived with the person with the disease, cannot fully understand what it means to lose EACH LITTLE BIT of function you have, your body literally destroyed in bits and pieces, every day. Thank you in advance for reading to the end. It's vitally important to us.

My adult stepdaughter Kristin was diagnosed in Nov 2018, after reporting leg weakness to us in September of that year. She is a single mother, with twin boys who were 14 at that time. She has bulbar onset, very fast progressing. She had to use an AFO (ankle foot orthosis) on one leg in Dec; two legs in January; a cane in February and a walker by March. In April we took our last full family vacation to a dude ranch, using a motorized scooter, walker, and manual wheelchair. It was at that point I had to stop treating patients in my physical therapy practice, as caring for Kristin, managing her emergencies, her quickly changing physical needs, her finances, and the upkeep on her home was more than two full time jobs for my husband and me.

By May Kristin could no longer weight bear for transfers, with full paralysis of her legs and most of her upper extremities except hands. We bought a new house for her and the boys that was wheelchair accessible after some remodeling. Her boys had been literally carrying her on their backs up and down the stairs every day. And continued to help her on and off the toilet until she could no longer stand. They were now 15. Imagine your own high school sons living this life.

In June 2019 she went full time on a feeding tube. In July she had an emergency tracheostomy and was placed full time on a ventilator, 8 months after diagnosis. She also endured a bilateral pulmonary saddle embolism, blood clots down her whole leg and outside her kidney. And then pneumonia. She was hospitalized a total of 40 days over 4 months. She could still use her fingers and thumb to write on a magic eraser board and communicate with us in her own words fairly efficiently. The last finger and thumb power was lost at the beginning of October, during her last big hospital stay of that year, 9.5 months after her diagnosis. She had to learn to use an eye gaze device, and communicate slowly and awkwardly by moving her eyes across a computer screen, leaving her out of group discussions and trying the patience of her caregivers and friends, and her patience with us. She developed a pressure sore that progressed despite wound care, and we were told to put her on hospice, June of 2021. She beat it after one year, and was kicked off hospice after 2 years, despite an appeal to Medicare, that we won saying she could stay on. (This is a problem that Medicare needs to fix). She had to go to the ED shortly after losing hospice as her feeding tube was plugged and she had a UTI, all treatable at home had she still been on hospice.

She has had 2 more UTI's. She is now antibiotic resistant, and is back on hospice. Every change on and off triggers a complete change in her equipment, supply providers, and primary physician, an enormous undertaking and stressful for Kristin.

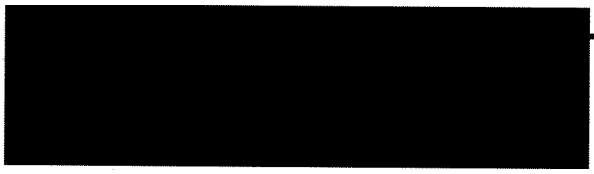
Her eye muscles have continued to deteriorate, as have the muscles of her eyelids. Once she could no longer use the eye gaze starting in Jan 2021, we resorted to slower eye movements and reciting an alphabet board to "talk" with her. Then it became side to side eye movements only, right for yes, and left for no. Then it became right movements only, so we had to ask questions in a way in which she could respond "yes" to. And that allowed her to share with us her wishes, her pains, her desire to change position, or change the TV channel. To say "yes" to questions such as "Are you

[redacted]

Access to therapies cannot come fast enough for those with ALS.
Furthermore, most people dealing with ALS along with their family/caregivers don't have the bandwidth to be advocating for themselves.

Google ALS
Watch the documentary Gleason

Or don't and just create access to therapies and resources for people with ALS.
They are living a nightmare.



I've lived a simple life. Married, raised 2 successful kids that now have families of their own.

Both retired, my husband and I planned on enjoying life and traveling a little.

I started having immune system problems. Tried to just work through them, tried to carry on with a normal life.

Visits with Dr. after Dr. and tests after tests.
Finally slammed with the diagnosis.

YOU HAVE ALS. I'm sorry.
Then I was sent home. Talk about feeling sick!

Average 2-5 years to live. NO CURE!
NO CURE! NO CURE!
NO CURE! NO CURE!
Get your affairs in order.
NO HOPE. Prepare to suffer as you die.

Your muscles will fail, your mind will be aware of everything happening. NO CURE!
You'll lose your ability to walk, lift your arms, use your hands. NO CURE! You'll lose your ability to swallow, choking on everything, choking on the phlegm your body produces, gasping for air.

Someone will need to be 100% available to feed you, bathe you, toilet you, NO CURE!
and move you.
Adjust your arm for you, adjust your fingers for you. NO CURE! Home health is $35.00 an hour.

Maybe with special equipment you can use a computer NO CURE! and your....
eye movement and be able to S L O W L Y express your need, whether you have a itch, a pain, CAN'T BREATHE or need your nose wiped.

The muscles that you use to breathe will eventually fail. NO CURE! You will try to gasp for air, but your lungs with no muscles will not expand.

ALS has been around for quite a long time. I never expected I would get this rare disease. I guess it's not that rare.
Estimated 1 out of 300 will get this disease in the coming years. NO CURE! The fight for ALS needs to be brought up to the forefront.
We need to have a hope not to die from this terrifying disease. It affects the whole family.

Please. I'm dying. I had hopes and plans. I want to interact with my loved ones. I don't want to suffer this death.

We need your help.

[redacted]

My husband was diagnosed earlier this year. He has lost the use of his legs and uses a motorized wheelchair. He is losing mobility in his arms. He has trouble clearing his lungs because the muscles used to cough have deteriorated. He is in constant pain.

In the last 3 months we have had to install a ramp so he can leave or enter the house, a stairlift so he can get to the upper level of our tri-level (,which by the way, we just got the main level renovated into our dream kitchen and living room). We did renovations in both bathrooms. Again, not knowing he would need different accommodations.

Before ALS, we spent lots of time traveling on our Harley-Davidson motorcycle, going salmon fishing and going on cruises. Now he can't ride, can no longer get into the boat to fish and cruising is not feasible. Now he spends his time sitting in a chair, watching TV and waiting to die.
This is not how people should have to spend their retirement.

We can't even afford the drugs that might help him.

SOMETHING needs to be done.

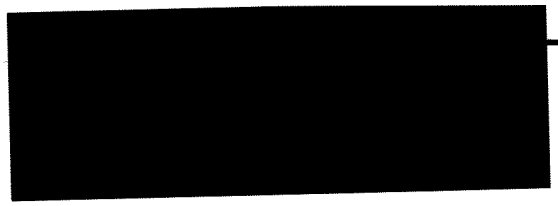
[redacted]

My story is probably pretty ordinary in many ways, and extraordinary in others, like many stories. I smoked for 30 years and quite smoking in 1992. Despite the fact that I quit, I was diagnosed with COPD in 2000, with about a third the lung function of others my age, height, weight, sex and ethnicity. My doctor advised weight loss; using diet and exercise, I was able to lose over 100 pounds over about 18 months, and as a result got off 02 completely (I'd used 02 24/7 for several years), put my c-pap in the closet and got a new wardrobe (clearly an important part!). I was able to stay off 02 for about 10myears, when I needed 02 for exercise and for flying. Now I use 02 for all exertion.

I was able to work until my planned retirement in 2009 and continued to work as a consultant in the field of disabilities, providing program assessments for organizations that provided vocational and residential supports to people with disabilities, primarily intellectual and mental health related disabilities. I was able to continue to do that virtually during COVID and finally retired in October, 2023. I moved to a senior living facility in 2010 where I live in independent living, but have access to memory care, assisted living, long term care and skilled nursing if needed. Because of the facility I live in, I have had very conservative care during COVID and access to all the COVID vaccines since they were first available. While I have had COVID once, it was long after the initial wave and was very mild, requiring no visits to a doctor and only a dose of Paxlovid.

The inexorable path of time has definitely taken its toll. I use a lot more 02 now that I used to and I am much slower than I was (and very annoyed by it!). It's harder and harder to continue to move throughout the facility to take part in programs and I find I'm spending more time in my apartment. I have been very involved in research for COPD through the COPD Foundation and PCORI and currently serve on the Executive Committees for three major studies: RELIANCE, EQuiP and FoCUseD. I am co-chair of the Patient Powered Research Network, a member of the Medical and Scientific Advisory Committee, and member of the Patient Engagement Committee all for the COPD Foundation. I am also a member of the Patient Advisory Committee for the American Lung Association. I can do all these things virtually, but it is harder and harder to travel to meet with other patients and professional colleagues as we work on equal access to appropriate 02 therapy for all (many people with high0flow 02 needs have no access to adequate liquid 02) similar to what's available in Europe. (A friend who went to Europe to speak at a conference was told that if would be illegal for the 02 provider to give him tanks in Italy: liquid 02 was mandated for everyone). We should be so lucky! Access to appropriate equipment and types of 02 for everyone who needs it is a huge issue requiring legislative change. Everyone has to breathe and everyone who needs 02 should get it in the most appropriate form possible. It's as close to a bi-partisan issue as you can find. My lungs don't have an R or a D tattooed on them!

There are so many things I want to do and can't. I feel I have lots of knowledge and I'm trying to share it with younger people who I hope will come along behind me and become advocates for people with COPD.



Hello. My name is Alec Koujaian and I am 25 years old. I am very happy to have the opportunity to share my story with you.

I have Niemann Pick Type C (NPC), but I don't let it slow me down. I graduated in 2021 with an Associate's degree in Fire Science. Unfortunately, I am not able to work in this field since I wear hearing aids but I do work at a local store for 25+ hours a week and have been for 5 years. I drive a car and have fun hanging with my friends. I am fortunate that I started treatment early enough before any of the typical symptoms of NPC would take hold such as seizures, dystonia, Ataxia, Narcolepsy, Swallowing issues, and cognitive decline. Unfortunately, my sister Hayley was not as fortunate and passed away on April 3rd 2020, from complications from NPC at the age of 20.

This is a cruel and devastating disease. It causes harm to your body every single second of every single minute of every single day. There are treatments to slow down the progression if started early but there is no cure. Therefore, our fight must go on in the in the memory of my sister Hayley and every single person who passed away from NPC. Our fight must go on in honor of those who are suffering every day from Niemann Pick Type C. Our fight must go on for all the kids yet to be born with NPC knowing very well what they and their families will endure. And our fight must go on to make sure that one day in the very near future, we will have a cure for NPC and to give hope to all. I am sure you will all be in this fight with us.

Thank You.

Alec Koujaian