

**FROM REGULATOR TO ROADBLOCK:
HOW FDA BUREAUCRACY
STIFLES INNOVATION**

HEARING
BEFORE THE
SPECIAL COMMITTEE ON AGING
UNITED STATES SENATE
ONE HUNDRED NINETEENTH CONGRESS

SECOND SESSION

WASHINGTON, DC

FEBRUARY 26, 2026

Serial No. 119–25

Printed for the use of the Special Committee on Aging



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

U.S. GOVERNMENT PUBLISHING OFFICE

63–835 PDF

WASHINGTON : 2026

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FROM REGULATOR TO ROADBLOCK: HOW FDA BUREAUCRACY STIFLES INNOVATION

Thursday, February 26, 2026

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

The Committee met, pursuant to notice, at 9:35 a.m., Room 216, Hart Senate Office Building, Hon. Rick Scott, Chairman of the Committee, presiding.

Present: Senator Scott, McCormick, Johnson, Moody, Gillibrand, Kim, and Alsobrooks.

OPENING STATEMENT OF SENATOR RICK SCOTT, CHAIRMAN

The CHAIRMAN. Good morning. The U.S. Special Committee on Aging will now come to order. Today we are here to ask a simple but important question, is the FDA doing everything Congress intended it to do to quickly get safe, effective treatments to patients with rare diseases who cannot afford to wait?

For more than 30 million Americans living with a rare disease, making sacrifices every day is just a part of life, but something they cannot afford to give up is time. Time means the ability to walk. Time means independence. Time means being able to speak, eat, or even recognize a loved one, and too often, time is exactly what patients lose while therapy sit in regulatory limbo. Growing up, I saw firsthand how a rare disease can affect a family. My family didn't have health insurance, and my brother had a rare hip disease. My mom had to drive 200 miles round trip just so he could get the care he needed. She made that sacrifice because care couldn't wait.

My brother couldn't afford to sacrifice time. Congress has been clear. On an overwhelmingly bipartisan basis we have given the FDA flexibility to move faster for patients with serious and life-threatening conditions.

In 2016, Congress passed the 21st Century Cures Act. In that bill and other bills that followed, Congress gave direction to the FDA, encouraged the use of real-world evidence, highlighting that rare disease drug development requires adaptability and urgency.

These laws are meant to help cut through bureaucratic delays and give patients access to the care and cures they so desperately need. Yet here we are, 10 years later, hearing from patients, physi-

cians, and drug developers that the system is not working as Congress intended.

I have heard from Commissioner Makary that he is working hard to fix longstanding problems at the FDA and I want to thank him for the work he is doing to try and make a strained system work better for patients. However, advocates here today will describe inconsistent review practices, shifting standards, and redundant, often late appearing data requests that in many cases may not be driven by safety concerns but by an overly cautious and rigid approach that puts bureaucratic processes ahead of patients.

As we will hear, the human cost of this regulatory slow walking is real. Many of the patients affected by these delays have no other treatment options. Patients from every State come and talk to our offices, and I am sure the same thing with the Ranking Member, sharing their irreversible declines in health that happen while they or someone they care about waits for a treatment that might never come.

It is heartbreaking to hear from families who are left watching their loved ones deteriorate, while promising therapies remain stuck in review. Meanwhile, small biotech companies struggle to survive years of uncertainty, even when their science is sound. Beyond individual patients, there are serious national security consequences that come with the FDA's inaction and delays.

Our adversaries have been accelerating their drug development and approval, attracting investment, talent, and clinical trials. FDA inaction here at home creates an economic and national competitive issue. Let me be clear, this hearing is not about weakening safety standards. Safety must always come first, but safety and speed are not mutually exclusive.

A system can protect patients while still acting with urgency, transparency, and common sense. Some of you may be asking why the Senate Aging Committee is tackling this issue when so many of those impacted by issues with rare disease treatments are young. Here is why. Part of caring for America's aging population is making sure that more Americans are given the opportunity to grow old.

It may sound cliché, but we are all aging. If something is standing in the way of a younger American making it to their senior years, it is absolutely the business of this Committee and something we need to try and fix. It is my hope that today's hearing will serve as a useful tool to help us understand what we can do to bring accountability, transparency, and efficiency to the process.

We are joined by an incredible panel of witnesses here today representing a wide range of perspectives, but all working toward a better future for people living with rare diseases. Now, we have a lot of members in the crowd that are here because rare disease drugs are very important to them, and I want to thank everybody for being here. Now, I would like to recognize Ranking Member Gillibrand for her opening statement.

**OPENING STATEMENT OF SENATOR
KIRSTEN E. GILLIBRAND, RANKING MEMBER**

Senator GILLIBRAND. Thank you, Chairman Scott. I really appreciate you calling today's hearing. Thank you to our witnesses and

the advocates who are here for Rare Disease Day on the Hill. It makes a big difference that you come together to make sure your loved ones are being heard and that the challenges and struggles that you go through as families and supporters are being understood by lawmakers.

Every one of us in this room today knows that when we have a friend, or a loved one, or a family member who has a rare disease, that the most important thing is finding a cure, getting the treatment, and making sure they survive. A disease is considered rare if it affects fewer than 200,000 people, but rare diseases actually aren't that rare. One in ten Americans is living with a rare disease.

As you know, many of these patients face substantial unmet medical needs. Because it can be really difficult and expensive for companies to develop these treatments and the FDA to evaluate them, Congress has provided the agency with significant regulatory flexibility to encourage both biotech innovation and rare disease therapies.

These include authorizing the accelerated approval pathway to speed up the drug review, establishing programs like the Rare Disease Endpoint Advancement Pilot to bolster novel endpoint development, and strengthening and expanding the use of patient experience data and real-world evidence in drug reviews.

These mechanisms are designed to help improve access to novel treatments for our patients, and they are supposed to provide drug sponsors with a predictable and consistent approach to addressing regulatory science challenges that are unique in rare disease therapy development and review, like designing complex clinical trials, developing appropriate endpoints, and using real world evidence, but it is not working how it should be. FDA's approach, transparency, and flexibility varies widely between its offices, divisions, and centers. I have seen a pattern of hesitation to use authorized flexibilities, limited communication with drug sponsors, failure to incorporate patient experience in real world evidence reviews, and FDA shifting its regulatory position on trial design at the last minute, rejecting drug applications, and requiring new clinical trials the sponsor may be unable to perform. This is heartbreaking for patients, and it is why we can't afford delays and disruptions in treatment.

Rare diseases can progress rapidly, cause irreversible harm, and in some cases premature death. This is also frustrating for drug sponsors who face increased costs and delayed timelines that impact the viability of their clinical trials, particularly in the United States. Uncertainty shapes behavior across the biotech ecosystem.

Without consistency and predictability, drug sponsors will continue to struggle with seeking FDA approval and will take their clinical trials elsewhere, like to China. This is bad for business, and it is bad for patients. If we want the U.S. to remain the global leader in biotech and we want American patients to have access to these novel treatments, things need to change.

Congress must hold the FDA accountable. We must make sure FDA fixes its inconsistent and unpredictable application of regulatory flexibility. It is essential for supporting innovation, while upholding the highest standard for safety and efficacy, in the approval of these rare disease drugs.

FDA appears to be moving in the right direction. With the rare disease evidence principles, the rare disease innovation hub, proposing new pathways for approval and trying to hire more reviewers, but it doesn't matter what agency leadership puts in a press release. It is about execution and implementation across all levels of that agency. Consistency from top to bottom.

Congress will ensure that happens by conducting oversight, encouraging application of authorized flexibilities, and providing adequate resources to restore agency capacity. I look forward to hearing from our witnesses and working with this committee to hold the FDA accountable because rare disease patients cannot wait.

The CHAIRMAN. Thank you, Ranking Member. I would like to welcome our witnesses, experts who are here to talk about how serious this issue is and the steps we can take to ensure patients with rare diseases are not left behind by regulatory delay. First, I want to recognize Annie Kennedy, Chief Mission Officer at the EveryLife Foundation for Rare Diseases.

Ms. Kennedy is a nationally recognized leader in rare disease policy and patient advocacy and works directly with patients, caregivers, and families navigating the drug development and approval process.

EveryLife represents the voices of rare disease communities across the country, and has long advocated for patients centered policies, regulatory flexibility, and timely access to life-saving therapies. Thank you for being here, and please begin your testimony.

**STATEMENT OF ANNIE KENNEDY, CHIEF MISSION
OFFICER, EVERYLIFE FOUNDATION FOR
RARE DISEASES, WASHINGTON, D.C.**

Ms. KENNEDY. Thank you, Chairman Scott, Ranking Member Gillibrand, and distinguished members of the Committee for convening this critical hearing. I am Annie Kennedy, Chief Mission Officer for the EveryLife Foundation for Rare Diseases. I am honored to be here alongside the hundreds of advocates who have joined us for Rare Disease Week on Capitol Hill.

Collectively, we are representing the more than 30 million Americans living with rare diseases. Today, there are more than 10,000 known rare diseases, about 70 percent of which start in childhood. For small patient communities facing progressive diseases, time is a commodity.

Traditional large placebo-controlled trials are often neither feasible nor ethical when considering the challenges and urgency of rare diseases. Beginning with the passage of the Orphan Drug Act in 1983, your leadership has provided tools that have rocketed the U.S. into the most competitive developer of rare disease products. Each landmark law since has reshaped our landscape.

In fact, tomorrow marks an anniversary of another watershed moment for our community here on Capitol Hill. The MD Care Act hearing convened in this exact same hearing room, presided over by Senator Arlen Specter, included a 13-year-old named Benjamin Cumbo. Twenty-five years ago, I watched with great pride as Ben asked Congress for actions that could help cure him and his friends

so that he could achieve his dreams of growing up, having a girlfriend, and serving his country.

Congress did respond. In that time, Congress has built a framework that incentivizes rare product development, authorizes regulatory flexibility, creates new pathways to approval, and embeds patient experience into review. While fewer than five percent of rare diseases currently have an FDA approved treatment, nearly 1,400 orphan-designated therapies are now changing the lives of patients and families.

Recently, this momentum has shifted. We are here today because our community has experienced worrisome trends with devastating consequences. While we are heartened by recent announcements of therapy development initiatives, such as the Rare Disease Evidence Principles Framework and the Plausible Mechanism Pathway and are eager to work with the agency on their implementation, our rare disease community has experienced a series of product application actions that seem misaligned with these recent public pledges to expand the use of regulatory flexibility.

Since the start of 2025, we have seen at least 23 complete response letters declining to approve rare disease therapies, many under accelerated approval, that suggest a hesitation to apply regulatory flexibility through surrogate endpoints, natural history studies, and external controls.

At that same time, advisory committee meetings for drugs and biologics declined by 65 percent compared to 2024, reducing opportunities for external expertise and patient insights to inform complex rare disease product decisions. We asked families who would be personally affected by recent regulatory decisions to reflect on their impact. These stories will be shared for the record. Story after story spoke to chilling consequences of recent regulatory delays and clinical trial hurdles.

As one mom shared about her son, Stone. My son is now receiving this experimental treatment, and he is thriving. For the first time since his diagnosis, his doctors have told us, with this treatment, a near normal lifespan is within reach for a disease that once came with a teenage expiration date that is nothing short of extraordinary. We are now living in fear, not because science failed, not because companies stopped fighting rare diseases, but because of regulatory inconsistency.

We are here today because congressional action is needed to ensure that this generation of patients will benefit from our existing rare disease treatment pipelines. We ask that Congress engage FDA to clarify its approach to accelerated approval for rare diseases, its consistent application of regulatory flexibility, and to urge the resumption of advisory committee meetings so that external expertise informs complex reviews.

We also urge Congress to resource the Rare Disease Innovation Hub to strengthen cross center coordination and to establish the Rare Disease and Condition Advisory Committee and a science focused drug development initiative. In closing, 25 years ago, I stood in this room filled with rare families.

Today, advances in science have put life-altering treatments within reach for many, but those advances were not in time for those who were in this with me 25 years ago. While Ben achieved

many of his dreams, he died two days before receiving his master's degree. We now have the opportunity to ensure that this generation of rare disease patients will benefit from today's therapy development pipelines.

Each time a promising therapy faces delays or demise, investment wanes, future scientific promise is unfulfilled, and lives are lost. Time is the most precious commodity for our rare disease community.

As Stone's mom implored while writing from his hospital bedside, we are closer than ever to rewriting the future of these diseases. Please don't let my generation become the next group of mothers who stand at gravesides instead of graduations. Thank you.

The CHAIRMAN. Thank you. Thank you, Ms. Kennedy. Now, I would like to introduce Dr. Jeremy Schmahmann, Professor of Neurology at Harvard Medical School, Founding Director of the Ataxia Center at Massachusetts General Hospital, and Principal Investigator for the Laboratory for Neuroanatomy. I said that correct, right?

He is a leading neurologist who treats patients with progressive and neurodegenerative diseases where time and access to treatment are critical. He has seen firsthand the consequences of delayed access to care and the irreversible loss patients can experience while waiting for regulatory decisions.

His testimony will round today's discussion and the real-world clinical impact these regulatory delays have on patients and families. Thank you for being here. Please begin your testimony.

**STATEMENT OF JEREMY SCHMAHMANN, MD, DIRECTOR,
MASSACHUSETTS GENERAL HOSPITAL ATAXIA
CENTER, BOSTON, MASSACHUSETTS**

Dr. SCHMAHMANN. Chairman Scott, Ranking Member Gillibrand, members of the Committee, thank you for convening this hearing, and for the opportunity to testify, and for your remarkable opening statements.

My name is Jeremy Schmahmann. I am the Martha and Robert Fogelman Chair in Ataxia, and Cerebellar Neurology at Massachusetts General Hospital, and Professor of Neurology at Harvard Medical School. I started the first Ataxia Center in the country, and I have cared for patients with spinocerebellar ataxias for 45 years.

I am the site principal investigator for Biohaven's study of trotiluzole in ataxia and my comments today reflect my personal and professional opinion, not necessarily that of my employer.

Senators, please help us fix the FDA. It has rejected trotiluzole, a drug that is safe—the first treatment to improve quality of life and slow progression in spinocerebellar ataxia. My patient Steve, for example, developed spinocerebellar ataxia type 3, also known as Machado-Joseph disease, in his late 30's.

Like his mother before him, he will become increasingly disabled, will need to use a wheelchair, become bedridden, and die young, but since starting trotiluzole a year ago, he has not changed. Mary, in her late 40's, has type two. After six and a half years on trotiluzole, she has not change.

These inherited neurodegenerative diseases worsen inexorably and in this business, staying the same is success. Like other rare diseases, ataxia is difficult to study, deteriorates slowly, and manifests differently even within families. There are 15,000 ataxic patients in America. Some affect hundreds of people, some just a few.

Now, Congress, as you have told us, recognized these challenges and passed legislation mandating that FDA use regulatory flexibility and real-world evidence in rare diseases like ataxia. The drug riluzole, used to treat ALS for 50 years, was reported to improve ataxia.

Based on this, and the plausible mechanism of action in spinocerebellar ataxia, Biohaven developed troriluzole, which metabolizes into riluzole, but is taken once a day with better brain penetration and fewer side effects. Early in the drug's development, an ataxic patient who stopped treatment after a year of open label therapy insisted they go back on troriluzole because they told us their condition worsened after stopping the drug.

Biohaven, to their credit, provided troriluzole to these patients and ran a one-year, double-blind placebo-controlled study. Patients with spinocerebellar ataxia type three improved compared to placebo. They were falling less, and they had fewer injuries. Biohaven requested approval of troriluzole for spinocerebellar ataxia type three based on these results.

The FDA refused to review the new drug application. Biohaven obtained FDA feedback and used a revised protocol to follow patients on drug for another three years, comparing them with patients in two natural history studies. In this real-world evidence study, troriluzole showed significant improvement across nine pre-specified FDA endpoints, slowing disease by 50 to 70 percent.

This is a dramatic result that was supported by patient and physician feedback. We were all shocked when FDA denied approval of this safe drug that makes people better. I wrote six letters to FDA leadership between 2023 and 2025, co-signed by 17 ataxia colleagues, asking FDA to review the application again and work with Biohaven to make the drug available, if necessary performing post-marketing studies. I never heard back.

Now, 300 patients, stable on troriluzole, will have to come off drug, and they are distraught. I met three times with FDA's Center for Drug Evaluation and Research. On each occasion, they did not heed the patients or the experts or considered the science. One panel member said to me, why should I listen to you?

The FDA's proposed path forward is another placebo-controlled trial that will take five to eight years, or a randomized withdrawal of the drug from patients benefiting from it. If this happens, patients on placebo will die. I believe this to be unethical, lacking charity, mercy, or kindness.

Senators, please, save our patients' lives. Use your authority to require that FDA consider real-world evidence and applies the regulatory flexibility you have legislated, and in so doing restore transparency, integrity, and competence to the agency. Thank you.

The CHAIRMAN. Now, I would like to recognize Ranking Member Gillibrand to introduce our next witnesses.

Senator GILLIBRAND. Thank you, Mr. Chairman. I want to introduce our next witness, Bradley Campbell. Mr. Campbell is the

President and CEO of Amicus Therapeutics, a biotechnology company focused on discovering and developing new medicines for people living with rare diseases.

During his tenure at Amicus, he led the global commercialization of Galafold, a medication used to treat Fabry disease in adults, which was approved by the U.S. Food and Drug Administration on an accelerated basis. Mr. Campbell brings over 20 years of experience in the rare and orphan disease fields. You may begin your testimony.

**STATEMENT OF BRADLEY CAMPBELL, PRESIDENT AND CEO,
AMICUS THERAPEUTICS, PRINCETON, NEW JERSEY**

Mr. CAMPBELL. Thank you very much, Chairman Scott, Ranking Member Gillibrand, the rest of the Senators on the Committee. It is my privilege to be here today to speak to you about our experience in developing drugs for people living with rare diseases. I am also honored to be alongside my fellow panelists.

I feel far less qualified than they to speak today, but I hope I can share some perspectives on the challenges and opportunities we have to help fix the system. I have had the privilege to work at Amicus for the last 20 years and have dedicated most of my professional career to developing new treatments for people living with rare diseases.

I thought I could begin with a patient story that I think captures the spirit of the testimony here today and the conversation we are having. At a recent patient meeting, we were discussing patient experience data and how we might make endpoints for clinical trials more meaningful for patients.

During a break, a young woman with Pompe disease took me aside and said, what would be most meaningful for her is if she could breathe on her own for just one minute. That would make the difference between her life and her death. This is not an approvable endpoint in Pompe disease, of course, but she depends upon a mechanical ventilator to breathe.

If that ventilator fails, if the battery dies, if an aid fails to clear a mucus plug, just that 60 seconds of her own breath could make the difference between her life and death. I think that comment is a very powerful reminder of why patients and caregivers must help us design better clinical studies with real endpoints that make a difference for them.

We can't ask patients to wait for years before approved treatments come when the difference between life and death can be that single breath. I think the rare disease innovation ecosystem in the United States has made enormous progress over the last 20 years, but it must now again adapt in speed, agility, and flexibility to keep the pace of innovation.

One of our own development experiences at Amicus I think sheds light on how regulatory flexibility and working together with sponsors and regulators can make a real difference in drug development. When we were developing our medicine Galafold for Fabry disease, we learned in early studies that in some patients the drug worked and some patients it didn't.

Through careful data analysis and close collaboration with the FDA and regulators around the world, we developed an assay that

could identify which of the thousands of genetic variants that cause Fabry disease might best respond to the therapy, and just as importantly, which ones may not.

The FDA ultimately incorporated that assay into our label and approved the first ever oral precision medicine for people living with Fabry disease. What does that mean? That means when sponsors and regulators work together, the result was an oral treatment option that has saved thousands of patients' years of biweekly infusions.

We know rare diseases are biologically complex. We know they are difficult to study. As we sit here today, 95 percent of the more than 10,000 known rare diseases lack an FDA-approved treatment. I think that is a statistic many of us are familiar with, but if you fast forward that pace of development, it will take us 150 years to only treat half of the remaining rare diseases.

Small and mid-sized biotechnology companies like Amicus, Biohaven, and others are the engine of rare disease innovation, but they can only succeed if the regulatory system adapts along with unmet medical need. I think there are three practical areas that we can work together to improve that very system.

First, we must start clinical trials faster. We know in other countries, those trials start in weeks, not months. We can reduce administrative requirements, leverage single IRBs, use AI and other digital tools to get into the clinic faster. We also must find better ways to measure efficacy. We can use biomarkers, innovative endpoints, accelerated approvals.

These are things the FDA has at its disposal right now, but we must use them more and we can make manufacturing inspections and rules work better. The single biggest delay oftentimes is inspections for getting patients access to medicines.

The FDA has tools like remote interactive inspections and relying on global regulators to reduce that inefficiency and let me close with just one final story. At a patient meeting last year, a man with Fabry disease told us when he was diagnosed in his 30's, he stopped saving for retirement because he thought there was no reason to think he could live that long. Fast forward 15 years, Fabry disease is now a treatable disease.

Advancement in treatments have changed that trajectory and for the first time he is thinking about a future he thought he would never have. I look forward to working together with the members of this Committee, and indeed with the regulators, the broad community here focused on rare diseases to find ways to ensure that we have a flexible, adaptable, agile regulatory system that can keep pace with modern innovation.

Thanks so much for the opportunity to testify and I look forward to taking your questions.

Senator GILLIBRAND. Thank you, Mr. Campbell. I want to move to introduce our next witness, Dr. Cara O'Neill. Dr. O'Neill is the Co-Founder and Chief Science Officer at the Cure Sanfilippo—the Cure Sanfilippo Foundation, dedicated to accelerating scientific development on disease and empowering families with the resources they need to navigate their journey.

Dr. O'Neill founded the foundation after receiving her daughter, Eliza, Sanfilippo's diagnosis in 2013. At the foundation, Dr. O'Neill

leads patient focused research efforts and awareness, working to bridge the gap between scientists, clinicians, industry, and family.

She was awarded the International 2020 Patient Advocacy Leader Award by World Symposium for exceptional contributions. You may begin your testimony.

**STATEMENT OF CARA O'NEILL, MD, FAAP, CHIEF
SCIENCE OFFICER, CO-FOUNDER, CURE SANFILIPPO
FOUNDATION, COLUMBIA, SOUTH CAROLINA**

Dr. O'Neill. Thank you, Chairman Scott, Ranking Member Gillibrand, and members of the Committee. On behalf of 15 million children with rare diseases in this country, I thank you truly for your concern.

I am Cara O'Neill, Chief Science Officer at Cure Sanfilippo Foundation, a Pediatrician, and mom to Eliza who has an ultra-rare genetic disease called Sanfilippo Syndrome, or MPS3, one of many forms of childhood dementia leading to progressive, irreversible brain damage. I would like to first acknowledge the critical public service of FDA and its staff who shoulder complex and heavy workloads every day.

We know the pressures are significant because we feel it too. Of late, we have seen many press releases highlighting new FDA policies and programs, which encourage us to look out into the future with hope, but today, the Committee has called us here with the recognition that current regulatory barriers are significantly impacting patients right now, and never more starkly than for degenerative conditions where time is the most crucial factor and where every regulatory flexibility must be leveraged to meet this uniquely urgent need.

We can see this illustrated in a story of three girls with the same deadly disease, but very different lives. Isabelle, or Izzy, was the first child with Sanfilippo that my husband and I met after our own daughter Eliza's diagnosis. Izzy was just 11, and the disease had already taken a tremendous toll. She could no longer walk independently, taking only a few steps if her mom held most of her weight.

Izzy had lost the ability to speak years before and could no longer eat or drink without choking, so relied on a feeding tube. She had seizures and increasingly severe abnormal movements that twisted her arms and legs into painful positions.

During one visit, Izzy's mom shared that she had come to accept this disease would take her daughter's life, but what she said next has always stuck with me. She said, in truth, I fear her suffering more than I fear death. At that time, my Eliza was close to four and in an extremely hyperactive stage of the disease, but she sang and talked with us. She played dress up and clapped around the house in my high heels. She rode her tricycle everywhere. She looked so healthy, but what was going on inside her body and brain was a much different picture.

Meeting Izzy put us face to face with Eliza's future, the concrete and cruel reality of what this disease would do. A medicine didn't come in time for Izzy. She suffered greatly and passed away just a few weeks before her 15th birthday. For decades, we have known the cause of this disease. We can precisely measure the levels of

toxic biomarker to determine whether a treatment is working and now we have the science to treat it.

Thanks to NIH funding and support from nonprofit foundations, including our own, a promising gene therapy was developed and propelled toward clinical trial at nationwide Children's Hospital in Ohio. While we anxiously were awaiting news the trial will begin, back at home we watched Eliza's sentences becoming shorter, her words less frequent. She became agitated and hardly slept.

The disease was taking hold. Two years later, in May 2016, the clinical trial finally began and Eliza, then six and a half, was so very lucky to be the first child to receive that gene therapy. It was her chance at a life different from Izzy's—a chance to grow up. Now at 16, it is clear that therapy changed her life. She surpassed average life expectancy, runs on the beach, plays in the water, uses picture cards to tell us how she is feeling and what show she wants to watch on TV. She can feed herself and goes to school every day.

These are simple but incredibly meaningful abilities that have a huge impact on her daily life, and children treated with higher doses earlier in life have even more remarkable outcomes. Like Caroline, who is now 10. She can read, play on a softball team, and learn to ski on her recent family vacation.

Despite these breakthroughs and nearly 10 years after the trial began, families outside the trial are still waiting for access. Why? Because last summer the drug was denied approval, not because of safety or how the children were benefiting, but for questions about manufacturing.

While this is an important issue, FDA could have used its flexibility to continue reviewing the application while addressing questions in parallel. You see, early on, trial data confirmed the drug's mechanism was more than just plausible, it was biologically effective, showing significant reduction of toxic biomarker within just six months after treatment in all the children.

Granting accelerated approval based on this biomarker would have brought treatment access to children years earlier, preventing further brain damage and changing the lives of so many children, like Sadie, who is here today—who is still waiting. This same drug application was recently resubmitted, but FDA issued another denial asking for yet more paperwork before agreeing to review it again.

Congress has given FDA the tools of flexibility it needs to accelerate approvals for these devastating diseases, but sadly flexibility and speed are not actually what most rare disease patients are witnessing.

Transformative therapies are at FDA's doorstep and so, with great respect, families are pleading for FDA to unlock the door and move with urgency so that our children can have a chance at the life they deserve. Thank you.

The CHAIRMAN. Thank you for your testimony. Thank you, Mr. Campbell, for your testimony. Now we will go to questions. Senator Johnson.

Senator JOHNSON. Thank you, Mr. Chairman. Again, I have to commend you for another excellent hearing here. At the start of the hearing, I received a text from Laura McLinn, who reminds me that 10 years to this day, as Chairman of Homeland Security I held

a hearing titled, Connecting Patients to New and Potential Life Saving Treatments. Her son, Jordan, who suffered from Duchenne Muscular Dystrophy testified at hearing—was certainly present there.

Two years later, that resulted in Right to Try, which was not easy to pass. I had to hold up the FDA user fee bill, had to water down Right to Try quite a bit to make sure that Big Pharma wouldn't sabotage it. They did sabotage it over in the House, but because of President Trump's leadership, he forced the House to pass the Senate version. Its main benefit is its name. It is very limited in its application, unfortunately.

People have the right to try. Laura has also begged me, begged me in a text to mention Ataluren and Deramiciocel, two investigatory drugs that are also being held up by the FDA for Duchenne Muscular Dystrophy. I think we probably are going to need another piece of legislation, probably Right to Try 2.0—something that is going to be far more effective than the current Right to Try, but I will tell you, reading this testimony this morning, you can maybe tell just by my passion, it enraged me.

It enraged me that these families, these patients are being denied effective treatments because of the regulatory roadblocks. Quick story and again, I want to ask questions, but a quick story. After I met the Duchenne Muscular Dystrophy community, they went up before a panel of FDA—this was probably in 2016, 2017, or 2018—begging. There are about 60 Duchenne Muscular patients' families begging the FDA, please approve this investigatory drug for our children.

Again, time is muscle, time is brain and that panel, I don't know who sat on it, listened to those 60 families begging them and said no, just like they said no—and I can't even pronounce these diseases and drugs. They say no time and time and time again. That has to change. Congress is directing the FDA, be more flexible—say yes.

You know, these patients understand the risks. They ought to have the right to try. Dr. Schmahmann—am I pronouncing that right?

Dr. SCHMAHMANN. Yes, sir.

Senator JOHNSON. I don't want you throwing anybody under the bus because I don't want this to impact future approvals but describe your meetings with CDER. To me, it is shocking to have one of those members of that panel say, why should we listen to you? Well, because you are a doctor at Harvard.

You are treating patients. You are having success. You are giving them a new lease on life, and you have got bureaucrats inside these agencies saying, why the hell should we listen to you? I want you going into greater detail—describe what those meetings are like.

Dr. SCHMAHMANN. Thank you, Senator. We have heard a few words a few times. Heartbreaking as the experience of patients and families going through this and the compassion that is required.

I saw none of that in the three meetings with the FDA. The members of the panel were like talking to a brick wall. There was no engagement, no dialog. In fact, they said as much, this is not

a dialog, this is not a collaboration. They do not seem to see the suffering of the patients, and they didn't hear the science.

They were rigid and inflexible and unyielding. The FDA worked with the company initially, but then they changed their mind later, and so, as the studies unfolded, everything came to a grinding halt. This drug in particular is safe. It metabolizes into a drug that has been there for 30 years in the market and is safe. Patients say it works. The doctors say it works. The study shows it works.

The double-blind first study showed it worked. The real-world evidence shows it works. Patients behind me, every one of them, talking to them yesterday, say it works. This drug works.

To paraphrase the Senator, what is their problem? My experience of the people on that panel, three times, as a private citizen coming for the first time to the FDA, was deeply distressing.

Senator JOHNSON. I have already texted Dr. Tracy Beth Hoeg and told her I have read your testimony. I will be sending her your testimony. I hope she listens to this. If I could just take a couple more minutes, Dr. O'Neill, you are obviously personally impacted by this.

Can you describe any meetings you have had similar to what we just heard? Again, the American people need to understand what these regulators are doing and not doing. Dr. O'Neill.

Dr. O'Neill. Thank you. You know, I will say that my interactions with regulators have been kind, so maybe a bit of a different perspective is they have listened. They have been interested to hear what we had to say. To hear the patient perspective. I think where we are challenged is that we don't see that translated into regulatory action.

Some of the decisions that are coming out are not benefiting patients right now. Listening is great, but two-way conversation and collaboration is actually what is needed, and greater transparency in how patient experience data and patient input is actually being integrated into these decisions.

Senator JOHNSON. My guess is that panel for Duchenne Muscular Dystrophy back in 2017 or whatever probably listened very nicely to the families, but they still said no. That is an unacceptable answer.

Again, you have my commitment. I am going to delve into this. We are going to right these wrongs. Thank you. Mr. Chairman, this is again an excellent hearing. We have got to followup on this. This is just completely unacceptable. Thank you

The CHAIRMAN. Thank you, Senator Johnson. Senator Alsobrooks.

Senator ALSOBROOKS. Thank you so much, Chair Scott. Also Ranking Member Gillibrand. I am so grateful to be here today joined by so many patient advocates, caregivers, family members.

I have heard from many Marylanders living with rare diseases and from their families, including dozens who have visited my office this week to share their priorities and their concerns. As I underscored with the NIH Director a few weeks ago, patients suffering from devastating diseases do not have time to wait for need-less delays to critical cures. For Marylanders with rare diseases, delayed access is not just an inconvenience, it is a matter of life or death.

For many with rare conditions, clinical trials are their last and best hope. These patients also depend on a regulatory process that is science driven and capable of turning research into real treatment. Instead of strengthening those foundations, this Administration is constantly disrupting clinical trials, slowing innovation, and undermining the pipeline to cures.

Scientific integrity should always guide decision-making, and we must protect the firewall between the Food and Drug Administration and political influence. President Trump and Secretary Kennedy continue to decimate critical parts of that system. The instability they have caused ripples across families, physicians, researchers, and innovators, and patients pay the price.

Ms. Kennedy, I would like to ask, over the past two weeks, we saw a striking example of political interference at the FDA involving a seasonal mRNA flu vaccine from Moderna. The agency first declined even to review the application, then reversed course just one week later after revised regulatory approach.

The abrupt change raised serious concerns about transparency, predictability, and political influence in what should be a scientific process. An episode many have described as regulatory whiplash. What does that kind of volatility signal about how the FDA is functioning right now, and why does that matter for rare disease reviews that depend on regulatory consistency?

Ms. KENNEDY. First of all, thank you so much, Senator, for being here and for all of you being here today, and for this important issue. I think first it is important to say that I am not an expert in vaccines, and I am here really to focus on rare disease, but I appreciate the question really asking about the trends that we are seeing and us being here really trying to follow the trends and understand what that means for rare disease.

I also agree with Dr. O'Neill that we have seen real intention from career staff and staff scientists at FDA around their engagement, but what we are concerned about is, to your question, what seems to be reversals in decisions, where there had been previous agreement, previous work with sponsors that was directing sponsors to move in one direction, and then regulatory decisions seemed to be yielding different decisions at this point.

As I stated in my testimony, we have seen recently 23 complete response letters issued in rare diseases that are delaying access to the patient community and having devastating consequences to our community. Many of those actually are decisions that are reversals in regulatory agreements that have been made previously.

Additionally, we are very concerned that previously, if there were to be a complex decision that needed to be worked through between a sponsor and the agency, an advisory committee would have been convened, and we have seen 65 fewer advisory committees convened in 2025 than 2024.

In fact, none since July. We are very concerned that the regulatory tools that are at the disposal of the agency to really work through some of these really complex decisions aren't being utilized.

Senator ALSOBROOKS. Thank you. Just very quickly, if I can also go to Ms. O'Neill. Finding new cures doesn't happen overnight, and it rarely happens in a single year.

Breakthrough therapies are built over decades of careful scientific work and discoveries, and NIH funded laboratories form the foundation for treatments that later move into clinical trials through regulatory review and ultimately into patient care.

When NIH research capacity is disrupted, as we have seen, and weakened, how does that set back the search for new cures long before therapies ever reach the FDA?

Dr. O'Neill. Thank you for your question. The NIH is a critical source of funding for innovation in this country and scientific innovation. It is interesting that when there were disruptions and uncertainty in the funding, we received a flood of requests about funding from our small non-profit foundation. I think non-profit foundations across the country were seeing that and, you know, we are not equipped to take up all of the pre-clinical and transformative science that NIH can do. The role of the NIH in supporting innovation is huge.

Senator ALSOBROOKS. Thank you.

The CHAIRMAN. Thank you, Senator. Senator McCormick.

Senator MCCORMICK. Thank you, Mr. Chairman and thanks to you and the Ranking Member for convening this and thank you all so much for being here today to help bring some of these critical issues to Americans and Pennsylvanians to light. Ms. Kennedy, more than 30 million Americans live with rare diseases, yet fewer than five percent have an approved treatment.

As you mentioned, since early 2025, the FDA has issued at least 23 complete response letters for rare disease therapies, while advisory committees use has declined dramatically. When late-stage rare disease applications raise concerns, what alternatives to issuing a complete response letter should the FDA use, including advisory committees or structured post-approval commitments, to resolve issues without restarting the entire process?

Ms. KENNEDY. Thank you. We appreciate that question. FDA has at its disposal, thanks to Congress, many types of engagements between sponsors and the agency. Many of those have been made possible thanks to the user fees.

We are concerned that many of those meetings and meeting types aren't occurring, and that the CRLs are being utilized as a way to perhaps maybe even clear the docket or create delays. There could be a lot of reasons why that might be happening, but there are meeting types that have been implemented that could enable engagement to answer questions that sponsors, and the agency might have.

We saw actually the agency deploy this during the pandemic, the COVID pandemic, where we saw real rapid, real time resolution to a crisis in our country and the agency was able to interact with sponsors. Get questions answered in real time and then we saw that CBER tried to operationalize that in other places and spaces.

We would really, as a rare disease community, like to see that operationalized within rare disease because we believe that our rare disease community has the urgency and unmet need that matches that of a pandemic, of a crisis.

We have individuals in this room who have very limited life expectancies. If we don't address what is happening in rare dis-

eases with that same sense of urgency, they would not be here with us if we were to convene this hearing another year from now.

Senator MCCORMICK. Thank you. Thank you for highlighting that urgency, and I think we feel it, and you are helping us to feel it. Thank you for that. Mr. Campbell, just on the issue of accelerating the process.

I was taken by the fact in preparing for this that some countries are moving much faster on rare disease therapies. The European Union's FAST-EU program caps multinational clinical trial authorization at 70 days. Australia allows many trials to begin almost immediately after an ethics approval.

What is going on here? What will happen if the United States fails to keep pace? What policy changes should we consider in the Congress, given what appears to be a much more streamlined approach in other places?

Mr. CAMPBELL. Thank you, Senator. I completely agree. I think, you know, the United States has been the beacon of biotechnology innovation for so many decades, and it is part of why we have more therapies approved today for rare diseases than we did, you now, decades ago.

I would acknowledge legislation like the Orphan Drug Act that led to that. As we said in our testimony and many of the panelists here today, we have now stopped keeping pace with innovation and I think one exact point, which I raised in my testimony as well, is speed to clinical trials. For me, on the one hand it is time for patients, and taking weeks, 70 days, would be a remarkable number.

I think Congress could work with the FDA to pass legislation to encourage, again, centralized IRBs, leveraging digital technology and artificial intelligence to help us do that. Reducing regulatory requirements. For sure, those things could speed us into the clinic. The other piece, I think, which is sitting behind this is our national competitiveness and in some ways our national security.

When we think about Australia, we think of Europe, collaborative nations, etcetera—there are other nations out there that perhaps we see in a different way, and from my perspective, whether you think of that as a security threat or whether you think of that as a threat to getting drugs to patients, in either case, I think Congress can take a leadership role in helping the FDA to speed through that process.

Senator MCCORMICK. Thank you all for being here.

The CHAIRMAN. Thank you, Senator McCormick. Senator Kim.

Senator KIM. Thank you, Chairman. Thank you to all of you coming out here. A couple words I just heard that I think really just hit the nail on the head. I would love your reactions to it. When we are talking about all the different problems that we are facing with the FDA, the bureaucracy or the workforce issues, I think the word that really hits it home is urgency.

I heard you use that. You know, I heard use that Ms. Kennedy. I feel like that is really what we are talking about here. Is like we need a government that is moving at the speed of urgency that the parents are trying to save their kids, right. Like, that we are struggling to understand what the actual purpose here is and the speed with which we need to move. Look, I got two boys. I got an eight-

year-old and a ten-year-old. I would do anything for them, you know.

I just like, how do we translate that into the urgency of a government trying to be responsive? I think that is where some of the disconnect hits on so many levels. You know, Mr. Campbell, you talked about it. You used the word national security. I used to work in national security. I was in Afghanistan and Iraq and elsewhere.

I saw this government move with urgency when they felt like lives were on the line, but like, why is it that we can't necessarily translate that to another circumstance where there are millions of lives on the lines and people just don't have the time to wait for this? I think that that is really a purpose. How do we talk about this as a national security priority?

The same reason we are trying to save lives abroad is the same reasons we are trying to save the lives here at home. Does that make sense to you, Ms. Kennedy? Am I kind of grasping the crux here of what we are trying to push forward?

Ms. KENNEDY. Yes, Senator, you absolutely are. Congress has recognized this urgency in statute and has enabled the use of regulatory flexibilities, and that is what is reflected in the accelerated approval pathway and the use of surrogate outcome measures and biomarkers in clinical trial design in rare disease.

What we are concerned about is that in many of these complete response letters, what we are seeing reflected is FDA, especially in one of the medical product centers, CBER, seems to be the trend that we are detecting backing away from a comfort level or use of the surrogate biomarkers.

What we have seen in rare disease is surrogates work. Surrogate biomarkers do save lives. We have more than 250 products that have been approved through the accelerated approval pathway, but fewer than 20 percent of those are for the non-oncologic, non-infectious rare diseases.

Which means there is a distinction between what is happening in the rare community that is in this room and the broader rare community. It is really important when we look at those statistics that we sort of look at what the different medical product centers are comfortable with and are doing, and that is why we—we know that the tools are available. We want to ensure that they are being utilized.

Senator KIM. Mr. Campbell, I wanted to bring you in on this because, you know, you have talked about this at length. Build off of what we just heard. How would expand use of adaptive trial designs or surrogate endpoints by the FDA lend itself to achieving better outcomes when it comes to rare disease approvals?

Mr. CAMPBELL. Yes, I think the first step is just use what we have available to us, right. If you look at oncology, I think in 2024, there were 8,000 different therapeutics in clinical trials that dwarfs the number in rare diseases today.

I think a large part of that is the much more welcoming use of accelerated approval and surrogate biomarkers. Our own product, Galafold, was approved on a surrogates biomarker. The competitor product also, Fabrazyme, was approved on a surrogate biomarker

and these things work. I get it, you know, rare diseases are biologically complex.

It is very difficult to understand how long it is going to take. You can't do randomized control studies in the same way you can with broader disease populations. When it is done right, as in the case of Fabrazyme, 10 years later, after using real-world evidence and a registry, they are able to confirm the original surrogate endpoint, and now it is a fully approved product. For me, the tools are all there. It is really more, as we have discussed, consistency and using the tools that exist. If we were to—oh please, go ahead, Senator.

Senator KIM. I just want to jump in here at the end. I mean the urgency on the trials and moving up forward on the approvals, but Mr. Campbell, I also want to raise another issue, which is just how long it often takes to build manufacturing facilities here in the United States.

You know, the level of slowness with the inspections themselves. I want that urgency on a manufacturing side as well. You know, what can you be showing us about the decisionmakings that manufacturers are going through especially in terms of being able to build this and manufacture this here in America.

Mr. CAMPBELL. Here at home. Thank you so much for the opportunity to address that, so just by background, Amicus, we work with external manufacturers. As a small cap company, we don't have the capital to build our own manufacturing facilities, and we certainly don't have an environment to be able to do that.

We work outside the United States. It takes three to five years to just to build a state-of-the-art manufacturing facility for protein therapeutics. It takes another one to two years then to get that facility inspected. You are talking five to seven years from when we want to do this to when it actually has medicine coming off the line for patients. In my mind, it is mutually beneficial to all of us, so create incentives—and they don't have to be financial incentives. Help with permitting. Help with inspections.

Give priority to inspections for homegrown manufacturing facilities. Create an environment that is actually supportive of bringing manufacturing at home, versus using, which is what we have seen over the last couple of years, more sticks to try to prevent—probably a more qualified person to speak to this, speaking in background. Let's use incentives instead of sticks to encourage that because I think the United States ecosystem, the patients, all benefit from doing that.

Senator KIM. Mr. Chair, you know, we have talked at length here in this Committee about the benefits on so many levels of having that manufacturing here in America, the speed with which we can move, the capabilities.

You know, these are some very concrete things that I hope we can followup on and really come up with a game plan here because it is just, honestly, it is just pathetic that we are just not able to do this with a greater level of speed given the skills and the talent and the resources of our country. We can and should be doing better.

Thank you for holding this hearing today.

The CHAIRMAN. Thank you, Senator Kim. Senator Johnson, do you have some more questions?

Senator JOHNSON. Yes. Thank you, Mr. Chairman. I mean, I think the elephant in the room here is, so we have got the laws in place. They maybe could be beefed up, but I think it is a personnel issue, right. I fear that not even necessarily the heads of the agencies, but possibly bureaucrats that have been there for decades, for whatever reason, they don't like a particular drug, and so they are able to sabotage it.

My question, how can we overcome the inconsistency from, you know, one bureaucrat to the next bureaucrat, changing administrations, or quite honestly, you know, a particular bureaucrat that has been in there for decades that just keeps blocking things. I mean, how do you get to the personnel issue? I will start with you, Ms. Kennedy.

Ms. KENNEDY. I think my experience differs from some on this panel in that we have seen great examples of models where we have had public meetings and public workshops where FDA has come together with the patient community, which I think is an incredibly important mechanism, to have meetings where we can have regulatory agreement around the use of certain innovative models in clinical trial design, surrogate endpoints, natural history studies as a control arm that had then allowed those programs to move forward.

Senator JOHNSON. I pointed out in a meeting like that, a panel, for Duchenne Muscular Dystrophy, 50 to 60 families, and they still said no.

Ms. KENNEDY. I love that reference. What you may not know, you probably don't know, is prior to being with the EveryLife Foundation, I was with the Duchenne community, and so that may have been an advisory committee.

Senator JOHNSON. Were you in that meeting?

Ms. KENNEDY. Yes, I was. Well, it depends on what meeting you are referring to. If it was an ADCOM, an advisory committee meeting, that advisory committee did vote no, but then the agency brought that internally and then overruled that.

Senator JOHNSON [continuing]. overruled it.

Ms. KENNEDY. That is a perfect example of the agency still has the authority to make the decision because they heard from the community and what we are concerned about right now is that the agency isn't engaging with the patient community.

Senator JOHNSON. Dr. O'Neill, in your testimony you talked about, you got your CO, the complete response letter. I mean, perfect bureaucratic type of—in other words, the no letter, right, and you got the no letter, not necessarily because of safety or lack of efficacy. It was because there is something in the manufacturing process, which again, a manufacturer, I understand that, but can you explain that. It seems like a pretty weak excuse where you could, we will fix the manufacturing process so this drug can be made available just talk about that.

Dr. O'Neill. Thank you. I am not an expert on gene therapy manufacturing, so I will say that. However, the sponsor was very transparent in reviewing the full CRL with our community so that we could understand truly what the concerns were. Many of them

were noted to be things like a crack on the floor not in the manufacturing area, or a tarp that was out back, or things that really are unrelated to our children.

Senator JOHNSON. Trust me, I have been through audits. I supplied packaging material for medical devices. You can find an excuse to, you know, write something up, pretty flimsy excuses.

Again, that is my concern. Dr. Schmahmann, in your case, it was based on real world evidence. It seems like the real-world evidence was completely in favor of allowing patients access to this drug. Talk a little bit about, you know, why you got a CLR, a no letter.

Dr. SCHMAHMANN. Thank you, Senator. You know, one of the thoughts that came to me as we are going through this whole process and hearing what happened to Sanfilippo with the crack in the floor in the factory is that this is a policy of death by technicality. These little, tiny glitches that the FDA is producing land up not approving drugs and patients die as a consequence.

I am glad to hear that there are people in the FDA who are doing what Congress requires them to do, but that speaks to the unpredictability and the erratic nature of the responses and the performance of the people in FDA. There are many ways to go forwards to use clinical trials and then use the new technology to bring treatments to patients faster that are safe and make a difference.

Science advances. The regulation is keeping up with the new advances, but it seems like the FDA is having trouble with that. The FDA must keep pace with the updates in science using the biomarkers, serum or imaging, using digital markers, using patient reported outcomes.

I developed the patient reported outcome measure for ataxia, understanding what patients are saying. The key issue here is that the real experts are the patients. The patients are the experts by experience. The patients are our research collaborators. We are all patients. Every one of us has something.

We are all patients. It may not be a rare disease, but this applies to us. We are talking about us, whether it is a rare disease or not. The approach that can be taken, including what was started at our institution, I think called a platform trial, where you can have one small group of controls and a number of other patient cohorts trying different drugs. There are innovations both in the clinical trial design and the biomarker space.

This is where we need to move, and the urgency is exactly what Senator Kim was talking about. There is an urgency now and some of the drugs on the table now, the ones you have heard about from Dr. O'Neill and myself, these should be approved this week. There is no reason not to.

Going forward, we need to find a way to enhance, to expedite, and make this a better process and have a sense that when you are going to the FDA, you know what you are getting. It is not just a random scatterplot of who is going to get what kind of a person there.

Senator JOHNSON. Isn't another root cause here is literally the doctors are no longer at the top of the treatment pyramid? They have been replaced by regulators. You talk patients are number one, but doctors are the ones that are most knowledgeable in this

equation, and you are shutting off to the side. What you are saying doesn't count because the regulators have replaced you in terms of making these decisions for patients. Isn't that a big problem?

Dr. SCHMAHMANN. You know, Senator, on your wall in your office yesterday, I saw your mission statement, which was triple, teamwork, respect, integrity, professionalism, loyalty, and education.

The FDA is not doing that. It is the opposite. Communication, dialog, teamwork between the physicians, the patients, the pharma who make the drug, the regulators, that is a two-way street. It is a dialog. In medicine, when we do rounds in the morning on our patients in the hospital, there is a discussion.

The physician is there, the residents are there, the nurse, the nurse practitioner, or the physical therapist, the patient and the family. It is a conversation, a discussion. This is not what we are hearing from across the board and certainly from the other rare diseases. We are here, the few of us.

Turns out there are 30 million people behind us, as you said. What we are bringing to you is the plea to make the FDA what it was supposed to be, which is what you regulated, and allow us to work in a collaborative manner across the board, not with this kind of hit or miss approach as to who you are going to get on a committee. You are looking for accountability.

In fact the leadership of the FDA, it is their responsibility to hold the feet to the fire of the people under that person's leadership. Not just to say good things, but to actually make them happen and bring new drugs to the American population including us, our patients, my patients, that are safe and effective.

Senator JOHNSON. Again, thank you, Mr. Chairman. I think this is an excellent hearing, excellent testimony. Both you and the ranking member, you pretty well diagnosed the problem here. I mean, in your opening statements, you laid out the problems. This is eminently fixable, and we have to fix it. Again, I am committed to working with you to do so but thank you for this hearing.

The CHAIRMAN. Senator Gillibrand.

Senator GILLIBRAND. Thank you. In 1972, the Federal Advisory Committee Act established advisory committees within the FDA to help provide independent expert scientific input on product reviews and policy topics.

In 2025, FDA canceled many advisory committee meetings and indicated that it would like to move away from involving advisory committees in the review of drug applications. For each of the witnesses, you can start Ms. Kennedy, how important is it to the rare disease community for FDA to restore the use of advisory committees?

Ms. KENNEDY. It is everything. We yesterday had one of our communities showcase in front of close to 800 members of the rare disease community how an advisory committee meeting helped inform a key regulatory decision for the VAR syndrome community by showing how an open public hearing enabled members of that community illuminate the nuance of a very complex regulatory decision in a very complicated regulatory review.

As Senator Johnson just highlighted, I have been a part of many advisory committee meetings for communities, including the

Duchenne community, and advisory committees don't always vote yes. That is not the point.

The point is for external experts, including clinicians, including those with statistical expertise and manufacturing expertise that are not always internal to the agency, to be brought to bear on regulatory decisions because we realize that with 10,000 rare diseases, it is not possible for FDA to always have all of that expertise internal.

Those committee hearings must be at the avail of the agency, but also those open public hearings must be available so that patient communities who are participating in clinical trials can share what their experiences in those clinical trials are. One of the challenges we have in clinical trial design is we don't always know what we are going to find when a clinical trial begins.

We design a clinical trial hoping that we are going to be able to select the best outcome measures, but sometimes patient communities who participate in those trials experience other benefits and those hearings enable us to hear from patients about what other outcomes were achieved so that we can make the best decisions possible for the patient community around safety and efficacy.

Eliminating those hearings eliminates the chance for FDA to make the decisions that are in the best interests of the patient communities possible.

Senator GILLIBRAND. Dr. Schmahmann and Dr. O'Neill, congressional actions have advanced how patient experience data is included in the development and evaluation of rare disease therapies. What is the importance of the patient voice in this regulatory process, and what more is needed to ensure FDA includes this information in its decisionmaking?

Dr. SCHMAHMANN. I agree that it is critical, Senator. I think that there is a deeper problem. If you don't listen to somebody else's advice in a complex story, that is the opposite of humility. It is a denial of the patient's humanity and it is sort of hubris. You don't want to hear what the patients have to say? Who are you? That is the problem.

This is all about the patients. To deny the patient voice in drug development and in drug design—and I agree completely with Ms. Kennedy here. Determining the end point when you start is fine if the disease is well known in the millions of people.

In our case, for example, the spinocerebellar ataxia, the first clinical trials that Biohaven did in the 2016s, we didn't know what would change. We had to take a guess and I worked with them in devising the scale, devising a trial. The patients then told us, you know what, I am falling less, I am not as fatigued, and my speech is better. There was a different outcome we didn't understand at the beginning. That is the epitome of regulatory flexibility.

There is a rule in medicine, listen to the patient, they are telling you the answer. The second piece is, ignore the patients at your peril. What we have here is denying of the patient's story. It is the peril not of us, but of the patient because now the drugs are not being approved.

I think you have hit the nail on the head here. If you are ignoring the patient, then why are you getting up in the morning and coming to do the work that you do with the FDA?

Senator GILLIBRAND. Well said. Dr. O'Neill.

Dr. O'Neill. Thank you. You know, obviously you have heard that patients are not outside of the drug development process. They are critical to it and advisory committees, as Annie had mentioned, are an important place where we can have that scientific dialog and hear from patients.

Their experience is also science. It is human science. The interaction needs to come way before that, because by the time we get to an advisory board, tens of millions of dollars have been spent, maybe a decade has gone by. We have not treated potentially that many patients who needed treatment.

Having a true collaborative dialog early in the process is essential and something—an opportunity that needs to be acted upon within the FDA. I think one other thing that we are understanding is key insights around risk tolerance. We also want safe medicines, but we also want the opportunity to save our children because those answers about a clinical trial come way down the road.

As Mr. Campbell explained, real-world evidence, post-marketing disease monitoring programs, this is where we need to be really focusing on these innovative ways. Maybe not so innovative, honestly, anymore, but more frequently used and supported ways to provide that longer term evidence to support accelerated approval.

Senator GILLIBRAND. Mr. Campbell, did you want to add?

Mr. CAMPBELL. For sure. I think what we keep coming back to, and I think you hear the theme, is you have all the tools in place. You have the advisory committees. You have accelerated approval pathways.

I think the frustration is when they are deployed inconsistently and without clarity from the sponsors and from the patient community and from the physicians in terms of how you end up, you know, meeting the expectation but then not coming to a positive resolution. There is one other piece that we haven't talked about, if I could just introduce that, which is the Rare Disease Innovation Hub. If we want to talk about things that Congress could proactively do.

We have a tool that is modeled after what was very successful in oncology, the Center of Excellence, but my observation would be is it is underfunded and probably under empowered to do what it needs to do.

When we think about advisory committees, when talk about staffing at the FDA, when we think consistency between reviewers, Congress could directly fund the Rare Disease Innovation Hub in a meaningful way that would allow us to train rare disease experts that could sit across review teams, across review divisions, and bring some of that consistency, that humanity, that humility, but that expertise that perhaps each of the individual teams or the new reviewer on the team doesn't quite have.

Again, I think we have a lot of the tools that we need. We just need to encourage the FDA to use them in the right way and that is one example we haven't talked about here today where Congress could fund that directly and allow the FDA to make it a much more valuable tool for rare disease drug development.

Senator GILLIBRAND. Thank you, Mr. Chairman.

The CHAIRMAN. You know, when you hear the testimony, I think all of us internalize it. I have got six grandsons and a granddaughter and you know, thank God they don't—you know, everybody has got problems, right, but you know, they don't have a rare disease that is going to shorten their life.

I can't imagine what a family is going through when they have a family member that has something and then they believe there is a possibility that something could change their life, and it doesn't happen. I mean, I would be pretty frustrated. I would be pretty—more than that. Ms. Kennedy, is it important for people to come to Congress and talk about their concerns with regard to the drug approval process?

Ms. KENNEDY. Well, I know you are asking me, but there are about 800 people on the Hill that would be happy to answer that question as well.

Throughout this time here this morning, starting with your opening remarks, we have cited many laws that have been transformational for our rare disease community, and every single one of them started with a member of the community meeting with their elected official and talking about a roadblock that could be transformed and turn into a resource and a tool.

Every single one of those laws has transformed lives and ultimately has saved lives. So the answer to your question is an emphatic yes, and we are so grateful for the time you take to be with our community, to listen to our community, to engage, and to become partners with all of us, so thank you.

The CHAIRMAN. Does the FDA appreciate when you guys come here?

Ms. KENNEDY. I think many do, yes. Maybe some no, but I think overall, over the years, I have been in this space 30 years and I think we have had strong partnerships with the agency and many times the agency has very much appreciated our support.

The CHAIRMAN. Dr. Schmahmann, what—from a clinical standpoint, what happens to patients with progressive neurologic diseases when access to treatment is delayed due to the regulatory process rather than safety concerns?

Dr. SCHMAHMANN. They progressively deteriorate. They lose function. They can't live their lives, go to work, spend time with their family, make a living, be productive citizens of society in that way. They become part of the family that people have to take care of instead of taking care of the families themselves. Then they become progressively debilitated and then they die young.

Then family members, in our case, see that. They see their future in the mirror. There is a high incidence of depression and, in fact, suicidality in this patient community as well. This is across the spectrum. This is not a motor control problem alone. This is a social, emotional, societal issue and the issue about medications that improve neurological function in real time work at the level of the physiology where brain cells are sick before they die.

If you have a medication, even though it is not a gene therapy, you have medication like troriluzole, where we know the mechanism, and you stop the neurons from being so hyperactive that they die, you actually improve function and you slow disease over time, so you are modifying the disease.

The absence of a medication that can treat the disease means that each day that this drug, triloriluzole, and others like it are not being approved means patients are losing brain cells and are closer to death. It is heartbreaking to see, as you all said at the outset, and we are hoping that this can change from today.

The CHAIRMAN. I think in your testimony you said that the FDA suggested withdrawing patients from compassionate use of care to evaluate whether their conditions would deteriorate despite physicians expressing the harm would be irreversible. So tell me about the—what are the ethical implications of that?

Dr. SCHMAHMANN. If you have a disease where there is a symptom like a migraine, for example, you can see if I stop the drug, will you get worse for a week or two, or a month, and I will put you back on drug, you are okay. In a neurodegenerative disease like these, and I am going to be—excuse me if I am provocative—the last time we had a catastrophe in medical science in the U.S. was between 1922 and 1972.

I believe there was like a 40-year period, 1932 to 1972, when people with syphilis were not treated so that the doctors could see what happened to them, and the patients were not told. That is a case study for every person who is going into human studies research in the United States.

We learn about that case. You cannot treat patients like guinea pigs. You have to have them on your story as part of the research collaborator, experts by experience. If we have a drug, as we do here, that is first safe and that bends the arc of the disease, and you want patients to come off that drug so you can see if they worsen, in other words if their brain cells are dying under your care, that is a poster child—it is Tuskegee version two, and it is entirely unacceptable. I reject it outright.

They should not have recommended that and whoever did, I would suggest they take updated education sessions on clinical trials and on human studies research. It is not okay, Senator.

The CHAIRMAN. I can't imagine doing that. Mr. Campbell, talk about inconsistent FDA standards, how it impacts timelines, costs, the ability of small biotech companies to survive. Is it easier to raise money if the FDA is inconsistent? Does that make your job easier?

Mr. CAMPBELL. No, is the candid answer, and you know, that is underlying all of this, right. We have created in the United States this rich ecosystem of innovation, which has been supported by Congress, supported by FDA over the years, supported by modern technology, and that brings in new companies that bring in new innovations and offer some of the therapies that we have talked about here today that are now stuck in front of this regulatory process.

The reality is, and this is in my written testimony, the reality is for many small and mid-sized biotech companies, it takes decades to become profitable, which means we are going hand-in-mouth begging for dollars from investors. If there is a clear path forward and investors can be confident of an eventual return, then they will keep investing and the innovation ecosystem keeps going and going.

If we continue to create this uncertainty, if we continue to create an uncertainty around manufacturing timelines, around approval timelines, around changing the goalposts again, I am confident that those investor dollars will go somewhere else.

I will tell you transparently, having gone to the recent J.P. Morgan Healthcare Conference, which I am sure folks know is the big investor conference in our industry, I heard more opportunities about Chinese therapeutics and companies than ever before, and I don't think that is an accident.

Ten, twenty years ago, we might have thought the science wasn't good. We might have distrusted the quality and the safety. I can tell you that the innovation there and the science is equally as good as ours.

We still have an advantage, but if we are not careful, we are going to lose that advantage, and at the end of the day, the American patients suffer, the American economy suffers, and I am convinced that that is a real threat, in addition to the most important piece, which is making sure drugs get to patients faster.

The CHAIRMAN. Dr. O'Neill, in progressive rare diseases, how should regulators account for the fact that clinical decline is often irreversible? Should the harm of waiting be weighed alongside uncertainty in the data? If so, how?

Dr. O'Neill. Thank you. Yes, to call back to Dr. Schmahmann's points around this and about exposure to not being on drug, the risks of not treating this disease are known. You know, these are not in question.

We know these children will be permanently, severely brain injured for the rest of their lives. There are critical, time-sensitive neurodevelopmental windows in childhood when it is important to intervene to be able to receive the maximum benefit. There is a continuum of this, but earlier is always better.

What we are still hearing as recommended to sponsors is that observational, or no treatment, or placebo controlled trials are being recommended for these pediatric conditions. This is very, very troubling when we know that they will become brain injured. We have also seen—you know, when parents ask me about this, I have to kind of step back and think, oh my goodness, I know what a perfect science experiment looks like.

Yes, that is the perfect science experience, but these are children. You cannot do good medicine unless you are putting the patients first and following the ethics of medicine and we have heard changes around the use of animals in preclinical studies. Just last April, the FDA published its roadmap to reducing animal testing in pre-clinic studies, and this says, I quote, "due to the limitations of animal testing as well as ethical concerns about animal testing, there have been increased focus within the scientific community on new approach methodologies."

We are concerned about the ethics of animal testing more than we are concerned about the ethics of allowing children to be brain injured in clinical trials, and I think we all need a gut check on that.

The CHAIRMAN. Would any of you like to talk about what patients and caregivers tell you about their willingness to accept un-

certainty or incomplete data when the alternative is no treatment at all?

Dr. SCHMAHMANN. I think it starts off with safety. Nobody likes side effects, and patients do want to know that the medications are safe, or the approaches are safe. Given that piece, if we can make a comment about safety, the degree to which the medication works or not is often something that patients, I think, are willing to take on.

We can certainly hear from the others about that and the other rare diseases. In our space, knowing that the medications we have available are safe, and have been shown in other circumstances, patients are not just willing, they are—we are getting emails every day from people around the world, what trials do you have for me that I can use to try and slow down the process of my disease?

Ms. KENNEDY. Yes. I really appreciate that question, and I think my response would be that for each subpopulation within each condition, within each targeted therapy, that consideration would be very different, which is why Congress authorized the use of the benefit-risk framework within the consideration of regulatory review. That is one of the things that we are concerned about is not being applied.

We don't know how it is being used. One of the things that we are asking for today is more questioning around how are these tools being utilized, because every community for every clinical trial within every subpopulation of that community will approach that threshold for risk tolerance differently.

That is a super important question, Senator, and we are just not sure that that is being questioned the way it was intended for the tailorization that is required for rare disease therapeutic development.

The CHAIRMAN. Mr. Campbell, can I ask you a separate question? How important is transparency from the FDA in maintaining trust with rare disease communities? What happens when explanations for delay are unclear or incomplete?

Mr. CAMPBELL. You know, I feel like as sponsors, manufacturers, we have a great duty to our patients. I think somebody—one of the Senators asked me why I am in this business. I will tell you, you know, it is for the patients, but when you have a chance to develop a therapy for people living with a rare disease, it sort of gets in your blood. You also, then you bear a great responsibility.

I feel, I think, like sponsors are at the front lines, in front of the agency trying our best to get those drugs over the finish line. If we fail to do that for any reason, we owe it to the patients, to the community, to the caregivers to give them an explanation. When there is no good explanation or when the explanation is a crack on the floor, you know, that is just not good enough.

I think I really do believe that sponsors bear some of that responsibility. I think it works best when we truly work together. Congress has the tools. The FDA has proven itself over time to be very effective in working with sponsors. I shared our story, which was an incredible, innovative regulatory science, medical science that helped thousands of patients.

If you don't have that transparency, and if you do not have that consistency then, you know, we all lose, and I really believe that

we are at the center of that. It pains me, you know, to hear these stories.

We are not in that position today as Amicus, but we owe a responsibility to these people who are giving their lives to participate in clinical studies who have so much hope, we owe them clarity and we all do. Everybody who is involved in that, including the regulators.

The CHAIRMAN. Ranking Member Gillibrand, you want to say anything before we close?

Senator GILLIBRAND. I would like the audience members who have pictures of their loved ones to stand please so we can see their loved one. Thank you for coming to represent them. Thank you all. I want to just thank our guest who is in the corner who has been so well behaved this entire time. I am very proud of her for being such a good girl. Just thank you all for being here today. This has been an extremely powerful hearing. We have gotten some amazing testimony, and I am very hopeful that we will find better solutions so that we can all work together to get these cures that our loved ones so desperately need. Thank you all.

The CHAIRMAN. I want to thank everybody for being here. I want to thank the Ranking Member for this. We have been doing this for a little over a year, and we have been able to do a lot of things together.

What we heard today was not abstract policy theory. We heard from Mr. Campbell that 95 percent of rare diseases still have no approved treatment. At the current pace, it could take more than a century to meaningful close that gap. We heard Dr. Schmahmann about a multi-year data set supported by real-world evidence and natural history comparisons, showing meaningful showing of disease progression, yet still unable to clear the regulatory bar.

We heard from Ms. Kennedy that at least 23 rare disease therapies received complete response letters in the past year, even as advisory committee meetings declined, raising concern about whether the flexibility Congress authorized is being applied consistently. We are reminded that for some patients, success is not an abstract endpoint, but the ability holds one breath long enough to survive another moment.

I recently spoke with Commissioner Makary. It was clear that the FDA's framework was built for common diseases, not rare to ones. He is implementing reforms like the plausible mechanism pathway, greater flexibility for gene therapies, and strengthening the rare disease innovation hub. We look forward to working with him to ensure those changes are applied consistently and urgently for patients. He inherited a broken system, and the FDA cannot be fixed overnight.

That said, he has made significant progress, and I am completely encouraged by the reforms President Trump has empowered Commissioner Makary to make at the FDA, and I know he cares deeply about getting results and making sure the United States remains the world's leader for innovation and treatment of rare diseases.

Taking together the testimony presented before our Committee today makes one thing clear, the question is not whether to protect safety, it is whether the system is moving with the urgency Congress intended and patients require. The Committee will continue

exercising oversight to ensure that flexibility enacted into law becomes reality in practice.

I look forward to continuing work with our members. If any Senator has additional questions for the witnesses or statements to be added, the hearing record will be open until next Wednesday at 5:00 p.m. Thanks everybody for being here.

[Whereupon, at 11:05 a.m., the hearing was adjourned.]

APPENDIX

Prepared Witness Statements

Testimony of Annie Kennedy
Chief Mission Officer
EveryLife Foundation for Rare Diseases
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Presented before the
United States Senate Special Committee on Aging
Hearing on
"From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation"
February 26, 2026 – SH-216



Summary of Testimony

Congress has Powered Rare Disease Therapy Development Progress

- Since 1983, Congress has created incentives and policies that recognize the inherent complexities in developing treatments for rare diseases.
- Congress has explicitly given the FDA authority to uphold the highest standards of regulatory safety and rigor, while applying tailored approaches (i.e. “regulatory flexibility”). Such approaches included:
 - o Establishment of the accelerated approval pathway
 - o Consideration of the totality of evidence in the regulatory review
 - o Inclusion of Patient Experience Data (PED) in clinical trial design & regulatory processes
 - o Utilization of innovative clinical trial designs and real-world evidence (RWE)
- Nearly 1,400 orphan-designated therapies are changing the lives of patients and families, but 95% of rare diseases remain without an FDA-approved treatment.

Progress is Uneven, but Some Developments Can’t be Ignored

- A series of FDA actions on rare disease product applications appears to contradict public pledges to expand the use of regulatory flexibility in the evaluation of rare disease therapies.
- At least 23 Complete Response Letters declining to approve rare disease therapies have been issued since the start of 2025, many of which were being considered under the accelerated approval pathway.
- In 2025, the FDA held 65% fewer advisory committee meetings for prescription drugs, biologics, and related topics than in 2024, reducing opportunities for external expertise and patient insights to inform FDA decisions. In some cases, meetings expected to discuss rare disease products that later received a negative regulatory decision were cancelled.

Key Opportunities

Congress can:

- Conduct oversight to better understand the FDA’s approach to:
 - o The application of the accelerated approval pathway to rare disease therapies;
 - o Resolving the inconsistent and unpredictable application of regulatory flexibility; and
 - o Resuming the use of Advisory Committee Meetings to receive external expertise on product reviews and key policy topics.
- Provide the necessary resources and direction to optimize the Rare Disease Innovation Hub’s ability to improve outcomes for rare disease patients through enhanced coordination and alignment between medical product centers.
- Urge FDA to establish a Rare Disease and Condition Advisory Committee to ensure the Agency can leverage external expertise and patient insights in its approach to rare disease regulatory reviews.

Testimony

Thank you, Chairman Scott, Ranking Member Gillibrand, and distinguished members of the Committee, for convening this critical hearing to explore how the Food and Drug Administration can enhance regulatory clarity and predictability – and foster a more patient-centered, efficient review process for rare disease therapies. These changes, if made, will strengthen U.S. biomedical leadership and ensure lifesaving therapies reach our rare disease patient community as soon as possible.

My name is Annie Kennedy, and I serve as the Chief Mission Officer for the EveryLife Foundation for Rare Diseases. I am especially honored to be here today on behalf of the more than 800 rare disease advocates who have joined us in Washington for Rare Disease Week on Capitol Hill. Our families have traveled great distances and from most every state – including each state represented on this committee – to be here this week – and we each proudly represent the more than 30 million Americans living with rare diseases.ⁱ

The Orphan Drug Act defines a rare disease as a condition that affects fewer than 200,000 people in the United States. Today, there are more than 10,000 distinct rare diseases,ⁱⁱ about 70 percent of which start in childhood.ⁱⁱⁱ Some of these are more common, such as Cystic Fibrosis and Duchenne muscular dystrophy. Others are so rare that they are considered N of 1 and are named by their genetic mutation. Collectively, our rare community comprises more than 10% of the U.S. population.

Congressional Efforts Yielded a Movement That Reshaped Methodology in Rare Disease

A stable and predictable regulatory environment is critical to the rare disease therapy development ecosystem. Over the past decade, our rare disease community has seen hundreds of life-altering and life-saving therapies become reality, and we appreciate that each and every day, researchers and drug developers are working to develop therapies for the 95 percent of the community that is still waiting for their first approved therapy.

For patient communities comprised of small numbers whose diagnoses typically occur after long, heartbreaking, and expensive diagnostic odysseys during which the disease has progressed – and function has declined – time is a precious commodity.

Randomized, double blind, placebo-controlled trials that are traditionally conducted in conditions with larger, well characterized, and slowly progressing disease populations are neither appropriate, nor ethical, when considering the challenges and urgency of rare disease.

Congress has long recognized that statutory “regulatory flexibility” is a means to accelerate treatments for patients living with rare diseases. Over the last two decades, your leadership has provided therapy developers and regulators tools that have not only rocketed the United States into renown as the most competitive developer of rare disease products – but most

importantly, have yielded life-changing medicine approvals for thousands of children and adults within our rare disease community.

More than 40 years ago, Congress enacted the landmark Orphan Drug Act (ODA) to create a designation, incentives and other processes to help evolve what to that point had been a largely neglected sector, devoid of approved products. Since that time, Congress has further recognized the complexities and challenges associated with rare disease therapy development – and has unleashed a decade-plus of innovation through the establishment of scientific, clinical, and regulatory infrastructure intended to create an environment of rapid and tailored development.

Through the 21st Century Cures Act, multiple FDA user fee cycles, the recent reauthorization of the Rare Disease Pediatric Priority Review Voucher program, and other actions, we have seen the advent of life saving therapy development incentives, the patient focused drug development movement, the establishment of the FDA Rare Disease Innovation Hub, and application of the accelerated approval pathway to rare disease – all while ensuring that the highest standards of safety and efficacy were upheld.

The application of the accelerated approval pathway to rare disease therapy development called for access to emerging therapies that have achieved safety and efficacy based on the earliest signals of promise, when considered against known alternative disease outcomes. And while over 250 therapies have been approved using the accelerated approval pathway, only 20% ^{iv} of these have been for rare non-oncological diseases.

As a result of Congress' leadership, rare disease patient advocacy organizations have witnessed improved engagement and understanding of the patient perspective through various approaches, including the Patient-Focused Drug Development workshops, the development of the FDA Benefit-Risk Framework, the formation of rare disease-focused initiatives within CDER and CBER, as well as reporting on the use of patient experience data within the regulatory review process.

Also transforming community engagement and sponsor development, legislation has spurred FDA's issuance of numerous guidance documents that are informing the conduct of patient-focused product development activities for drugs, cell- and gene-based therapies, diagnostics, and medical devices that has been critical to our pipelines.

In fact, nearly 1,400 orphan-designated therapies are changing the lives of patients and families.^v

These past Congressional efforts yielded a movement that reshaped methodology.

And while this movement and the critical application of methodology have yielded benefit for some, we have only just begun. Still, the vast majority of our communities living with the more

than 10,000 rare diseases still have no FDA approved treatments. To date, fewer than five percent of rare diseases have an FDA approved treatment – and none have been cured.

In other words, the majority of our nation’s rare disease community are living with rapidly progressive and debilitating conditions for which there is no treatment. This is the challenge before us today. Unfortunately, despite four decades of positive scientific momentum, progress has stalled.

Momentum Has Shifted

We are here today because our community has experienced worrisome trends with devastating consequences.

While we have been incredibly heartened by announcements flagging support of rare disease therapy development initiatives such as the Rare Disease Evidence Principles (RDEP) framework and the Plausible Mechanism Pathway, our community has experienced a series of FDA actions on rare disease product applications that seem misaligned with recent public pledges to expand the use of regulatory flexibility in evaluating rare disease therapies.

- Since the start of 2025, at least 23 Complete Response Letters (CRLs) declining to approve rare disease therapies have been issued – many of which were being considered under the accelerated approval pathway.
- Several of the recent CRLs include comments that indicate a hesitation to apply regulatory flexibility on issues such as the use of surrogate endpoints, natural history studies, external controls, and real-world evidence.
- Previously, novel product reviews encountering complex discernment might initiate the convening of a product – or topic – specific advisory committee for the inclusion of insights of external experts to inform decision making.
- Yet in 2025, the FDA held 65% fewer advisory committee meetings for prescription drugs, biologics, and related topics than in 2024^{vi}, sharply reducing opportunities for external expertise and patient insights to inform FDA decisions. In some cases, meetings that were expected to discuss rare disease products – that later received a negative regulatory decision – were cancelled.

Congressional Action to Ensure Today's Patients Will Benefit from Robust Rare Disease Treatment Pipelines

In order to ensure that this generation of patients living with rare diseases benefit from the innovation within our nation's robust therapy pipelines, we ask that Congress conduct oversight of the following:

- The application of the accelerated approval pathway to rare disease therapies;
- Resolving the inconsistent and unpredictable application of regulatory flexibility; and
- Resuming the use of Advisory Committee Meetings to receive external expertise on product reviews and key policy topics.

We also ask that Congress provide the necessary resources and direction to optimize the Rare Disease Innovation Hub's ability to improve outcomes for rare disease patients through enhanced coordination and alignment between medical product centers.

Finally, within the remit of the Rare Disease Innovation Hub, we urge FDA to establish a Rare Disease and Condition Advisory Committee to ensure the Agency can leverage external expertise and patient insights in its approach to rare disease regulatory reviews. While not a product-review committee, this would provide a clear mechanism for FDA to obtain the necessary perspective from rare disease stakeholders to inform this work.

Closing

While the FDA has taken actions to implement rare disease related provisions of the user fee bills and created new rare disease infrastructure through the Rare Disease Innovation Hub, the impact of these and other actions has not yet been fully realized for the benefit of the rare disease community.

The uneven application of rare disease policies and recent actions across the agency are resulting in increased unpredictability and risk that we fear could slow or prevent promising therapies from reaching those who need them most.

At a time when advances in science and understanding of diseases have put life-altering treatments within reach for many communities, the uneven application of regulatory tools created by Congress is threatening our rare disease patient community's future.

Time is the most precious commodity for rare disease community.

And when a promising therapeutic target faces delays or demise due to the complexities in rare disease and strain on the existing regulatory infrastructure, investment wanes, future scientific promise is unfulfilled, and lives are lost.

About the EveryLife Foundation for Rare Diseases:

The [EveryLife Foundation for Rare Diseases](#) is a 501(c)(3) nonprofit, nonpartisan organization powered by the rare disease community to improve health outcomes by driving change through evidence-based policy, leading science-driven policy and regulatory research, activating the community to advocate for their rights and needs, and strengthening the rare disease community.

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¹ National Institutes of Health- National Center for Advancing Translational Sciences. (n.d.). Genetic and rare diseases information center.

Genetic and Rare Diseases Information Center. <https://rarediseases.info.nih.gov/>

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³ Nguengang Wakap S, Lambert DM, Oly A, Rodwell C, Gueydan C, Lanneau V, et al. Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database. *Eur J Hum Genet.* 2020;28(2):165–73.

⁴ [Expediting treatments in the 21st century: orphan drugs and accelerated approvals](#) | *Orphanet Journal of Rare Diseases* | Springer Nature Link

⁵ Food and Drug Administration: Office of Orphan Products Development. (n.d.) *Orphan Drug Product Designation Database*.

<https://www.accessdata.fda.gov/scripts/opdlisting/ood/index.cfm>

⁶ <https://insights.citeline.com/pink-sheet/product-reviews/us-advisory-committees/us-fda-sees-advisory-committee-volume-collapse-in-2025-T265ZITIFRIBHAT7PFGREWACM/>

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**Written Testimony for the Senate Special Committee on Aging
 "From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation"
 Hart Senate Office Building, Washington, DC
 February 26th, 2026**

Chairman Scott, Ranking Member Gillibrand, Members of the Committee:

Thank you for convening this very important hearing, and for inviting me to testify about my patients and the situation in which they find themselves and to share with you my personal experience with the FDA.

I have been caring for patients with cerebellar ataxia for 45 years. I started the first Ataxia Center in the US at the Massachusetts General Hospital in 1994. I serve on the National Ataxia Foundation's Medical Research Advisory Board, and I received lifetime research achievement awards from both the National Ataxia Foundation and from the American Academy of Neurology's Society for Cognitive and Behavioral Neurology. I discovered the role of the cerebellum in intellect and emotion and described the cerebellar cognitive affective syndrome that bears my name, and developed the Patient Reported Outcome Measure of Ataxia that ensures the patient voice is included in patient care and clinical trial design in the ataxias. I am a site principal investigator for the natural history study of ataxia and for Biohaven's study of troiluzole in ataxia.

I do not speak for Mass General Brigham, Harvard Medical School, or Biohaven Pharmaceuticals. I do not own stock in Biohaven, have no equity in it, and am not their employee. Research funds received from Biohaven for the conduct of clinical trials and brain imaging studies are monitored by regulators and grant administrators at my institution. My consulting time is reimbursed by Biohaven, but I have no financial interest in the outcome of their study.

The cerebellum is a fist-sized structure at the back of the brain that contains 80% of our brain cells. It is a critical regulator of motor control, as well as of emotional and cognitive processing. Ataxia is the term used to describe disorders of the cerebellum. The spinocerebellar ataxias are inherited brain diseases that progressively destroy the cerebellum and related structures, degrading quality of life and leading to early death. They affect patients in the prime of life but can also come on in childhood. People with ataxia cannot maintain balance and walking, they stumble and fall, injuring themselves repeatedly. Their speech becomes slurred and difficult to understand. Arm and hand control are degraded so they have difficulty writing, typing, feeding themselves. Eye movements and in some cases, vision are impaired which affects reading and driving. Fine-tuned cognitive processing is affected, and patients face multiple emotional challenges. As the disease inexorably progresses, patients need walkers and wheelchairs, until

they are bedridden. Impaired swallowing leads to aspiration pneumonia, and after 10 to 25 years of progressive degradation of quality of life, patients die an early death. Compounding the misery is the fact that these are autosomal dominant inherited diseases, they pass from one generation to the next, each child of an affected parent having a 1-in-2 chance of inheriting the gene, knowing what is in store for them. Further, spinocerebellar ataxias are rare, affecting about 15,000 people in the US, with 50 different forms of dominantly inherited ataxia, and 100s of recessive ataxias. The most common ataxias number in the few thousands, the rarest affect 10 – 30 identified patients.

Studying rare diseases like these is exceptionally difficult. Progression is inevitable but slow, the manifestations differ for each disease, and there is substantial heterogeneity even within families. Clinical trial design requires deep knowledge of these diseases and their manifestations. Recognizing these challenges, Congress has come to the defense of the American people. Congress authorized the FDA to use regulatory flexibility in rare diseases through the Orphan Drug Act of 1983, and required the use of real-world evidence in regulatory decision making in the 21st Century Cures act of 2016. Congress then passed the Accelerating Access to Critical Therapies for ALS Act in 2021 which was enacted to foster the development of safe and effective drugs to improve the lives of people living with ALS and other rare, similarly fatal, neurodegenerative diseases.

Spinocerebellar ataxia is such a disease. There have been no cures for ataxia or ways to slow progression. All we have had is symptomatic relief. This has caused despair for patients and frustration in the medical community.

Until triloriluzole came on the scene.

Italian studies in the early 2010s showed that riluzole, the drug used to treat ALS for the past 30 years, seemed to improve ataxia. Based on this finding and the plausible mechanism of action as a treatment for spinocerebellar ataxia, Biohaven developed triloriluzole, which metabolizes into riluzole, but the pill is taken just once a day, with better absorption and brain penetration, and a remarkable side effect profile that is similar to placebo.

Biohaven triloriluzole program is the first registrational trial in spinocerebellar ataxia which spans over 8 years and is the largest clinical trial dataset for spinocerebellar ataxia to date. At every step of the clinical development program Biohaven relied on input and collaboration with the ataxia experts across the globe and incorporated FDA feedback into each protocol. Results across the program, which included two clinical trials and a Real World Evidence (RWE) Study, show consistent evidence that triloriluzole delays disease progression in spinocerebellar ataxia patients, decreases risk of falls, with worsening of symptoms when patients discontinue drug. In my own clinic, this is exactly what I have observed, and continue to observe, in the ongoing Expanded Access Program.

As a clinician who has treated these patients for decades, I can tell you that the stability I see in patients on triloriluzole does not happen in the absence of an effective treatment.

To their credit, Biohaven continued with their clinical program while interacting with FDA on the protocol for their RWE Study to generate additional efficacy data to support a resubmission in all genotypes. Biohaven designed a 3-year study, submitted the protocol and statistical analysis plan to FDA for review and input, and followed all the FDA guidelines including 9 FDA-sanctioned prespecified endpoints. In this study they compared the results of patients on triloriluzole with statistically matched, untreated spinocerebellar ataxia patients from two rigorously designed

natural history studies, conducted by experts in academic medical centers in the US and in Europe.

The results of the 3-year external control study showed that triloriluzole slowed the disease by 50 - 70%. This dramatic observation was supported by the patients' reports of their experience and confirmed by the ataxia physicians.

But the FDA issued a complete response letter, rejecting the triloriluzole new drug application. I have written 6 letters to FDA leadership between 2023 and 2025, cosigned by 17 ataxia colleagues around the country, asking FDA to review the application and work with Biohaven to make the drug available, if necessary, performing post-marketing studies. I emphasized that each day without treatment leads to irreversible neuronal loss and functional decline. I have never heard back from the FDA.

Now, despite appeals by the experts, the company, and the patients, the triloriluzole expanded access program is about to end. There are nearly 300 patients on drug across the country and mounting numbers on a wait list to start treatment. I follow many of these compassionate use patients myself, and we see stabilization.

Because of FDA action, or inaction, these patients, stable on triloriluzole, will have to come off drug. Knowing they will worsen, we are starting to hear from patients how distraught and outraged they are. This medication is safe, it is well-tolerated, and to reiterate, it metabolizes into a drug that has been on the market for 30 years. We are at a loss to understand how this has been allowed to take place.

This brings me to my personal experience with the FDA. I have met on 3 occasions with the Center for Drug Evaluation and Research (in person: White Oak campus, Silver Spring MD, October 5th, 2023, and July 25th 2025; teleconference, September 18th 2025). On each occasion we were unable to convince the committee to heed the patients, or the experts, or consider the science. They did not engage in meaningful discussion and explicitly stated that the purpose of the meeting was not for collaboration or a dialogue. One panel member said to me: "Why should I listen to you?"

In neurodegenerative ataxias, stability represents meaningful therapeutic success. These patients do not remain unchanged for multiple years without an effective intervention. The long-term data, including real-world evidence from the natural history study, show that triloriluzole slows disease progression relative to untreated patients. Congress has directed the FDA to apply regulatory flexibility in rare diseases and to consider real-world evidence when randomized trials are impractical. Despite this, the FDA has declined to consider these data and has instead focused on the original short-term primary endpoint. We are therefore faced with rare, fatal, inherited diseases, a drug that is safe, and converging clinical, longitudinal, and real-world evidence that it meaningfully slows progression. Yet it remains unavailable to patients outside clinical trials and is now to be denied even to those patients on the expanded access program.

In the complete response letter, the FDA's only proposed path forward is to require another large, double-blind, placebo-controlled trial. In this rare disease context, such a trial would take five to eight years to complete and would require withholding a drug that has been shown to slow decline. During such a trial, patients will worsen and die from their disease. There was even the suggestion by FDA to perform a randomized withdrawal study. This would entail blinding patients

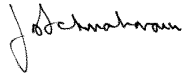
to whether they were being taken off treatment and then seeing if they worsen to further prove the effect of the drug. My colleagues and I find either approach to be unethical. It violates the principle of beneficence in human studies research, to act with charity, mercy, and kindness to promote the well-being of others.

The FDA mission is to protect the health of the American public by assuring the safety, efficacy, and security of drugs, and to speed innovation. Based on my personal experience of the FDA during both the last administration and the present one, and my knowledge of this patient population, of the diseases that afflict them, and of the impact of troriluzole bending of the arc of their disease, it is my opinion that the FDA is violating its mission, and ignoring Congressional mandates and the voice of the American public it is their duty to serve and protect. I have personally observed the behavior of the CDER committee and experienced the unresponsiveness of FDA senior leadership to direct appeals by national experts. The FDA as currently functioning is opaque, unpredictable, inequitable, and inconsistent in its approach to drug evaluation and approval.

There is an urgency to this. Our patients are losing access to a medication that is saving their lives. And the same denial of timely access to safe and life-altering therapies appears to be happening to many of the 30 million Americans who collectively are living with rare diseases.

I therefore ask Congress, please, help us save the lives of our patients. Use your authority of oversight to require that FDA applies the regulatory flexibility you have legislated, consider real-world evidence, and restore transparency, competence and integrity to the agency.

Thank you again for convening this hearing and for the opportunity to testify.

A handwritten signature in black ink, appearing to read "J. Schmahmann".

Jeremy D. Schmahmann, MD, FAAN, FANA, FANPA



Testimony from Bradley Campbell, President and Chief Executive Officer, Amicus Therapeutics

“From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation”

February 26, 2026

9:30 A.M.

Chairman Scott, Ranking Member Gillibrand, and distinguished committee members:

My name is Bradley Campbell, and for the last 20 years, I’ve worked at Amicus Therapeutics, a Princeton, New Jersey-headquartered company whose mission is to develop and deliver transformative medicines for people living with rare diseases. Since August 2022, I have had the honor and privilege of serving as President and CEO.

I am also a member of the Board of Directors of the Biotechnology Innovation Organization (BIO), the Advisory Board of the Duke Margolis Institute for Health Policy, and the Corporate Advisory Board for the National Tay-Sachs and Allied Diseases Association.

As I speak with you today, I would note that Amicus is in the process of being acquired by BioMarin Pharmaceuticals, but my remarks today are based on my thirty years of experience in drug development, and in particular the twenty years I have spent at Amicus.

Amicus has successfully developed and commercialized three products that treat two life-threatening lysosomal storage disorders. These rare genetic disorders are caused by the body’s inability to break down substances it normally would, leading to progressive, often irreversible, and potentially fatal organ and muscle damage.

These medicines are a small molecule drug chaperone for Fabry disease (Galafold), and a two-component therapy for Pompe disease that combines an oral small molecule enzyme stabilizer (Opfolda) with an infused biologic enzyme replacement therapy (Pombiliti).

I am grateful to Chairman Scott, Ranking Member Gillibrand, and the distinguished members of the Senate Special Committee on Aging for the opportunity to speak today about Amicus’ experience developing medicines for serious and life-threatening rare diseases since our founding in 2002.

I am proud to speak today alongside my fellow panelists Cara O’Neill, rare disease mom and Chief Science Officer at the Cure Sanfilippo Foundation, Annie Kennedy, Chief Mission Officer at the EveryLife Foundation, and Dr. Jeremy Schmahmann, Professor of Neurology at Harvard Medical School.

I would like to thank the many members of the rare disease community who are in the room with us today, and in the Capitol this week, in celebration of Rare Disease Day, and to build on the powerful legacy of the Orphan Drug Act (ODA), passed by Congress in 1983.

Similar to the ODA, the reauthorization of the FDA’s Pediatric Priority Review Voucher program on February 3 is another example of how bipartisan Congressional action, informed by

rare disease advocates, can help drive meaningful advances in rare disease research and drug development. It is critical that we protect and strengthen existing incentives for orphan drug development while we address other regulatory and policy issues.

On behalf of all of us at Amicus, I want to thank the many patients and families in the U.S. and around the world who have made our work at Amicus possible, and to share how their insights have made our work better.

For example, at a recent patient advisory group meeting, we were speaking with Pompe patients about “patient experience data,” and how to make it more quantitative, which, in turn also makes these data more measurable—very salient to today’s discussion of regulatory frameworks.

During a break between sessions, a young woman came up to me and said that while clinical trials in Pompe disease often measure “forced vital capacity,” she depends on a mechanical ventilator to breathe. Therefore, she said, what would truly make a difference in her life was if she could just hold her breath for one minute. Why? Because if her ventilator battery fails, or she falls, or if an aide has to clear a mucus plug from her trachea tube, those 60 seconds could mean the difference between life and death.

That led all of us to reflect on how many breaths we take each day, and how easily we take for granted that the next one will always follow the last.

Her comment remains one of the most profound *and* simple examples of why it is critical to listen to the voice of patients and caregivers in designing clinical trials and regulatory endpoints that reflect what truly matters to the rare disease community.

The core message of my testimony today is straightforward and builds on this insight: the rare disease innovation ecosystem, as currently regulated, and which historically has done so much in supporting the development of new therapies for people living with rare diseases, ***must*** adapt in speed, flexibility, and scale to meet the magnitude of unmet medical need facing American patients.

We cannot ask patients to wait years for new treatments when the difference between life and death can be a single breath.

Working Together to Get Treatments to Rare Disease Patients Faster

To understand why this is true, I would like to share more about Amicus, both our successes and setbacks.

Since our founding in 2002, Amicus has grown from a small start-up into a global organization of more than five hundred team members supporting three approved medicines and the patients who rely on them.

But our success was never a given, and definitely not a straight line.

When we were developing an oral chaperone treatment for Fabry disease (Galafold), we initially planned for it to be used by all adult patients with Fabry. However, our early trials showed that

migalastat worked well for some patients, but not others. Through deeper analysis of trial data and in close dialogue with regulators, Amicus developed and validated an assay that could identify which out of the thousands of known genetic variants were responsive to treatment—and just as importantly, which were not.

The FDA ultimately incorporated this concept of “amenability” directly into the drug’s labeling. The result was Galafold became the first oral precision therapy for Fabry disease, matched to patients most likely to benefit.

This is a concrete example of regulators and sponsors learning together, rather than treating trials as one-shot, binary verdicts. The result is a more convenient oral treatment option that frees a subset of Fabry disease patients from the hours-long burden of bi-weekly infusions and relieves the health care system from the added costs that come from hospital and clinic-based infusions.

The lesson is consistent: innovation is not just about creating new medicines in the lab. It requires working collaboratively with regulators, patient advocates, researchers, and more to build regulatory pathways that are flexible and designed to adapt as they learn—

providing patients and clinicians with novel treatment options as well as more data about how to apply those options to optimize health outcomes for people living with rare diseases.

But as with so many other biotechs, not every Amicus research program developing a novel medicine has crossed the proverbial finish line of FDA approval.

In epidermolysis bullosa (EB), a devastating skin disease, we launched what was at the time the largest ever trial for EB, but promising early data were contradicted in a Phase 3 trial that showed some efficacy but failed to beat placebo on the primary endpoints.

Rather than shelving the data in our archives, we communicated everything we learned with the EB community, including investigators, patient leaders, regulators, and even other companies working in the EB space.

We did this fully and deliberately, so others could build on what we had learned rather than spend scarce resources and precious patient time on ground we had already covered.

Since then, the FDA has approved the first topical gene therapy for dystrophic EB and the first cell-based gene therapy specifically for recessive dystrophic EB—proof that responsible data sharing can help move the whole rare disease community forward.

So, for Amicus, after more than 20 years in drug development, while we now have three approved drugs, we have had many more programs that were discontinued.

Rare diseases are incredibly complex and inherently more difficult to study than more common, better understood diseases. That is one reason why the vast majority of biotech companies fail, and even when they succeed, the time to get to consistent profitability and sustainability is measured in decades, not years. Amicus was founded in 2002 and became profitable only at the end of last year.

Research supported by the U.S. National Institutes of Health (NIH) estimates 95 percent of the 10,000-plus known rare diseases still lack effective, FDA-approved treatments. That means roughly 9,500 rare diseases lack treatment today.

If we keep the current pace of innovation, averaging 31 orphan-designated novel approvals per year across CDER and CBER over the last five years,ⁱ then developing treatments for half of all known rare diseases (~5,000 conditions) would take approximately 161 years.

We know that America's small and mid-size biotech companies are the engine for new medicines overall, and for rare diseases in particular.ⁱⁱ I firmly believe that these companies will be better able to create new medicines, faster, if we adopt more flexible, agile regulatory frameworks and fully harness new tools including artificial intelligence. These approaches should also be harmonized between the U.S. FDA and other advanced regulatory agencies to minimize the collection of data that does not meaningfully advance our understanding of patient safety or product efficacy.

The FDA has reached much the same diagnosis. The creation of the Rare Disease Innovation Hub (RDIH), Rare Disease Evidence Principles (RDEP), and many other FDA programs all acknowledge that conventional drug development paradigms and evidence standards simply do not work for many rare and ultra-rare conditions.

These are all welcome efforts, but we need to transition from meetings and pilots to agency infrastructure to train staff on how to consistently implement novel approaches and best practices, convene external expert working groups to resolve scientific and regulatory bottlenecks, and de-risk promising new biomarkers.

I believe there are three fundamental areas where we need to concentrate our efforts to modernize regulations and make rapid progress without sacrificing patient safety or public health.

A. Start Clinical Trials Faster—Without Lowering Safety Standards

Other country regulators have adopted or are building faster pathways that allow early-phase trials to activate in weeks rather than months. In January 2026, the European Union launched FAST-EU (Facilitating and Accelerating Strategic Clinical Trials) to cap the time to authorization of multinational clinical trials at 70 days.ⁱⁱⁱ Under Australia's Clinical Trial Notification (CTN) system, many trials can begin almost immediately after local ethics approval.^{iv} What these models have in common is that they are shifting early clinical learning, investment, and trial leadership away from the United States. U.S. reforms should:

- Reduce administrative burdens on trial sites and sponsors by standardizing documents and processes, including clinical trial contracts, informed consent, and modular e-consent.
- Enable integration of new artificial intelligence tools to analyze complex datasets and for predictive enrollment, adaptive randomization, and site ID.
- Support single Institutional Review Boards (IRBs), and leverage cloud services to centralize document collection and enable real-time data quality monitoring.

- Expand the use of decentralized and hybrid trials, master protocols and platform studies, RWE and external controls for decision making and remote monitoring.
- Provide Congress with routine reports on rare disease trial transformation that reflect key success metrics.

B. Use Biomarkers and Innovative Endpoints to Assess When Medicines are Working

Policymakers should support and expand FDA's capability to convene stakeholders and design fit-for-purpose biomarkers and endpoints, as well as building internal knowledge management systems that enable reviewers to apply those tools consistently and predictably. This starts with

- Sufficiently funding and staffing the Rare Disease Innovation Hub to convene more public, multistakeholder efforts that prioritize, develop, and operationalize a growing set of reusable endpoints (including composite endpoints) and biomarkers across rare diseases.
- Investing in systematic reviewer training and support so sponsors know that innovative and flexible approaches will be utilized consistently across divisions and centers.
- Harmonizing FDA and EMA expectations for high quality real-world evidence (RWE)—especially in rare pediatric populations—so it can support decisions and, where appropriate, labeling quality.
- Finalize and expand Platform Technology Designation (PTD) to enable carryover of validated assays, analytics, and chemistry and manufacturing control (CMC) elements across platform modalities (including gene therapy and gene editing), with transparent cross-center criteria and routine reporting on PTD.

C. Make Inspections and Manufacturing Rules Work Better for Rare Disease Medicines

For rare and low-volume therapies, manufacturing and inspection can become rate-limiting steps to patient access. To keep pace with innovation and the unique challenges with rare disease low volume products, FDA should:

- Expand the use of Mutual Recognition Agreements (MRAs) with other advanced regulatory agencies and expand the use of Remote Regulatory Assessments (RRAs) to reduce duplicative in-person inspections.
- Streamline foreign facility inspections by using Artificial Intelligence to prioritize risk-based inspections. This would conserve FDA inspection resources for high risk/high priority inspections and share burdens more equitably with other trusted regulatory agencies.

In addition, Congress should pass the Biomanufacturing Excellence Act of 2025 (H.R. 6089 and S. 3188) which directs the National Institute of Standards and Technology (NIST) to establish a National Biomanufacturing Center of Excellence (COE) to advance manufacturing methods to ensure innovative products can move rapidly from clinical to commercial scale.

Conclusion

Let me leave you with one final story. At an Amicus Patient Advisory Board meeting last year, one of our Fabry patient advisors said that he had stopped saving for retirement when he was first diagnosed in his late thirties. What he found online about Fabry disease at the time, was that life expectancy for men with Fabry disease was only into their late fifties.

But advances in treatment for Fabry disease, including earlier diagnosis, and better management of disease complications are extending lives and changing expectations.

That gentleman is now saving for retirement. For him, for the woman with Pompe disease who told us she needed 60 seconds to breathe, for the many patients we have learned from, and even more, around the world—we need to have a regulatory framework that can accelerate bringing these patients new treatments.

Please join me in helping to make a future to look forward to the reality for many more adults, children, and families living with rare diseases, including the advocates standing in this room today.

Thank you, and I look forward to answering your questions.

ⁱ This does not include supplemental New Drug Applications, or supplemental Biological License Applications (sNDA or sBLA). Drugs with Orphan designations are exempt from the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c) requirements... It also does not include label indications for drugs that were originally approved for non-orphan indications. While the total number of available treatments for rare diseases is higher, we believe that counting Orphan Designated approvals is the best way to measure the rate of innovation in rare disease drug development.

ⁱⁱ Biotechnology Innovation Organization. America's Innovation Engine: The Power of Small and Mid-Sized Biotechs. https://www.bio.org/sites/default/files/2026-01/the_power_of_small_and_mid-size_biotechs.pdf

ⁱⁱⁱ <https://www.aifa.gov.it/en/fast-eu>

^{iv} Steyn N, Davis S. *Australia: The Regulatory and Reimbursement Environment*. Third in a three-part series. Parexel; August 28, 2023. Available at: [https://www.parexel.com/application/files/resources/assets/Australia%20Regulatory%20Market%20Access%20Article_Third%20in%20a%20three-part%20series%20\(1\).pdf](https://www.parexel.com/application/files/resources/assets/Australia%20Regulatory%20Market%20Access%20Article_Third%20in%20a%20three-part%20series%20(1).pdf) (accessed Feb. 18, 2026)



Written Testimony of:
Cara O'Neill, MD, FAAP
Chief Science Officer & Co-Founder
Cure Sanfilippo Foundation

Mother of Eliza, age 16, with Sanfilippo Syndrome (MPS III)

On: From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation

Before the: U.S. Senate Special Committee on Aging, February 26, 2026

Chairman Scott, Ranking Member Gillibrand, and Distinguished Members of the Special Committee on Aging:

Thank you for your attention to the urgent, unmet needs of rare disease patients and to the 15 million children affected by rare diseases who are awaiting treatments that would allow them to grow up. I'm honored to provide testimony on behalf of our rare disease community regarding the impact that FDA processes and regulatory actions have on patients' timely access to safe and effective therapies.

My name is Dr. Cara O'Neill, and I am the Chief Science Officer and Co-Founder of [Cure Sanfilippo Foundation](#). Cure Sanfilippo Foundation is a U.S. nonprofit dedicated to accelerating scientific development and access to a cure or therapeutic options for all affected by Sanfilippo Syndrome, driving advocacy to improve care and outcomes, and empowering families with information, guidance, and support to navigate the journey. My daughter, Eliza, is also personally affected by this ultra-rare, neurodegenerative disease, also considered a form of 'childhood dementia' or 'childhood Alzheimer's'.

While there have been advancements in rare disease policy and legal statutes over the past two decades, significant opportunities remain to address the desperate needs of 95% of the rare disease population, who still lack approved therapies. FDA review teams and leadership have tremendous responsibility and conduct complex work across thousands of disease states.

Recently, a renewed focus on FDA modernization has set forth a vision of positive change. Additionally, FDA leadership has announced several new policies and programs, including the Rare Disease Evidence Principles and, most recently, the Framework for Accelerating Development of Individualized Therapies for Ultra-Rare Diseases. We commend these efforts to add to existing expedited frameworks for drug development in rare diseases with small patient populations.

These emerging policies and programs, however, are not currently poised to help existing late-stage drug development programs and those under current review reach deteriorating patients within the urgent timeframe needed. Many rare disease communities, like ours, are at risk of losing therapies that are already demonstrating substantial benefit.



This is most evident for those with degenerative diseases, where time is the most-critical factor in accessing treatment. Due to the progressive and devastating nature of these conditions, regulatory practices must leverage every available flexibility authorized by Congress to prevent further irreversible disability and early death.

In the following testimony, you will find real-world stories about the impact of delayed time-to-treatment access in Sanfilippo syndrome (mucopolysaccharidosis type III or MPS III), a form of childhood dementia.

Time: The Most-Critical Factor in Pediatric Neurodegeneration

The impact of timely access can be seen in the lives of three children, all diagnosed with the same deadly form of childhood dementia, but with very different outcomes.

Izzy was 11 years old when we first met, shortly after our daughter, Eliza, was diagnosed with the same disease, Sanfilippo syndrome (MPS III). Izzy could no longer walk independently and had lost the ability to speak years earlier. She could no longer eat or drink by mouth without choking, requiring tube feedings for her nutrition. She suffered from seizures and movement disorders that twisted her arms and legs into painful positions.

Sanfilippo syndrome is caused by single-gene mutations that result in the accumulation of toxic levels of heparan sulfate, leading to progressive and irreversible brain damage.

During one of our visits, Izzy's mother shared that she had come to accept that the disease would take her daughter's life. But what she said next has always stuck with me:

"I fear her suffering more than I fear her death."

At that time, my daughter Eliza was around four years old and in the extremely hyperactive stage of the disease. But she still sang and talked with us. She played dress-up and clopped around the house in my high heels. She rode her tricycle everywhere. She looked healthy, but we knew that the disease was continuing to damage her developing mind and body.

Meeting Isabel put us face-to-face with Eliza's future: the concrete and cruel reality that lay ahead if she could not receive a treatment.





For Izzy, a treatment didn't come in time. Heartbreakingly, she did suffer a great deal before passing away just weeks before her 15th birthday.

We know exactly what causes the disease. We can precisely measure the levels of the toxic biomarker (heparan sulfate) to determine whether a treatment is working. And now, we have ways to treat it.

Thanks to NIH funding and support from non-profit foundations, including our own, a promising gene therapy was developed and propelled towards a clinical trial at Nationwide Children's Hospital in Ohio. Parents like us anxiously awaited news of the trial opening.

During this time, we noticed that Eliza's sentences were becoming shorter and her words were becoming less frequent. She was becoming more agitated and hardly slept. The disease was taking hold.

In May 2016, the trial finally began. Eliza, by then six-and-a-half years old, was able to receive the gene therapy at the first starting dose. We felt so lucky that she would have a chance at a future different from Izzy's; a chance to grow older and be healthy.

Now, at age 16, it's clear that the treatment changed Eliza's life. Surpassing average life expectancy, she can run on the beach and play in the water. She uses picture cards to tell us how she's feeling, and what show she wants to watch on TV. She can use a fork to feed herself and goes to school every day. Simple, but incredibly-meaningful abilities that have a positive impact on her everyday life.

Children, like Caroline, who were treated at an even earlier age and with a higher dose, have demonstrated even more remarkable outcomes. Now, at 10 years old, Caroline can read books, is on a softball team, has playdates with her friends, and even learned to ski on her family's vacation last week!

An entirely different future is in store for the few children who were able access treatment in the clinical trial. But despite these breakthroughs, and nearly a decade since the trial first began, children outside of the trial are still waiting for access - all while continuing to suffer more brain damage, month by month.

Last summer, patients' hopes were dashed when the drug was denied approval - not for safety issues or concerns about how the children were responding to the treatment, but because of questions about the manufacturing process. While an important issue, a flexible regulatory approach could have allowed the application review to proceed while addressing any outstanding questions in parallel.

Data early in the trial confirmed that the drug's mechanism was not just plausible; it is undeniably biologically effective. The levels of toxic biomarker (heparan sulfate) dropped significantly just six months after treatment in all the children. Earlier use of



Accelerated Approval based on the scientifically-sound biomarker would have changed the lives of so many children.

After being resubmitted, the clock was stopped again when the FDA requested additional paperwork before agreeing to proceed with the review.

Unfortunately, this is not an uncommon story across the rare disease community, with other diseases and conditions experiencing similar non-approvals despite strong evidence.

Congress's vision of speeding approvals for serious conditions through regulatory flexibility and the enactment of laws to enable this objective is simply not being realized for most rare disease patients and children suffering from progressive, debilitating diseases.

Transformative therapies are on the FDA's doorstep, and others are moving through the pipeline. Respectfully and sincerely, patients and their families ask decision-makers at the FDA to unlock the door.

Sanfilippo Syndrome (MPS III)

[Sanfilippo syndrome](#), or mucopolysaccharidosis type III (MPS III), is a group of four devastating, rare genetic disorders causing progressive neurodegeneration and other debilitating multisystemic effects in children. Single-gene mutations lead to insufficient production of the enzyme needed to properly break down the naturally-occurring molecule heparan sulfate.

Toxic amounts of heparan sulfate accumulate, causing severe and irreversible brain damage, particularly during the sensitive neurodevelopmental periods of early childhood.

While seemingly typical during the first couple of years of life, children go on to experience broad cognitive regression and loss of basic skills such as the ability to talk, walk, and eat by

PROGRESSION OF SANFILIPPO SYNDROME (MPS III)

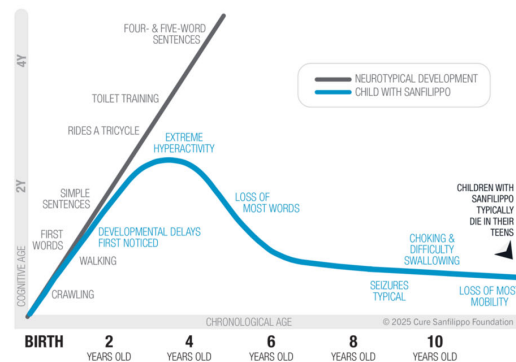


Figure represents studies of disease impact in rapidly-progressing forms of Sanfilippo Syndrome.



mouth. Over the ensuing years, these children suffer many other disease-related symptoms, including seizures, movement disorders, autism, significant behavioral and sleep disturbances, hearing and vision loss, and, in the most-common form of the disease, have an average life expectancy of just 15 years.

There are no FDA-approved treatments for any form of Sanfilippo syndrome.

Regulatory Flexibility is Essential in Rare Disease Drug Development

Over the past four decades, Congress has codified the FDA's authority and obligation to exercise regulatory flexibility for serious and life-threatening conditions and rare diseases. These regulations highlight several key provisions:

- 1) The development of medicines for rare diseases requires modified frameworks and innovative trial designs;
- 2) The FDA has the authority to use flexible evidentiary standards;
- 3) The FDA has been directed to consider disease severity and unmet need when evaluating benefit-risk; and
- 4) The FDA has been directed to incorporate patient perspectives.

In 2025, rare genetic neurodegenerative disease programs experienced a marked increase in Complete Response Letters (CRLs), an official communication from the FDA to a drug sponsor indicating that the review cycle for a marketing application (NDA, BLA, or ANDA) is complete, but the product cannot be approved in its current form.

Our analysis of publicly-available FDA data and sponsor disclosures identified seven CRLs and only two approvals for these rapidly-progressive conditions, compared with four approvals out of five applications in the prior year. Many of the affected programs were pursuing Accelerated Approval.

The deficiencies cited in the CRLs raise the question of whether the FDA is indeed using its regulatory flexibility in rare diseases. In 2025, CRLs increasingly emphasize trial design and evidentiary rigor over well-established, disease-causing biomarkers, such as heparan sulfate in MPS disorders. In ultra-rare, heterogeneous diseases with very small patient populations, trials will never resemble those conducted in common diseases. Requiring perfection in such settings risks denying progress altogether.

Increased Utilization of Accelerated Approval is Needed

Key Congressional legislation created the Accelerated Approval pathway, enabling regulatory flexibility in the evaluation of treatments for serious, life-threatening conditions. While the Accelerated Approval pathway is not exclusive to rare diseases, it is well-suited to address the needs of serious and life-threatening rare diseases. However, to date, 80% of drugs approved under Accelerated Approval have been for cancer



therapies. Based on an internal analysis of the last two years, only 12% of non-cancer rare diseases received approval via this accelerated pathway.

There remains a gap between therapies that demonstrate biologic plausibility and a regulatory system that struggles to translate that plausibility into timely, consistent decisions. Recent FDA statements and draft guidance acknowledge the mismatch between standards appropriate for common diseases and those feasible in ultra-rare conditions. Draft guidance is an important step. However, meaningful impact will depend on consistent implementation of both existing statutes and new initiatives. Regulatory flexibility must be applied not only in theory, but in practice.

The Accelerated Approval pathway, as codified in 21 CFR 314 Subpart H and 21 CFR 601 Subpart E, expressly permits FDA approval based on surrogate endpoints, such as biomarkers or intermediate clinical endpoints, that are reasonably likely to predict clinical benefit.

The use of biomarkers is an essential approach to achieving FDA approval for conditions that do not fit traditional drug-development frameworks.

Acceptance of heparan sulfate as the primary disease-causing biomarker for Sanfilippo syndrome (MPS III) and other forms of neurologically impairing MPS (MPS I, II, VII) reached [consensus](#) through a [scientific convening of the Reagan-Udall Foundation for the FDA](#) in February 2024. Key opinion leaders affirmed that:

- Elevated heparan sulfate is the primary pathologic cause of disease.
- Natural history data demonstrate a predictable pattern of cognitive decline.
- Changes in cerebrospinal fluid (CSF) heparan sulfate levels are reliably measurable and reasonably reflect brain tissue heparan sulfate accumulation.
- A reduction in heparan sulfate levels reflects the biological activity of drugs targeting the primary disease mechanism.

Manufacturing Process Flexibility

Regulatory flexibility must extend beyond clinical trial design to all aspects of the review, including Chemistry, Manufacturing, and Controls (CMC). CMC requirements for gene therapies are inherently complex and manufacturing processes evolve and require refinement over time.

In the case of a Sanfilippo syndrome gene therapy and a number of other rare disease treatments, letters denying approval (CRLs) or communications delaying regulatory processes cited only CMC concerns, not safety or efficacy concerns. Dosing of patients in the Sanfilippo gene therapy clinical trial was allowed to continue, reassuring that the agency continued to consider the drug product safe for use in children. Despite established safety, the path towards approval is currently on hold again as the agency requested additional paperwork that is typically reserved for review during the



time of on site inspection. Timelines that are delayed due to administrative burdens further limit children's access to treatment, leading to more neurological damage.

Product safety and consistency are essential, however, Congress recognizes that therapies for life-threatening diseases may require a flexible, risk-based approach. This includes post-approval commitments to address manufacturing questions. When therapies demonstrate promise in progressive diseases, we must allow regulatory flexibility in CMC reviews to prevent delays in getting treatments to children.

Trial Designs that Delay Treatment Lead to Irreversible Brain Damage

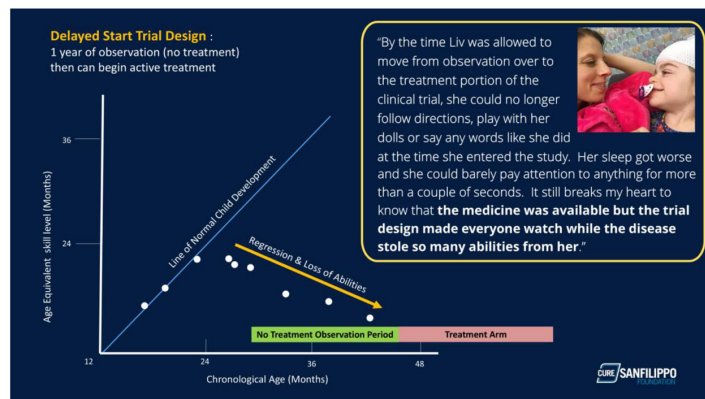
Cognitive decline and neurodegeneration are central features of many pediatric rare diseases, including Sanfilippo syndrome. Brain development unfolds within well-defined, time-sensitive windows from early childhood through adolescence. During these critical periods, exposure to toxic substrates, such as heparan sulfate, has particularly harmful and irreversible effects. In Sanfilippo syndrome and other neurological MPS diseases, continued accumulation of heparan sulfate toxin directly damages the central nervous system.

The FDA has appropriately acknowledged that traditional, large, randomized-controlled trials are often infeasible in very small patient populations. Yet sponsors of ultra-rare pediatric programs continue to report regulatory requirements for randomized or "no-treatment" comparator arms, even in progressive neurodegenerative conditions. In practice, this means some children are knowingly assigned to sustained periods without therapy, during which irreversible brain injury will certainly occur.

When a primary disease-modifying therapy is responsive to a scientifically-sound biomarker for a neurologically progressive condition, innovative trial designs are an ethical necessity. External comparators, adaptive designs, patient-as-their-own-control, and biomarkers as surrogate endpoints can provide rigorous data for efficacy evaluations while minimizing preventable harm. In diseases in which neurons are lost daily, clinical trial design must adhere to both scientific standards and the biological reality of irreversible decline.

Consider a little girl from Pennsylvania named Liv. In a previous clinical trial, the protocol required an observation period of one year during which children were not given treatment, prior to them being switched over to the treatment arm of the trial. During that year while awaiting treatment, Liv suffered irreversible developmental regression.

Today, similar programs targeting neurocognitive disease symptoms face requirements for randomized control arms in small pediatric neurodegenerative disease populations.



**Image depicts Loss of cognitive abilities during the delayed start period of an enzyme replacement clinical trial.*

Importance of Patient Representation in Drug Development & Regulatory Review

The 2012 reauthorization of the Prescription Drug User Fee Act (PDUFA V) formally advanced the concept of Patient-Focused Drug Development (PFDD), signaling Congress’s intent that patient experience be systematically integrated into regulatory decision-making. In 2016, Congress enacted the landmark 21st Century Cures Act, which further codified PFDD into the FDA’s statutory framework, reinforcing that patient input is not optional but core to the agency’s mission. Since that time, patient organizations and advocates have become increasingly engaged in drug development activities, and the practice of PFDD continues to be adopted more widely.

Meaningful patient engagement strengthens regulatory science across the continuum of drug development. Patients and caregivers bring uniquely-valuable, disease-specific, lived experience necessary to inform study feasibility, treatment targets, degree of change constituting meaningful benefit, realistic risk tolerance in life-threatening conditions, and broader risk/benefit considerations.

FDA has made progress in developing and hosting patient engagement efforts such as the [Patient Engagement Collaborative](#), internally and externally-led PFDD meetings, and Listening Sessions. It is unclear whether [FDA’s Patient Representative Program](#) is still active, or to what extent representation is filled in rare disease review divisions. Further, a reduction and halting of product-specific advisory committee meetings has occurred.



Additional Opportunities to Integrate Patient Representative Insight

- 1) **Re-prioritize advisory committees:** Advisory committees provide a transparent venue for scientific dialogue among key stakeholders. These are typically public forums and provide a window into complex regulatory decisions. Last year, the number of ad-coms decreased substantially. Integrating patient/caregiver perspectives and real-world expertise into scientific discussions allows decision-making to be rooted in the primary goal of public benefit while also providing important case example learnings for the entire drug development community.
- 2) **Revive and/or expand FDA's Patient Representative Program or councils:** Revive and/or expand formal, standing councils of trained patient representatives to engage with FDA review divisions on an ongoing basis. These councils could provide rare disease-specific insight into lived experience, trial feasibility, acceptable risk, and what constitutes meaningful benefit from the patient perspective.

Unlike one-time listening sessions, these councils may operate longitudinally, allowing for structured, bi-directional engagement through the development lifecycle (e.g., early trial design, endpoint selection, and post-approval or CRL). This would build on, but not replace, other PFDD initiatives by moving from one-time input to continual partnership. Working through the Rare Disease Hub would allow focused coordination to serve the rare disease community.

The Economic Reality of Ultra-Rare Drug Development

There are currently no approved treatments for any type of Sanfilippo syndrome, despite the disease being discovered in 1963. In ultra-rare diseases, early medical research and even clinical trials are often partially funded by family efforts - lemonade stands and 5K races - to support non-profit advocacy foundations funding research. NIH funding is also instrumental in supporting basic and translational steps needed to reach the point of a clinical trial. In recent years, NIH has created critical clinical trial funding sources, though these are limited.

Moving basic science to a clinical trial requires many millions of dollars. In rare diseases with very small populations, large pharma is often not interested due to the complexities, uncertainty, and limited returns involved in rare disease drug development. Therefore, companies involved in rare disease are often small, startup biotechs.

Over the last 10 years, we've seen eight promising Sanfilippo syndrome therapeutic programs abandoned. Many of the companies developing these drugs cited the financial burden of extended, uncertain regulatory timelines and pathway as reasons for shelving promising treatments. A number of these companies have gone out of business while attempting to maintain

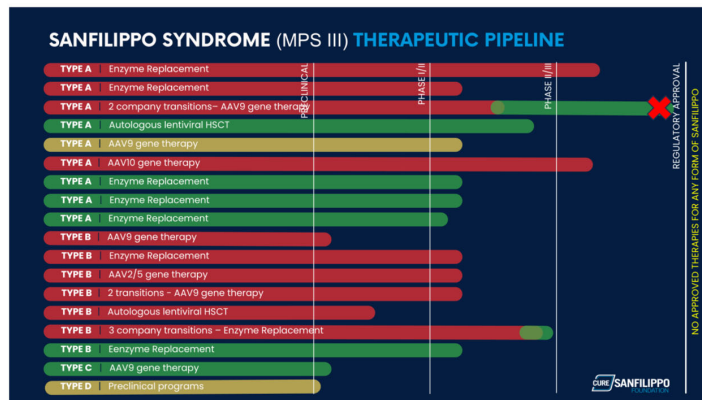


their programs in Sanfilippo. Shifting regulatory opinion on study comparator arms, study design, and recognition of meaningful surrogate biomarker change lead to further uncertainty among investors and companies.

Parents have watched their children stabilize and continue to grow and learn while receiving treatment in clinical trials, only to have that promising treatment taken away. Most of these children never get access to another treatment.

Sanfilippo syndrome is not an isolated case. Many rare disease programs face similar obstacles. Small biotechnology companies, which develop the majority of ultra-rare therapies, often cannot withstand prolonged regulatory uncertainty, shifting evidentiary expectations, or extended review timelines.

Without FDA's greater use of flexibility, consistency, and transparency, we will continue to see companies turn their backs on rare disease drug development.



* Image depicts Sanfilippo syndrome therapeutic landscape



Proposed Actions and Conclusion

We commend FDA leadership for their numerous public statements supporting rare disease treatments and for developing new initiatives, such as the Rare Disease Evidence Principles and draft guidance for individualized therapies. While new programs are welcome, Congressionally codified programs already exist that offer the regulatory flexibility required to advance urgently-needed therapies and can be utilized to address the needs of patients today.

We respectfully request Congressional oversight to ensure consistent application of existing statutory flexibility:

1. **Use Accelerated Approval as Congress intended.** When a treatment clearly improves the underlying biology of a fatal rare disease, approvals should enable timely access before further irreversible disease progression.
2. **Increase acceptance of innovative trial design in rare diseases** where large or randomized trials are not feasible or ethically appropriate.
3. **Apply flexibility across all aspects of the rare disease review process**, from trial design to biomarkers to manufacturing.
4. **Provide clear, consistent expectations early in development** to build trust that regulatory opinion and guidance will not shift in later development stages.
5. **Increase transparency across the FDA review process** by integrating the patient representation into all aspects of drug review and reprioritizing advisory committees.

In children with progressive neurodegenerative diseases, biology does not wait for policy implementation, administrative refinement, or prolonged debates over biomarkers. These conditions move forward every day. Brain cells die. Abilities are permanently lost.

We are not asking for lower standards. We are asking that the standards and flexibility Congress has already authorized be applied consistently, transparently, and proportionately in the context of ultra-rare, life-threatening disease. Regulatory flexibility, including Accelerated Approval and use of biomarkers, are not concessions; they are tools deliberately created for situations where traditional development paradigms do not fit.

Please accept our gratitude to this Committee for elevating the unmet needs of patients suffering from rare diseases. We hope that you will continue your support in ensuring that the regulatory framework already in place is used with clarity, consistency, and urgency. For children facing irreversible neurodegeneration, time is the most precious and limited resource. Our shared responsibility is to close the gap between scientific possibility and regulatory execution so that no child is left waiting for a therapy that could alleviate suffering and save their life.

"You have the power to move with urgency. Please do not make families like mine wait while our children disappear in front of us. Because while you are deciding, I am watching my son disappear." - Beckham's father from Georgia

More comments from families of children with Sanfilippo syndrome in the **Appendix** below.

Appendix: Family Comments



Below are comments provided by parents of children with Sanfilippo syndrome (February 2026)

What does time mean for you and your child with Sanfilippo syndrome?

A delay of 6 to 12 months means losing parts of my son that I will never get back. Every single second matters for Beckham. Not months. Not weeks. Seconds. I have already watched him lose so much in such a short period of time. He used to sing in the car. Now there is silence. He used to talk. Now the only word he consistently says is "daddy." And I live with the fear every single day that one day, he will stop saying it. I won't know when the last time was. I won't be prepared for it. It will just be gone. That is what time does to children like Beckham.

A delay of 6 to 12 months means 6 to 12 more months of watching my son slip away from me. It means more moments where he seems lost. More moments where he cannot communicate. More moments where I see pieces of him disappear.

It means his brothers losing their little brother piece by piece. It means our family living with the pain of watching someone we love fade in front of our eyes while we wait for help that may come too late.

Every second matters because every second is time I may never get back with my son as he is today.

A delay is not just time on paper.

It is time that this disease uses to take my son from me.

Brandon Hutcheson, Georgia
Child: Beckham "Bex" Hutcheson, age 4

Time is not on our side with Sanfilippo Syndrome. With each moment that passes, more brain damage occurs. Delays of six or 12 months or so means that Simon loses more words, more cognitive ability, and more memory. It means that Simon's neuromuscular scoliosis, avascular necrosis, and bilateral sensorineural hearing loss worsen. Resulting pain, agitation, and hyperactivity increase. Inflammation and oxidative stress continue to drain the light from our Simon's beautiful face. Sadness and confusion take over as he loses his abilities to count, spell, identify colors, dance, and run.

Alina Gorniak, Texas
Child: Simon Croke, age 9



Since FDA delay of UX 111 in July 2025, Lottie has already lost many more ASL signs and word approximations. Lottie no longer uses any ASL sign or sound consistently. Lottie has forgotten several songs that she used to get excited for. A delay of six more months will most likely mean that Lottie will need a G-tube, we anticipate seeing fewer laughs, and we believe we will continue to see a decline in her receptive skills as well.

Abby Milburn, IL
Child: Lottie, age 5

Delays mean that my daughter Veda can no longer speak. She doesn't color anymore or dance and sing to her favorite songs. Her body is starting to slow down and I see my daughter fading when I look into her eyes. I don't want this to happen to other families. Our children need a treatment when they are born, not when Sanfilippo has already started to steal them away.

Christin Ulrich, Florida
Child: Veda Ulrich, age 6

In just 6 months, Jacob has lost his ability to eat solid foods without struggling through each bite. It takes Jacob an hour to eat dinner. Eating is one of the things that Jacob has always enjoyed, and something as a family we have always celebrated. He is also much less mobile. While he attends our local high school in a special program, he is not as actively involved as he was just last spring.

Christine Moon, New York
Child: Jacob Moon, age 16

Time, for our family, is not measured in years. It's measured in windows. Our son Emmett has Sanfilippo Syndrome, a progressive and terminal neurological disease. He has not started seizures yet. He is still gaining some skills. He still has some words. But we are seeing the slowing, fewer words, subtle physical decline. We know what comes next. A delay of 6 or 12 months is not a minor setback for children like Emmett. Six months can mean lost brain cells that cannot be recovered. Twelve months can mean the difference between treating a child who is walking and talking and one who no longer can.

Stephanie McCabe, Saskatchewan, Canada
Child: Emmett Doucette, age 6



My name is Ashley, and I am the mother of Sadie, who has Sanfilippo syndrome, a progressive and fatal neurodegenerative disease.

At this stage, Sadie is actively losing skills. Over the past 2 years, she has lost most of her speech, memory and had a significant cognitive decline. These losses are permanent.

A 6–12 month delay in treatment is detrimental—it results in irreversible decline. During that time, children like mine can lose communication, cognitive function, and the ability to safely engage with the world. By the time a treatment becomes available, it may be too late for it to provide meaningful benefit.

For our children, a delay is not just time—it is loss.

Ashley Haywood, NC

Child: Sadie, age 9

Further decline of cognitive abilities & functional abilities like speaking, eating/drinking, and ambulation

Krystal Cooley, SC

Child: Dawson, age 7

Time, for us, is not measured in years. It is measured in losses.

Sanfilippo Syndrome is progressive and unforgiving. Every 6 or 12 months of delay means more skills lost, more regression, more pain, more sleepless nights, and fewer abilities my children may ever regain. It means watching communication fade, mobility decline, and personality slowly disappear.

For most families, a year is time to plan. For us, a year can mean the difference between walking and not walking, speaking and never speaking again. Delays are not administrative, they are irreversible.

Soraya, Al Chouf Baakleen Lebanon

Children: Sama Chaaban and Aram Chaaban

They are just losing their capabilities, skills and health... until they get disabled or die after just because there is No cure for Sanfilippo type A syndrome

Khaled Chaaban, Lebanon

Children: Sama Chaaban & Aram Chaaban



With Sanfilippo syndrome, time is on our side. A six-month delay can cost a child the ability to speak, and a year the ability to move. For us, time isn't an abstraction, but rather concrete, lost skills that cannot be regained. Every month of waiting reduces the chances of effective therapy and increases the burden on the family. We don't ask for time; we fight for it, because for our child, every day counts.

Eugenia Sotnikova, Novosibirsk city, Russia
Child: Alexandr Sotnikov, age 7

FDS delays will cause further regression and cognitive delays for individuals with sanfilippo syndrome. The accumulation of toxic heparin sulfate continues to cause significant damage each and every day. The future for my two daughters is very uncertain. Seizures may return, language may be lost, motor skills will diminish and quality of life will deteriorate for Margaret, Bridget and our whole family.

Kathy Lindquist, New York
Children: Bridget & Margaret Lindquist

He will lose the ability to talk and can't make any progress

Astrid, Germany, Bavaria
Child: Charlie, age 4

Bir aylık gecikme bile bizim için çok uzun bir süre (Even a one-month delay is a very long time for us.)

Mehmet vural, Türkiye
Child: Zeren, age 6

Leni is just two years old and full of love, laughter and life. She has not yet experienced the regression, brain damage, and very worst symptoms of Sanfilippo Syndrome. If she is able to access treatment before this begins (usually around 3 years old) she has the chance of a near normal life. Once the regression begins it cannot be reversed. Sanfilippo Syndrome is rapidly neurodegenerative and relentless. A delay of 6 months could be the difference between our sweet girl losing her ability to talk or not, and a delay of 12 months could be the difference between her losing her ability to walk or not. Sanfilippo Syndrome does not respect approval



timelines, these children need treatment now to give them the best possible chance at life - they can't wait. Delays also have a huge mental impact on the parents, families and loved ones of these children. We are advocating tirelessly for Leni to get access to treatment before it is too late. It is exhausting fighting for your child's right to live every single day and shifting timelines are absolutely heartbreaking when the impact of this is so catastrophic. Every day that Leni cannot access treatment toxic waste builds up inside her tiny body. We are watching her grow and develop into a beautiful little human with the haunting knowledge that if she is unable to access treatment and quickly she will lose everything, including her life. Time is precious, and time is our enemy.

Emily Forrester, Kent, UK
Child: Leni Forrester, age 2

Time is everything! 6-12 months could result in loss of skills, new medical issues, and the potential for a medication to now not be effective when it could have made a meaningful difference would it have been administered sooner.

Lauren Barber, Michigan
Child: Autumn Barber, age 7

Time is scarce with Sanfilippo. We know that the earlier Louisa can get access to a therapy or a clinical trial the better and greater the chances are for her to progress positively and not to lose skills. Time is also scary with Sanfilippo as since the diagnosis, the disease feels like a Sword of Damocles hanging over our family, it feels like a race against time. 6 months or 12 months feel like an eternity now.

Lennart Sieweke, Potsdam, Germany
Child: Louisa

Right now, Lydia has no regression. The next 6 months are crucial for her as it's the expected to begin to decline with far more brain damage taking away her quality of life. There are treatments & science out there that give these children a better quality of life, that will be filled with pain & suffering without it. It's our only chance of hope for our child.

Morgan Rachal, Louisiana
Child: Lydia Rachal, age 3



Frankie used to wake up every morning singing. She was full of joy, energy, humor, and affection. She had rich language, spoke in sentences, loved to sing, and even had funny jokes. She gave the most amazing running hugs. It only took Sanfilippo Syndrome 3 months to take it all. Over the course of 3 months, all of Frankie's words and songs were taken. She didn't know how to engage in play anymore, and she struggled to pick up a toy. She could no longer feed herself independently. She used to climb rock walls, and then she struggled to know what to do on a playground. At 5 years old, Sanfilippo Syndrome stole our daughter and in just 3 months. To us, 6 or 12 months means everything.

Gabrielle Price, Washington
Child: Frankie Price, age 6

Looking back 6 months is looking at a different child of mine. Looking back 12 months makes the difference even more stark. In 6 months, my child has lost her ability to communicate even more so than she did over the previous 6 months. She continues to grow in discomfort and what seems like pain as the disease continues to progress throughout her body. Delays of any kind mean simple experiences with her now could be taken away permanently.

Andrew Price, Washington
Child: Frankie Price, age 6

Living with Sanfilippo Syndrome means living against a clock that never stops ticking. While other families plan for the future in milestones gained, we brace ourselves for milestones slipping away. Time is not something we take for granted — it is something we fight for. Six months may not sound like much in the world of drug development, regulatory timelines, or funding cycles. But for our child, six months can mean:

- the difference between speaking in sentences and struggling for words
- the difference between walking independently and needing support
- the difference between sleeping through the night and relentless exhaustion
- the difference between understanding us and slowly drifting away

Twelve months can mean even more. It can mean losing skills that will never come back. It can mean further cognitive decline. It can mean more seizures, more behaviors, more regression. It can mean watching your child change in ways no parent should have to witness. For families like ours, delays in research, clinical trials, or funding are not abstract timelines. They are lived in real time. They are birthdays passed. Holidays changed. Abilities fading. Time is everything.

Christiane von Rosbitzki, Germany/Hessen/Rödermark
Child: Theresa von Rosbitzki, age 4



Time for a child with Sanfilippo is not abstract. It is physical. It is visible. It is measurable in lost words, lost abilities, lost moments. My daughter Payton was diagnosed at age five. She is eight now, and every day we watch pieces of her slip away. Time is not neutral for families like ours—it is a force that actively harms our children.

A six-month delay in access to a therapy for most conditions might be frustrating. For Sanfilippo families, six months can mean the difference between a child still being able to walk independently or not. A year can mean losing the ability to speak, to feed themselves, to sleep through the night, to recognize loved ones. These are not hypothetical possibilities; for us, they are the reality of the disease's trajectory.

When we hear "six months," we do not think of a bureaucratic interval. We think of six months of skills eroding. Six months of watching Payton's world shrink. Six months closer to losing abilities she will never get back. Six months of our family grieving in advance for what Sanfilippo will take next.

Twelve months feels like an entire chapter of her life that could have been lived differently—with more comfort, more connection, and more dignity—if safe and effective therapies were accessible when they are ready instead of after prolonged, unintended delays. For us, time is not just precious; it is life-altering. Delays take from our children what no therapy can restore.

Ally Geronzin, Arizona
Child: Payton Geronzin, age 8

I watched my daughter lose her ability to communicate in a 4 month span, -going from saying, "Mom, come on" to nothing. Currently, she loves food and is still able to eat and she loves to run and is still mobile. Those skills could easily slip away in a few months without treatment.

Rebecca Jordan, Ohio
Child: Liv Jordan, age 11

Loss of words, increasing headaches and aggression, loss of mobility, worsening gi issues, toileting accidents. His personality is fading with every passing day.

Nancy Rubino, Massachusetts
Child: Merrick Rubino, age 11



What does a chance at a better quality of life look like for your child and your entire family? What would be different in their and your lives?

A better quality of life means I don't have to keep watching my son drift further away while I stand there unable to reach him.

There are moments now where I look into Beckham's eyes, and I don't know if he fully understands or recognizes what's happening around him. I talk to him, and I don't know if he can respond the way he wants to. I see him struggling, and I see the frustration in him. And as his dad, there is nothing more painful than knowing he's still in there, but I can't fully reach him anymore.

A better quality of life means he doesn't have to live in that place of confusion. It means he can feel comfort instead of frustration. It means he can feel safe, peaceful, and connected to us instead of slowly slipping further away.

It means his brothers don't have to grow up watching their little brother lose more of himself. They deserve to have real moments with him. They deserve to hear his voice, see his smile, and feel like their brother is still there with them—not just physically, but emotionally.

For our family, it would mean relief from the constant heartbreak. Right now, every day feels heavy. Every day feels like we are waiting for the next piece of him to be taken. A better quality of life would mean fewer of those losses. It would mean more peace for him and more peace for all of us.

It would mean Beckham could live with comfort, dignity, and love, without this disease continuing to take more from him than it already has.

He has already lost so much. A better quality of life means he doesn't have to lose everything.

Brandon Hutcheson, Georgia

Child: Beckham "Bex" Hutcheson, age 4

A clinically proven treatment would mean that the progression of his disease would slow. He'd be in less pain, experience less agitation, and hyperactivity. Simon would hold on to the skills that he worked so hard to achieve like playing basketball, putting together floor puzzles, and building with blocks. Our family's lives would be filled with more joy and happiness than stress, anticipatory grief, and heartbreak.

Alina Gorniak, Texas

Child: Simon Croke, age 9

Currently, Sanfilippo syndrome affects all parts of our lives. Lottie is the oldest of our four children. Her younger siblings even are one year-old are all more independent and less in need



of the constant monitoring that Lottie is in need of. In general simply syndrome hangs over our family like a dark cloud. Some days the grief is already so immense it makes doing any mundane activity astronomically hard.

Better quality of life for Lottie could mean so many things. One improvement would be getting to independently feed herself safely and for a longer period of time. Another improvement to her quality of life would be better sleep so that she experiences less daytime, exhaustion, and is able to have more fun with her younger siblings and to just be a kid. In general, if Lottie could receive treatment of some kind, I think that it would relieve some of the heaviness that we have felt since receiving lots of diagnosis and overall improving the quality of life for our entire family.

Abby Milburn, IL
Child: Lottie, age 5

Our daughter can't tell us where her pain is. With earlier treatment we might have been able to keep her speech so she could tell us where she is having pain. Now we have to rely on body language to figure out where she is hurting. Nothing is worse than the helpless feeling of hearing your child cry and not knowing what is wrong or how to help.

Christin Ulrich, Florida
Child: Veda Ulrich, age 6

Jacob was diagnosed on the "late" side. He was 7. I always say how ridiculous at 7, it was a late diagnosis, but in this world it was late. Our entire focus for Jacob has been maintenance. We are extremely lucky to have a support team that understands the importance of maintaining all of Jacob's skills. So for Jacob to continue to maintain his voice, his mobility, his ability to participate in everything his family and friends do are vital. If Jacob's sleep could improve everyone's quality of life would improve!

Christine Moon, New York
Child: Jacob Moon, age 16

It means fewer sleepless nights because his brain is calmer.
 It means less pain and discomfort he cannot explain to us.
 It means preserving the words he still has — or even gaining a few more.
 It means holding onto his ability to walk, to laugh, to engage with his sister.



Right now, we live in anticipation of decline — seizures, loss of mobility, loss of communication. A better quality of life means slowing that progression. It means giving him more time as the child he is today.
For our family, it would mean breathing a little easier.

Stephanie McCabe, Saskatchewan, Canada
Child: Emmett Doucette, age 6

For my child living with Sanfilippo syndrome, a better quality of life would mean less pain, more consistent sleep, and the ability to hold onto the skills they still have.
It would look like being able to communicate basic needs instead of crying in frustration. It would mean fewer behavioral challenges driven by discomfort they cannot express. It would mean moments of connection that last longer—recognition, interaction, and engagement with the world around them.
For our family, it would mean stability where there is currently constant decline. It would mean fewer sleepless nights, less medical and safety crisis management, and more time simply being present together.
A chance at better quality of life does not mean expecting a cure. It means preserving what is still there for as long as possible—and reducing suffering in the time we have.
That would change everything.

Ashley Haywood, NC
Child: Sadie, age 9

It breaks my heart to see my child hurt or struggle in school and at home with ADLs so anything that helps would improve our families quality of life. We want our kids to have a normal life and experience all the things other kids get to experience

Krystal Cooley, SC
Child: Dawson, age 7

A better quality of life would mean less suffering, less neurological pain, better sleep, fewer behavioral crises, and the possibility of preserving the skills my child still has.
It would mean hearing their voice longer. Seeing them hold onto the ability to recognize us. Having moments of connection that are not overshadowed by decline.
For our family, it would mean living with hope instead of constant anticipatory grief. It would mean being parents again not just caregivers managing degeneration. It would mean stability, dignity, and the chance to build memories that are not defined by loss.



Soraya, Al Chouf Baakleen Lebanon
Children: Sama Chaaban and Aram Chaaban

Their life is essentially changing from a happy kid to sadness and dullness since they are losing almost everything. Walk, chewing, focusing, speaking and their senses.

Khaled Chaaban, Lebanon
Children: Sama Chaaban & Aram Chaaban

For us, improving our quality of life means restoring contact and communication. We would no longer have to guess why our child is crying. Understanding our child's needs would reduce our sense of helplessness.

Eugenia Sotnikova, Novosibirsk city, Russia
Child: Alexandr Sotnikov, age 7

For Margaret & Bridget a better quality of life means the difference better stabilizing their skills or losing them. Margaret & Bridget would require increase level of care and increase of support. As working parents it would be life changing for my entire family.

Kathy Lindquist, New York
Children: Bridget & Margaret Lindquist

He can learn, he can play with his cousins and friends, he can dance and sing. All the things he loves to do right now

Astrid, Germany, Bavaria
Child: Charlie, age 4

Hereey çok güzel olurdu ama en önemlisi kızımız artık hayata daha güzel bakardı (Everything would be wonderful, but most importantly, our daughter would have a more positive outlook on life.)

Mehmet vural, Türkiye
Child: Zeren, age 6



Our family are faced with two totally different futures - one is extremely dark if Leni is unable to access treatment now, and the other is a near normal life. As parents it is our responsibility to protect our child and give them the best possible life - and without treatment options we are unable to protect our baby. If Leni is unable to access treatment she will lose the ability to walk, talk, run, play, laugh, eat and eventually die in her early to mid teens. She will suffer physical pain, mental distress, seizures and insomnia that can last for days. As a family we will have to cope with all this, whilst navigating a gruelling schedule of medical appointments and trying to give our little girl the best possible life. If she is able to access treatment in the next year Leni and our family will be able to lead a near normal life. The difference is dark and light, life or death.

Emily Forrester, Kent, UK
Child: Leni Forrester, age 2

Sanfilippo is a terrible disease. As a family we dread watching Autumn suffer even more than her death. Anything to help improve her quality of life could make a HUGE difference for our family regardless of if it extends her life or improves her cognitive function. The sleep deprivation, pain, and frustrations from lack of communication result in extreme caregiver fatigue and suffering for Autumn and our entire family.

Lauren Barber, Michigan
Child: Autumn Barber, age 7

Less symptoms would mean for Louisa to have a more normal life, a life that every child deserves. A carefree life and a life where she doesn't stand out in a negative way because of her hyperactivity, impulsivity and lack of focus. For us as parents it is simply heartbreaking to see our child suffering, or being underdeveloped versus other same aged children in terms of speech or worse, to see Louisa being excluded sometimes due to behavioral issues, because she is perceived as being "too much".

Lennart Sieweke, Potsdam, Germany
Child: Louisa

Lydia can talk to us, laugh with us, play with us.. a typical toddler. With the science and drugs coming about, this wouldn't take her childhood away from her. Her childhood wouldn't be filled



with pain & suffering. She would be able to retain skills she has & keeping playing along side of her big sister.

Morgan Rachal, Louisiana
Child: Lydia Rachal, age 3

Learning that our daughter has a terminal diagnosis absolutely crushed us. To learn that not only is it terminal, but that you'll have to endure losing her piece by piece and face the extreme challenges of caregiving -- I still don't have the words for the cruelty of it all. Sanfilippo Syndrome causes great suffering for both the child and the family. A chance to ease that suffering and give a better quality of life is something we'd do anything to have. For us, it looks like less pain for Frankie, the chance to see her smile more, less distress for the whole family, better sleep for the whole family, and her retaining any skills that she has. If our days with Frankie have to be numbered, we just want them to be as good as possible.

Gabrielle Price, Washington
Child: Frankie Price, age 6

Frankie isn't able to smile much these days. I hope that doesn't mean she doesn't feel joy or excitement. I hope that those feelings are happening inside herself just without a way to be expressed. A chance at a better quality of life could give her simple pleasure. It would mean freedom from restlessness, pain, and discomfort as well as the opportunity to express herself in ways that she isn't now.

Andrew Price, Washington
Child: Frankie Price, age 6

A chance at a better quality of life would change everything -- not just for our child, but for our entire family.
 For our child, it would mean comfort.
 Less pain. Fewer restless nights. A body that feels calmer instead of constantly overwhelmed.
 It would mean holding on to skills instead of losing them. Keeping words. Keeping understanding. Keeping the ability to connect with us.
 It would mean more time where our child feels safe in their own body.
 More laughter.
 More connection.
 More life -- lived with less suffering.

Christiane von Rosbitzki, Germany/Hessen/Rödermark



Child: Theresa von Rosbitzki, age 4

Even small improvements would change everything.

A therapy that could lessen Payton's pain, help her sleep, or slow the daily decline would not only improve her life—it would reshape our entire family's reality. Better sleep means she could wake up more regulated, and so could we. Less pain means more comfort in her day, fewer moments of distress that she cannot communicate, and more opportunities for her to participate in family moments.

Retaining skills—communication, mobility, feeding—would extend her independence. It would allow her to keep engaging with the world, even in small ways. The ability to express a want, a feeling, or a need is something many families take for granted, but for us, even a little more connection would be life-changing.

For our family, improved quality of life doesn't mean a cure. It means preserving the joy she still has. It means fewer emergency interventions and less fear. It means being able to plan beyond the immediate crisis. It means allowing Payton to experience more of her childhood, instead of watching it disappear sooner than it should.

A therapy that could give us even modest improvements would not just lessen suffering—it would give us back moments we're losing far too quickly.

Ally Geronzin, Arizona

Child: Payton Geronzin, age 8

Spending quality time with your family is what life is all about. Feeling well and having a good night's rest are critical firsts.

Rebecca Jordan, Ohio

Child: Liv Jordan, age 11

Ability to live past his teenage years, retention of mobility and ability to continue eating all his favorite foods by mouth, remembering all the family members he loves by name.

Nancy Rubino, Massachusetts

Child: Merrick Rubino, age 11

How would you weigh the benefits and risks that could come with potential and promising therapeutic options?



I know what the outcome of Sanfilippo Syndrome is. I know this disease will take my son's life. I am already watching it take pieces of him every day. I have watched him lose his words. I have watched him lose his independence. And I know, if nothing changes, it will continue until it takes him completely.

So when I think about risk, I think about it differently. The greatest risk is doing nothing.

Doing nothing means accepting that my son will continue to suffer and that he will die from this disease. That is not something I am willing to accept without fighting for him.

Any potential treatment represents a chance. Not a guarantee—but a chance. A chance for him to keep what he still has. A chance for him to stay connected to his brothers. A chance for him to have more time with the people who love him.

I understand there are risks with any new or promising therapy. But there is also certainty in doing nothing. And that certainty is losing my son.

As his father, I am willing to accept reasonable risks if it means giving Beckham a chance at more life, more comfort, and more time with his family.

I cannot stand by and watch this disease take him without trying everything possible to help him.

Beckham deserves that fight. And I will never stop fighting for him.

Brandon Hutcheson, Georgia

Child: Beckham "Bex" Hutcheson, age 4

The natural progression of Sanfilippo Syndrome ensures that our son passes away by his 18th or 19th birthday, and since he's already 9, the latter years of his are going to be far from pleasant. Without treatment, his fate is to die of this disease before he completes his second decade of life. So, we are eager to try a promising treatment that could only improve his quality of life.

Alina Gorniak, Texas

Child: Simon Croke, age 9

As a family, we are very willing to try therapeutic options that come up. We are often asking Lottie's doctor about potential repurposed medication's, and are always looking into other types of holistic medicine when it seems that there is a lack of options in the medical world.

Abby Milburn, IL

Child: Lottie, age 5



Our children die a painful death. That is a certainty without any medical intervention. Parents have the right to try a drug, even if the risk is high and the outcome isn't certain. Our children deserve, at the very least, an opportunity to try a drug to ease their pain and possibly increase their quality and quantity of life.

Christin Ulrich, Florida
Child: Veda Ulrich, age 6

At 16, I think we have long come to terms with Jacob not qualifying for treatments because of his age. But I would sign Jacob up for anything that would keep Jacob as he is now forever!

Christine Moon, New York
Child: Jacob Moon, age 16

We understand that Sanfilippo Syndrome is progressive and ultimately fatal. The outcome, without intervention, is certain.
 So when we weigh benefits and risks, we are not comparing treatment to a healthy future. We are comparing treatment to continued decline.
 That changes the equation.
 We educate ourselves. We ask questions. We consult specialists. We look at data. We understand that innovative therapies, especially in rare disease, come with uncertainty. But doing nothing also carries risk.
 The risk of seizures.
 The risk of losing speech.
 The risk of losing mobility.
 The risk of losing our child far too soon.
 We are willing to try promising therapies because the alternative is guaranteed progression. If there is a chance to preserve brain function, to slow decline, to reduce suffering, that matters. We are not asking for perfection.
 We are asking for opportunity.
 As parents, our job is to protect our child. In a disease like Sanfilippo, protection means being willing to take carefully considered risks for the possibility of more time, more skills retained, more quality of life.

Stephanie McCabe, Saskatchewan, Canada
Child: Emmett Doucette, age 6



As a parent of a child with Sanfilippo syndrome, I am making decisions in the context of a disease with a known and devastating outcome.

Because progression is certain and irreversible, I weigh risk differently. The risk of doing nothing is continued and predictable decline.

My child, Sadie, participated in a Phase 1 clinical trial for two years. That was not an easy decision—but it was an informed one. We accepted uncertainty because the alternative was guaranteed loss.

That experience reflects my willingness to pursue promising therapies, even when risks are present. I am not looking for perfection or certainty—I am looking for a chance to slow progression, preserve skills, and improve quality of life.

In diseases like Sanfilippo syndrome, even small benefits matter. More time with retained abilities, better sleep, or reduced discomfort can significantly impact both the child and their family.

Families like mine understand the risks. We live with the outcome of this disease every day. We should have a voice in determining what level of risk is acceptable when the alternative is already known.

Ashley Haywood, NC

Child: Sadie, age 9

We would be very willing to try any treatment to stop or delay the progression of this disease as it is inevitable. If it gives us more time and improves functional status, we feel it is worth it.

Krystal Cooley, SC

Child: Dawson, age 7

Sanfilippo Syndrome has a certain and devastating outcome. Without treatment, progression is guaranteed.

When the alternative is continued neurological decline, we are willing to consider reasonable risks associated with promising therapies. We understand that innovative treatments carry uncertainty but the certainty of doing nothing is far worse.

We are not asking for reckless decisions. We are asking for urgency, flexibility, and compassion in evaluating therapies for children who do not have time to wait. We are willing to try treatments that offer even a chance to slow progression or preserve function.

Soraya, Al Chouf Baakleen Lebanon

Children: Sama Chaaban and Aram Chaaban



Since this disease is progressing day after day, promising therapeutic treatments will be the hope to find the proper cure, so the kids can retrieve their nice moments and abilities instead of going straight forward to death

Khaled Chaaban, Lebanon
Children: Sama Chaaban & Aram Chaaban

We fully recognize that Sanfilippo syndrome is a progressive disease with a predictable, unfavorable outcome without intervention. The natural course of the disease guarantees loss of skills, a decline in quality of life, and a shortened life expectancy. Since the natural course of Sanfilippo syndrome leads to severe disability and early death, the risk of inaction is unacceptable to us. Even partial improvement (stabilization of skills, improved sleep) is a significant victory for us. We are ready to try various treatment methods. Our motivation is extremely high, as we fight for every day of our child's quality of life.

Eugenia Sotnikova, Novosibirsk city, Russia
Child: Alexandr Sotnikov, age 7

Margaret and Bridget are 100% willing to try therapeutic medications and or treatments to maintain their level of independence. They understand their diagnosis is often called "childhood Alzheimer's." They know what Alzheimer's looks like and that's not something they want to happen to themselves. They both have said themselves they are willing to participate in these types of treatments for the potential improvement-quality of life. They trust the science, they understand the data is strong. They trust the many pharmaceutical companies that have been working on this for years and years. There are no other options for them. They asked for your help today because today is their best day, tomorrow they are a little bit worse.

Kathy Lindquist, New York
Children: Bridget & Margaret Lindquist

We can see how he keeps his quality of life longer. We could see if he makes progress in language

Astrid, Germany, Bavaria
Child: Charlie, age 4



Biz her türlü ciddi çalışmanın içinde olmak istiyoruz (We want to be involved in all kinds of serious work.)

Mehmet vural, Türkiye
Child: Zeren, age 6

Without treatment our little girl will suffer the most cruel and catastrophic decline you can imagine, losing all physical and mental function and eventually her life to this horrific condition. When premature death after years of suffering is the reality we are facing without treatment it is worth any risks associated with experimental treatment options. It simply cannot be any worse than the outcome of Sanfilippo Syndrome, so the potential benefits far outweighs the risk. We are willing to try anything to save our little girl from the horrific future that awaits her.

Emily Forrester, Kent, UK
Child: Leni Forrester, age 2

As parents of children with Sanfilippo syndrome, we live with the reality that this is a progressive, terminal disease marked by profound neurological decline, suffering, and ultimately the loss of our children. Because of this, many of us — myself included — are willing to accept a high risk-to-benefit ratio when it comes to experimental therapies. When the alternative is watching your child gradually lose skills, awareness, mobility, comfort, and life itself, the calculus of risk changes. What might be considered “too risky” in other medical contexts feels different when time is limited and options are nonexistent.

Our family made the decision to travel internationally during a global pandemic so our daughter could participate in a clinical trial. I am a Nurse Practitioner, and my Husband is an Engineer. We chose to participate very educated on the scientific process and potential risk/benefits of the treatment. We knowingly sacrificed financial stability, physical safety, and emotional security. She ultimately did experience a complication from the treatment, and it is possible that the long-term benefit will be minimal. Even in hindsight, we do not regret the decision to participate.

We do not regret it because when faced with a disease that guarantees suffering and decline, doing nothing is not a neutral choice — it is simply accepting the inevitable. As parents, we needed to know that when an opportunity arose — one that so few families ever receive — we did everything within our power to try to help our child. Families affected by Sanfilippo understand the risks. We live the risks every day.

Lauren Barber, Michigan



Child: Autumn Barber, age 7

Since the outcome is certain and devastating, we would be willing to try everything that could give us more quality time with Louisa.

Lennart Sieweke, Potsdam, Germany
Child: Louisa

The disease is terminal. In a flat line, she will die early in life after pain & suffering. The risk I am willing to take for my child to have a better life outweighs anything. More happy days. More walking, more talking, more laughing, more playing. No suffering.

Morgan Rachal, Louisiana
Child: Lydia Rachal, age 3

We would do anything to try and help Frankie. Sanfilippo Syndrome is absolutely relentless and we'd give anything to ease its burden. Though we know therapies can have risks, we also know exactly what happens if we don't try. The potential to help our daughter is worth the risk.

Gabrielle Price, Washington
Child: Frankie Price, age 6

Doing nothing means guaranteed regression. Guaranteed loss of skills. Guaranteed suffering over time.

Yes, there may be risks. There may be side effects. There may be unknowns. But the disease itself is a known, relentless risk. Every month without intervention means more neurological damage that cannot be reversed.

We are willing to participate in clinical trials because we can only win!

Christiane von Rosbitzki, Germany/Hessen/Rödermark
Child: Theresa von Rosbitzki, age 4

Sanfilippo has a known and devastating progression. Without intervention, outcomes are certain, and they are heartbreaking. Because of that, families like ours think about risk differently than those facing conditions with stable or predictable futures.

For Payton, whose abilities decline every day, the risk of doing nothing is the greatest risk of all.



We understand that any therapy—especially innovative or first-in-class treatments—comes with uncertainties. But we also live with the certainty of a disease that will continue taking from her unless something interrupts its course. When the alternative is guaranteed loss, the potential benefits of a promising therapy, even one with some risk, carry enormous weight.

We are thoughtful, informed, and deeply invested in evidence and safety. But we are also parents watching our daughter lose skills she had only months before. That urgency is real, and it makes us willing to pursue therapeutic options that could give her a chance at a better future, even if they are not perfect. Payton has not yet had the opportunity to participate in a clinical trial—with her involvement so far limited to data-only research—but we would absolutely consider a treatment-based trial if it were available and scientifically promising.

When families like ours advocate for earlier access, it is not out of desperation—it is out of rational, informed hope grounded in the reality of the disease's progression. We are asking for the chance to try, before time makes trying impossible.

Ally Geronzin, Arizona
Child: Payton Geronzin, age 8

My daughter was the first in the US to receive enzyme replacement through a cranial port in the United States. I have zero regrets and would do it again. We need our attempts to gain access to treatment to become a reality.

Rebecca Jordan, Ohio
Child: Liv Jordan, age 11

There are not many risks worse than this terrible progressive disease itself. We are hoping every day to hear that the therapy that could save Merrick's life will finally be accessible to him. We are willing to move to raise money, to go into debt—anything to get him this treatment.

Nancy Rubino, Massachusetts
Child: Merrick Rubino, age 11

If you could speak directly to the leaders at FDA, what would you say?

I need you to understand that this is my son's life, and I am the one who has to watch him die while waiting for decisions I have no control over.



Every day that passes, Sanfilippo Syndrome is taking more from Beckham. I am not reading about it. I am living it. I see it in his silence where his voice used to be. I see it when he seems lost. I see it when he struggles with things that once came naturally to him.

And while this is happening, I am forced to wait. Waiting for people who have never met my son, who will never know his laugh, his smile, or the way he says "daddy," to decide whether he gets a chance.

You are not the one who has to sit down with his brother, who is in kindergarten, and try to explain why his little brother is changing. You are not the one who has to answer questions no parent should ever have to answer. You are not the one who has to watch the confusion and sadness in his brother's eyes while trying to stay strong yourself.

That choice should not belong to someone who has never looked into my son's eyes.

That choice should belong to me.

I am his father. I am the one who loves him. I am the one who has to hold him, comfort him, and live with whatever happens. I am willing to accept the risks if it means giving him a chance. I am willing to fight for him with everything I have.

What I am not willing to do is stand by and watch him die while waiting for permission to try to help him.

You have the power to give families like mine a chance. You have the power to move with urgency. You have the power to recognize that time is something children like Beckham do not have.

Please do not make families like mine wait while our children disappear in front of us.

His name is Beckham. He is four years old. He is a son. He is a brother. And he deserves the chance to fight for his life.

Because while you are deciding, I am watching my son disappear.

Brandon Hutcheson, Georgia
Child: Beckham "Bex" Hutcheson, age 4

Please approve clinically proven treatments TODAY. Ask for clarifying details about the manufacturing facility and production TOMORROW. Our kids' lives can't wait.

Alina Gorniak, Texas
Child: Simon Croke, age 9

If I could say one thing to FDA, it would be that my child's life is in your hands. You have the power and the ability to save her life.

Abby Milburn, IL
Child: Lottie, age 5



The time is now! Our children are not a number on a page. They are real, they are here and they are worthy and deserving of an FDA approved treatment!!

Christin Ulrich, Florida
Child: Veda Ulrich, age 6

Please stop delaying treatments for our children! Please understand that families just want more time with their babies,

Christine Moon, New York
Child: Jacob Moon, age 16

Please remember that behind every data point is a child whose disease does not pause while decisions are being made.

Sanfilippo Syndrome is relentless and progressive. Our children are losing brain function every single day. We do not have the luxury of time.

We understand the responsibility you carry. We want therapies to be safe. We want them to be effective. But we also need urgency to reflect the reality of diseases where decline is certain and irreversible.

Stephanie McCabe, Saskatchewan, Canada
Child: Emmett Doucette, age 6

To the leaders at the U.S. Food and Drug Administration:

Please understand that for children with Sanfilippo syndrome, time is not without consequence. Every month of delay means irreversible loss—of skills, of connection, and of quality of life that cannot be regained.

I am not asking you to lower standards. I am asking you to match the urgency of your process to the reality of the disease.

Families like mine are willing to accept risk because we live with the certainty of what happens without treatment.

We need a system that moves with that same understanding—because our children do not have time to wait.

Ashley Haywood, NC
Child: Sadie, age 9



Our children are the most important thing in the world to us and the time we have is invaluable. Any delay in the approval of treatments leads to further progression of this disease.

Krystal Cooley, SC
Child: Dawson, age 7

Please see our children not as data points, but as lives on a clock that is moving too fast. Regulatory timelines that may seem reasonable in other contexts are devastating in rare, rapidly progressive diseases like Sanfilippo. We ask you to act with the urgency this disease demands. Every day, week and month matters. Every delay costs something that cannot be recovered. Our children do not have time. Please do not let the system take what the disease has not yet taken.

Soraya, Al Chouf Baakleen Lebanon
Children: Sama Chaaban and Aram Chaaban

This is a life-threatening, progressive condition with zero alternatives, which fits the criteria for urgent Fast Track or Accelerated Approval.

Khaled Chaaban, Lebanon
Children: Sama Chaaban & Aram Chaaban

I would say, "Look into my child's eyes." If you saw how this disease is stealing their smile and skills day by day, you would understand why we are begging for speed. We are not asking you to abandon safety; we are asking you to understand our urgency. Please stand with us in this race against time. Please hear the voice of patients: we are willing to take risks for the sake of hope. Don't expect perfection when children's lives are at stake. Speed up the approval process, because tomorrow may be too late. Your signature on the approval is more than just a document; it is a gift of life for children who no longer have hope.

Eugenia Sotnikova, Novosibirsk city, Russia
Child: Alexandr Sotnikov, age 7

I would ask the FDA to expedite the process for pediatric ultra rare diseases. We are not asking for shortcuts. Safety is a number one priority. But time is not on our side. These kids cannot



wait. We need the system to change for children with rare disease. Improving the quality of life is a significant change for parents and families with sanfilippo syndrome . It affects the entire body and the whole system. If a child's sleep could improve, digestion could improve, be seizure free, and less pain would result in happier days for everybody involved. Less hospital visits, less emergencies, less uncertainty. A person's quality of life is subjective and cannot be measured by the FDA or others who are not living with rare diseases. Having 2 daughters with Sanfilippo Syndrome causes enormous complications and tremendous suffering on our family and everyone who knows us and loves our girls.

Kathy Lindquist, New York
Children: Bridget & Margaret Lindquist

Please give our children a chance for a better life. They do not have an opportunity to have a normal life, to grow up and have their own families. So please help us make their short lives as happy as possible.

Astrid, Germany, Bavaria
Child: Charlie, age 4

Sanfilippo Syndrome is cruel, relentless, rapid and irreversible. It leaves no part of our children untouched and the impact is catastrophic for both the child and the families and people who love them. The science is there, treatment options exist, we just cannot access them - and that is absolutely devastating and incredibly frustrating. This is even harder to accept when it's lives that are at stake, and even more so when it is children. There is a window of opportunity to prevent this awful decline if a child receives treatment early enough, but that window doesn't remain open indefinitely and what has been lost cannot be recovered. Delays and regulatory processes are a matter of life and death - and I ask you to consider how you would feel if this was your child, and your reality. It is a race against time, and time is the one thing our children do not have. You must expedite drug approval protocol for rare diseases now, to save our children's lives. When what's at stake is a child's life, these issues cease to be political or administrative and become something profoundly moral.

Emily Forrester, Kent, UK
Child: Leni Forrester, age 2

We respectfully urge the FDA to ensure that regulatory processes and evolving evidentiary standards do not unintentionally delay access to promising therapies for rare, fatal pediatric conditions. In progressive neurodegenerative diseases with no approved treatments and no



options to improve quality of life, timing is critical and delay results in irreversible loss. Families facing certain decline and premature death are willing to accept substantially higher levels of risk and uncertainty, and regulatory frameworks should reflect the urgency and reality of these devastating diseases.

Lauren Barber, Michigan
Child: Autumn Barber, age 7

Please don't lose yourself in details and rigid processes - the speed of the process is critical and will save our children's lives. Evaluate wisely what the benefits of a treatment/clinical trial can mean for the children and their families.

Lennart Sieweke, Potsdam, Germany
Child: Louisa

As a mother, when my daughter was born.. I felt as if her life was all in my hands to take care of her well being. Now that I know she has a terminal disease with treatments on the way with the science working, I feel as if her life is also in the hands of the FDA. These are OUR children. It's our duty to give children the absolute best quality of life we possibly can. Time is ticking, these treatments are my daughter's ONLY chance at life.

Morgan Rachal, Louisiana
Child: Lydia Rachal, age 3

Frankie showed us exactly who she is before Sanfilippo Syndrome caused a sharp, fast regression. Smart, joyful, funny, loving, brave, the best big sister. Full of life. To see so much of her be taken is a pain we endure every day. To know that there's more pain to come is a fear we face every day. If it's too late for Frankie, we hope that it's not too late for others and for the children who will continue to be diagnosed with Sanfilippo Syndrome. We hope for a world where children can get access to therapies sooner. Time isn't on our side. 6 months can mean everything.

Gabrielle Price, Washington
Child: Frankie Price, age 6

If the system can be improved to expedite the rate of scientific discovery that can tangibly improve lives and experiences of families like mine, it should be done. I don't consider



experimental treatment to be an assured thing that could help my child. But I sure as hell want the option to try.

Andrew Price, Washington
Child: Frankie Price, age 6

Please see the urgency the way we live it.

For you, timelines are quarters, review cycles, regulatory pathways, and data sets. For us, timelines are skills lost, words forgotten, nights without sleep, and parts of our child slipping away that we will never get back.

Sanfilippo Syndrome does not pause while paperwork moves forward. It does not wait for the next meeting. Every month of delay means irreversible neurological damage. Time is brain — and our children are losing it in real time.

Our children do not have time for perfect.

They need thoughtful speed. They need regulatory courage. They need leaders who understand that in ultra-rare, rapidly progressive diseases, the cost of waiting is measured in childhood itself.

Christiane von Rosbitzki, Germany/Hessen/Rödermark
Child: Theresa von Rosbitzki, age 4

If I could say one thing to the leaders at U.S. Food and Drug Administration, it would be this:

Please don't let the perfect become the enemy of the possible when children like my daughter Payton are losing abilities every single day.

For families living with Sanfilippo, time is not theoretical—we watch its consequences unfold in real time. Every delay, even when unintentional, has a human cost that can never be undone.

We are not asking you to lower standards of safety or effectiveness. We are asking you to recognize that for diseases with certain and devastating progression, inaction is not the safer option. The risk of doing nothing is guaranteed harm.

Please let urgency, compassion, and flexibility guide your decisions for rare diseases. Our children cannot wait. They don't have that luxury.

Ally Geronzin, Arizona
Child: Payton Geronzin, age 8



If it were your child, you would want treatment. It's here, it's available. Let us give it to our kids so they can live their best lives.

Rebecca Jordan, Ohio
Child: Liv Jordan, age 11

We wish the FDA felt the same urgency to save my son's life that we do. Every day we hope to hear good news that could turn the tide for this disease. With AI tools science breakthroughs will continue to progress more and more rapidly, and the FDA needs to figure out how to speed up their own processes for the good of everyone.

Nancy Rubino, Massachusetts
Child: Merrick Rubino, age 11

Questions for the Record

U.S. SENATE SPECIAL COMMITTEE ON AGING

"FROM REGULATOR TO ROADBLOCK: HOW FDA BUREAUCRACY STIFLES INNOVATION"

FEBRUARY 26, 2026

QUESTIONS FOR THE RECORD

Annie Kennedy**Senator Raphael Warnock****Question:**

Over the past few decades, the FDA has adopted strategies to accelerate the development of treatments for ultra-rare diseases. These strategies have included the Support for Clinical Trials Advancing Rare Disease Therapeutics Pilot Program, Rare Disease Evidence Principles, and the Plausible Mechanism of Action Framework. However, there are many rare diseases that still need treatments.

What would be the advantages of the FDA extending the above strategies to other rare diseases? How can Congress ensure the FDA balances acceleration and thoroughness in its review of potential rare disease treatments?

Response:

We have been following closely the recent agency announcements, including the Rare Disease Evidence Principals (RDEP) initiative, the Plausible Mechanism Framework, the establishment of the Rare Disease Innovation Hub in 2024, and the implementation of new guidance documents and regulatory science pilot initiatives contained in PDUFA VII (10/1/2022 - 9/30/2027).

The application of these programs and policies can shape the prospects of rare disease therapy development for a given community, drive investment into one area and out of another, and determine how patient advocacy organizations allocate precious resources. For a variety of reasons the ways in which available guidances, programs, and pathways can be applied to different subpopulations of rare diseases differ. Multiple factors have led to some rare disease communities having greater success in leveraging FDA's regulatory flexibility including population size, therapeutic modality, disease characterization, extent of diagnostic delays, age of onset, and others.

We are encouraged by the intent signaled by FDA's most recent initiatives, RDEP and the Plausible Mechanism Framework, however, more information is needed to understand how the Agency plans to operationalize these new approaches for products in today's pipeline and beyond, and which subpopulations of rare diseases stand to benefit initially, and over the longer term.

We encourage additional dialogue and input from the community into these new initiatives as even the best ideas need the benefit of robust dialogue and operational details for them to have the intended effect.

Specific to the RDEP announcement - this announcement appears to be responsive to calls for more predictability in the regulatory process, but more details will be needed before we have a detailed reaction. Many rare disease communities may not realize the program's benefits due to its narrow focus; however, it can provide valuable insights for expansion if appropriate metrics and evaluation methods are incorporated from the outset.

We are eager to hear more details on how RDEP will be operationalized, as well as a better understanding of how RDEP's requirements for pre-specifying the trial requirements will be handled, given the nature of many rare disease trial designs.

Regarding the Plausible Mechanism Framework, we are encouraged by the release of the draft Guidance, and what it represents for the eligible communities for whom traditional approaches to clinical trials and regulatory requirements are fundamentally at odds with the reality of their conditions. We are grateful to the FDA for taking on this challenge of ensuring no disease is too rare to deserve treatment. And we are incredibly grateful to the many families and experts who applied their personal expertise to yield transformational change.

We also recognize that for many in our rare disease community, the Plausible Mechanism Framework will not apply, and we urge FDA leadership to continue pursuing solutions that will ensure the tools and policies that Congress has created over decades, are deployed in a predictable and consistent manner that can unleash scientific innovation and speed safe and effective therapies to patients across the

more than 10,000 rare diseases. The EveryLife Foundation team is in the process of closely reviewing the recently released draft Guidance.

Regarding the Rare Disease Innovation Hub and opportunities yielding from PDUFA VII Pilot Programs, we are hopeful that the opportunities stemming from these PDUFA VII investments will be applied more broadly across rare disease product development. The Rare Disease Innovation Hub is well positioned to be a catalyst of progress by spearheading the dissemination of data, case studies, and other learnings resulting from these pilots and experiences with the application of regulatory flexibility tools more broadly.

Since 1983, Congress has created incentives and policies that recognize the inherent complexities in developing treatments for rare diseases. Congress has explicitly given the FDA authority to uphold the highest standards of regulatory safety and rigor, while applying tailored approaches (i.e. "regulatory flexibility"). Such approaches include:

- Establishment of the accelerated approval pathway
- Consideration of the totality of evidence in the regulatory review
- Inclusion of Patient Experience Data (PED) in clinical trial design & regulatory processes
- Utilization of innovative clinical trial designs and real-world evidence (RWE)

Nearly 1,400 orphan-designated therapies are changing the lives of patients and families, but 95% of rare diseases remain without an FDA-approved treatment.

Congress must continually ensure that FDA review statutes keep pace with the science and are designed to work across the spectrum of rare diseases, from n-1 to just under 200,000, and from pediatric to adult populations. Congress should look to address gaps more regularly, ideally more often than the typical practice of moving regulatory legislation alongside the five-year PDUFA reauthorization window allows. Congress should regularly engage in dialogue with the Agency leadership and rare disease stakeholders, seek comprehensive metrics to understand how the Agency is applying regulatory flexibility, and ensure the Agency has adequate resources, such as funding for the Rare Disease Innovation Hub, to optimize their ability to apply tailored approaches to rare disease product evaluation.

Question:

As part of his sweeping reductions-in-force (RIFs) of Department of Health and Human Services (HHS) employees, HHS Secretary Robert F. Kennedy dismissed 3,500 Federal Drug Administration (FDA) employees in April 2025. The RIFs targeted employees across the agency, including advisory committee staff.

You mentioned that the FDA held far fewer advisory committee meetings in 2025 relative to 2024 and that this drastic drop meant fewer opportunities for experts and patients to share information to inform the FDA's decision-making. What are the ramifications of last year's RIFs at the FDA for the development and treatment of illnesses that do not yet have a cure?

Response:

Significant leaders the rare disease community has built relationships with over the years have either resigned or been laid off in the last 12 months, resulting in the loss of powerful allies and institutional knowledge that have generated the progress the rare disease community has seen over the last decade. However, thousands of committed public servants remain, and the EveryLife Foundation, together with our community, is committed to policies that will support and enhance the Agency's rare disease capacity and expertise.

Rare disease product reviews occur in every division and product Center at the FDA. With the appropriate resources, the Rare Disease Innovation Hub is poised to enhance its role as the FDA's coordinating office to optimize rare disease expertise, processes, and engagement with stakeholders across all therapeutic areas, including drugs, cell and gene therapies, and medical devices. Given the departure of experienced staff, the importance of a robust Rare Disease Innovation Hub is magnified. The Hub's first full year of operations has laid the foundation for meeting this moment of opportunity if institutional support and resources are enhanced.

Question:

How can Congress conduct oversight over the FDA to ensure the agency continues to hold advisory committee meetings and review rare disease treatments?

Response:

We are concerned about the dramatic decline in opportunities to leverage external scientific, clinical, and patient-community insights to inform deliberations on complex rare-disease product reviews. While not every product application requires an advisory committee, where relevant, their use was one of the few ways the Agency

discussed its approach to the review in public and heard from clinicians who treat patients and run trials, and from the patients and families who took part. This additional insight affords review teams with another data point to consider among the totality of evidence they must balance when determining how to apply the regulatory flexibility tools that Congress has authorized.

As I encouraged Congress in my testimony, Congress should conduct outreach to the Agency to understand its approach to the following:

- The application of the accelerated approval pathway to rare disease therapies;
- Improving the predictability and consistency of the application of regulatory flexibility; and
- Resuming the use of Advisory Committee Meetings to receive external expertise on product reviews and key policy topics.

Based on this engagement and the Agency's responses, we encourage Congress to identify opportunities for additional public dialogue with the Agency and rare disease stakeholders to identify a path forward that will ensure sustainable, transparent, and predictable processes for leveraging external expertise in relevant product reviews and to inform overall rare disease regulatory science approaches moving forward.

U.S. SENATE SPECIAL COMMITTEE ON AGING

"FROM REGULATOR TO ROADBLOCK: HOW FDA BUREAUCRACY STIFLES INNOVATION"

FEBRUARY 26, 2026

QUESTIONS FOR THE RECORD

Bradley Campbell**Senator Raphael Warnock****Question:**

Approximately one in ten Georgians live with a rare disease. Many of these individuals, including older adults, do not have access to life-saving treatments due to incomplete scientific knowledge of their disease and limited funding. Families seeking treatments that were reviewed under a priority voucher program are also experiencing delays due to the prolonged FDA approval process.

How can Congress reduce regulatory barriers to expedite the FDA's approval process for rare disease treatments while maintaining the safety and quality of these treatments?

Response:

Senator Warnock, thank you for this thoughtful question. As noted in my testimony, I believe there are low-hanging fruit that we can seize while still maintaining FDA's "gold standard" for safety and efficacy:

- Speeding up approval of early phase clinical trials
- Harnessing innovative endpoints based on biomarkers
- Expanding the use of real-world evidence
- Streamlining manufacturing inspections

In cases where there is residual uncertainty about the durability or extent of patient benefit for promising therapies, real-world data should be collected post-approval via the Accelerated Approval pathway.¹ If that data does not bear out patient benefit, the agency should consider withdrawing that treatment in consultation with the patient community. When it comes to rare diseases, patients and their families are the true experts, and their voices need to be respected as such.

FDA already has Congressionally granted authority to do everything I listed above. The challenge is simply doing them consistently. This is where Congressional oversight is vital.

Question:

How do bipartisan initiatives like the FDA Pediatric Priority Review Voucher program, which I was glad to see reauthorized recently, help incentivize innovation for rare disease treatments?

Response:

Senator Warnock, we are deeply grateful to Congress for reauthorizing the FDA's Pediatric Priority Review Voucher (PRV) program.

Small and mid-size biotech companies are the driving force behind U.S. drug development for all diseases, but particularly for rare diseases. These companies are often pre-commercial, meaning they are years-to-decades from sustainable profitability.

When a company with a PRV voucher receives FDA approval, the sponsor can sell that voucher, sometimes for hundreds of millions of dollars. That funding is a critical lifeline for continued operations when the alternative is bankruptcy.

Rare pediatric diseases that have benefited from PRVs include pediatric neuroblastoma, the most common cancer in infants; spinal muscular atrophy (SMA), the most common genetic cause of infant mortality; and epidermolysis bullosa, which causes fragile, blistering skin.

There were no treatments for any of these diseases before Congress created the PRV program in 2012.

¹ Examples of rare-disease therapies that entered the market via FDA Accelerated Approval and later converted to full approval include sparsentan for primary IgA nephropathy, agalsidase beta for Fabry disease, and delandistrogene moxeparvovec-rokl for Duchenne muscular dystrophy.

The PRV program has no cost to taxpayers, but when investors are considering whether to fund an early-stage rare disease company, having a PRV designation can be decisive.

Statements for the Record

Statement for the Record
U.S. Senate Special Committee on Aging
Hearing on the MINI Act
On Behalf of the ALS Association

Chairman, Ranking Member, and Members of the Committee:

On behalf of the ALS Association and the families we serve across the country, thank you for the opportunity to submit this statement in strong support of the MINI Act.

Amyotrophic lateral sclerosis (ALS) is a rapidly progressive, fatal neurodegenerative disease. There is no cure. Most people diagnosed with ALS live just two to five years from symptom onset. The disease robs individuals of their ability to walk, speak, eat, and eventually breathe all while their cognitive awareness often remains intact.

For people living with ALS, time is not an abstraction. It is everything. The MINI Act represents a meaningful and compassionate step toward reducing unnecessary administrative burdens and delays that prevent individuals with terminal illnesses from accessing critical supports and services. People living with ALS often face complex eligibility requirements, repeated documentation demands, and procedural hurdles at the very moment when their physical capacity is declining most rapidly. These bureaucratic barriers cost precious time they simply do not have.

Congress has previously recognized the urgent nature of ALS by eliminating the Medicare waiting period for individuals with ALS through the ALS Disability Insurance Access Act. The MINI Act builds on that bipartisan legacy by ensuring that individuals facing terminal diagnoses are not forced to navigate duplicative or prolonged processes to receive the benefits and assistance for which they qualify.

Every delay in access to care, home modifications, assistive technology, or income support has real and immediate consequences. Delays can mean the difference between remaining at home with family and entering institutional care. They can mean the difference between accessing life-prolonging interventions and going without.

The ALS Association strongly supports policies that:

- Streamline access to benefits for individuals with terminal illnesses;
- Reduce redundant medical certification requirements;
- Improve interagency coordination; and
- Recognize the urgent realities of rapidly progressive diseases like ALS.

The MINI Act reflects common-sense governance rooted in dignity, efficiency, and compassion. It acknowledges that when a physician has confirmed a terminal diagnosis, our systems should respond with urgency and humanity, not paperwork and delay.

We urge the Committee and the full Senate to advance the MINI Act swiftly and continue bipartisan efforts to improve quality of life for people living with ALS and other terminal conditions.

Thank you for your leadership and your continued commitment to older Americans and people living with serious and life-limiting illnesses.

Respectfully submitted,

Melanie Lendnal

Melanie Lendnal
Senior Vice President, Policy & Advocacy
The ALS Association



February 24, 2026

Chair Scott, Ranking Member Gillibrand, and Members of the Committee

Re: Senate Aging Committee hearing, "From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation":
Submission to the Record

The Huntington's Disease Society of America (HDSA) is a leading national organization dedicated to the care and cure of Huntington's disease. At HDSA our focus is to promote and support research to find a cure for Huntington's disease (HD); help people and families affected by the disease; and educate the public and clinicians. We do this through our network of chapters and Centers of Excellence around the country.

I am submitting this testimony to share my concerns about current FDA regulatory decisions and their impact on the HD community.

Huntington's disease is a rare, inherited, and ultimately fatal neurological disorder. Often striking in the prime of a person's life. It causes a progressive decline in a person's ability to think, move, and function independently. If one parent has HD, their children have a 50 percent chance of inheriting HD. There is currently no treatment that slows or stops the progression of HD. It progresses from symptom onset to death over approximately 15 years often beginning in the prime of life.

People living with HD and their families are willing to take risks to stop the progression of the disease. Nearly three-quarters of respondents to the 2024 HDSA HD Symptoms and Treatment Impact Survey said they would accept treatment risks to gain five years with no disease progression, and almost 35% were willing to accept risks for even three years of halted progression.

When FDA policies are unclear, inconsistent, or unpredictable, it creates additional barriers for therapies that may represent our only hope. I am concerned about lack of transparency in decision-making for HD therapies, inconsistent application of regulatory standards, and failure to adequately account for the realities of small patient populations. I respectfully urge the Committee to direct the FDA to:

- Consider benefit/risk tolerance of people living with HD when making decisions about trials for HD treatments and cures.
- Utilize natural history studies for HD and other rare disease trials.

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- Be clear, transparent and public about its decisions related to HD trial decisions, including recent statements about uniQure's AMT-130.

Following this cover letter are personal stories from members of the HD community that bear witness to the devastating realities of the disease and the urgent need for treatments that can stop its relentless progression.

Thank you for the opportunity to submit testimony for the record. I appreciate the Committee's attention to the needs of HD patients and families. For our community, innovation is not optional — it is survival. It represents more time, more independence, and more life.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Amy Gray", written in a cursive style.

Amy Gray
President and Chief Executive Officer
Huntington's Disease Society of America
agray@hdsa.org

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My name is Sherrie England, and I live in Maryville , Tennessee. I am a family member of someone that is living with Huntington's disease. I am submitting this testimony to share my concerns about current FDA regulatory decisions and their impact on the Huntington disease (HD) community.

HD affects normal daily life in so many different ways. Slowly losing speech, eating food and drinking liquids, mobility, memory issues, ability to hold employment, do household chores and driving are just a few examples of the effects of HD.

My family has been and is affected by HD, my great grandfather, grandmother, mother and now my older sister. None have been able to participate in clinical trials to possibly offer some relief or delay the progression of the disease.

Respectfully submitted,
 Sherrie England
 Maryville, Tennessee
 englanddavid@bellsouth.net

My name is Jerry Saunders, and I live in Southport, CT. My father and two sisters were afflicted with Huntington's Disease. I am submitting this testimony to share my concerns about current FDA regulatory decisions and their impact on the Huntington disease (HD) community.

HD had devastating effects on my father and sisters; their diseases progressed in unique ways for each of them. They each regressed from lives of competence and relative contentment through a period of deterioration cognitively, physically, and emotionally over a period of years. HD was a death sentence for all of them.

My father was a veteran of WWII. He was the first in his family to attend college, which he did with the help of the GI Bill. He was a professional educator, and active in veterans' organizations, including as a Commander in a local DAV organization. He was particularly skilled in woodworking; in fact, he taught high school Industrial Arts. I remember my dad being a good father when I was young; playing with me, reading to me, coaching my baseball team, etc. By the time I was about 12 years old, when my dad was around 38 years old, while we did not

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understand what was going on, my dad started showing initial but impactful HD symptoms (undiagnosed; "out of nowhere"). He became irritable and depressed, acted violently towards others verbally and then physically. He could not hold down a job either as a teacher in the schools or at numerous other vocations he attempted. Our family had many resultant difficult relationship problems and our financial situation was fragile. Symptoms started out subtle, but never improved despite many attempted interventions mostly through the VA. In fact, symptoms progressed markedly over the years, until my dad spent the last years of his life non-ambulatory, almost non-verbal, needing caretaking for 100% of his daily needs. My father died of complications of HD at age 65.

My younger sister began experiencing psychological and physical symptoms of HD (undiagnosed until my father was diagnosed, years later) by the time she was a teenager. She was a very bright and socially successful child; but she was not able to consistently overcome inexplicable episodes of depression and anxiety that began when she was about 13 and got progressively worse. Psychiatric and other medical/neurological interventions seemed to help at times, but only briefly. When our dad was diagnosed with HD, she realized why she was having such struggles. With the HD diagnosis, she could only envision an horrific future for herself, with no way to effectively treat it. My "little sister" died by suicide at age 31.

My older sister also lost the HD lottery. She, too, inherited the defective gene. She was a brilliant, talented, creative child and student. Just a few years after completing her Masters degree in counseling, and working to help others in various professional settings, her more subtle HD symptoms were evident. She courageously fought throughout adulthood to live her life, but this disease is horribly destructive and unstoppable. She ultimately lived in a nursing home in her last years. My "big sister" died of complications of HD at age 58.

Respectfully submitted,
 Jerry Saunders
 Southport, CT
jsaunders1012@gmail.com

My name is Patrick Eannotti Sr. and I live in Ansonia CT. I have lost at least 12 family members to Huntington's disease and counting. I am submitting this testimony to share my concerns

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about current FDA regulatory decisions and their impact on the Huntington disease (HD) community.

I watched my 2 younger sisters suffer and die from this horrible disease, and neither reached their 50th birthday. We are now into our 4th generation of family members having HD. When will there be a cure? I'm 64 and praying something will be done to stop the progression before I die.

Respectfully submitted,
 Patrick Eannotti Sr.
 Ansonia Ct
 peannotti@sbcglobal.net

My name is Joan Foor and I live in Cathedral City California. I was born in Pennsylvania to a family affected by this horrific disease. My grandfather, mother, brother, several aunts and cousins inherited H.D. My mother was unable to get support back in the 50's and just recently my cousin decades later had the same difficulties-wherein nursing homes once they found out she had Huntington's they would not accept her as a patient. And yet, her husband and daughter were worn out trying to get food or nourishment into her frail 75-pound body. She was alert and did her best to cooperate but choked on her food as her extremities flailed about banging against her padded bed rails.

I am sharing these facts as a daughter and sister who did everything possible to keep my mother and brother alive. I bore no children as I worried for fear of getting the disease myself. Every time I stumbled or dropped an item the fear came to my mind, "Am I getting the disease?" I am submitting this testimony to share my concerns about current FDA regulatory decisions and their impact on the Huntington disease (HD) community.

Respectfully submitted,
 Joan Foor R.N (retired)
 Cathedral City, CA
 jf4436@aol.comEmail

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My name is Stephanie Khoury, and I live in Milwaukee, Wisconsin. I am at risk of living with Huntington's disease and live with family members who tested gene positive. I am submitting this testimony to share my concerns about current FDA regulatory decisions and their impact on the Huntington disease (HD) community.

As a child, experiencing a parent with HD was traumatizing, tragic, and painful. Not only did I lack a maternal figure, I had to watch someone, someone who I should've known but instead as a stranger, deteriorate before my eyes. I couldn't explain what was happening or relate to any of the peers or adults in my life. It was isolating. Even after her passing, seldom do people understand the trauma I lived with as a child. In the present, the ever-impending doom of my brother's sickness as well as my own potential sickness, looms over my daily life like a thick fog. I can never be at peace. I never will be at peace. This is the experience of many children of HD parents like myself.

My brother participated in a clinical trial. This trial occurred hours away and was worrying to experience even from a distance. There was an overlying anxiety over his physical and emotional wellbeing.

Respectfully submitted,
Stephanie Marie Khoury
Milwaukee, Wisconsin
stephaniekhoury434@gmail.com

My name is Sarah Khoury, and I live in Milwaukee, WI. I am living with someone gene positive with Huntington's disease. I am submitting this testimony to share my concerns about current FDA regulatory decisions and their impact on the Huntington disease (HD) community.

My husband is gene positive, and while he does not currently display any HD symptoms currently, his mind is constantly torn away in the anxiety of what will come. With no cure in sight, our anticipation of losing him fills my heart with sorrow each day.

We were blessed to have an HD free child through numerous PGT-IVF grants, and he is the light of our life. Our hope is that he will not have to see his father become ill, as my husband watched his mother slowly fade away.

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Respectfully submitted,
 Sarah Khoury
 Milwaukee, WI

My name is Christina DeGryse, and I live in Birmingham, Michigan. I am a family member of someone living with Huntington's disease. I am submitting this testimony to share my concerns about current FDA regulatory decisions and their impact on the Huntington disease (HD) community.

For families like mine, this disease is not theoretical, it is deeply personal. We have watched loved ones deteriorate year by year, knowing there is nothing available to slow or stop the progression of this devastating illness.

Respectfully submitted,
 Christina DeGryse
 Birmingham, Mi
christinazivan@gmail.com

My name is Janet Brandt, and I live in Milwaukie, OR. I am living with Huntington's disease. I am submitting this testimony to share my concerns about current FDA regulatory decisions and their impact on the Huntington disease (HD) community.

Due to my Huntington's Disease I had to retire 5 years early from my C level executive job. The financial impact of this is of course significant. Besides the financial impact there are ongoing and worsening physical symptoms. Currently there are some symptom management options, but no cure for this disease.

To that end, my sister (also a Huntington's victim) and I both signed up with the Seattle Center for Excellence. We are committed to being a part of a cure so that our children and grandchildren may not have to suffer the way that we have.

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My sister did participate in one clinical trial. So far, I made it to a level of testing that included a brain MRI to see if I would qualify for a brain surgery, and I didn't. However, we're both still willing to help with the research any way that we can.

Respectfully submitted,
Janet Brandt
Milwaukie, OR
janet.brandt23@yahoo.com

My name is Patricia Huffman, and I live in Richmond, Texas. I am the spouse/caregiver of someone living with Huntington's disease. I am submitting this testimony to share my concerns about current FDA regulatory decisions and their impact on the Huntington disease (HD) community.

My husband, Jon Huffman, and I are both retired pharmacists. Our ability to remain in the workforce, in a profession we loved, was greatly diminished by Huntington's disease. My husband retired at age 52, and I retired at 60. We lived modestly and saved carefully for retirement with this possibility in mind. However, losing access to employer-sponsored health insurance was a consequence I did not anticipate. Marketplace health insurance subsidies reduced our premiums to a manageable level and proved to be a better option than COBRA.

I also did not anticipate the emotional impact of leaving my profession. I struggled deeply with the loss of purpose, the challenge of finding joy in daily routines, and the severed connection with colleagues who had long been an important part of my life.

As science-minded individuals, Jon and I eagerly pursued participation in clinical trials as soon as he received his Huntington's disease diagnosis in 2014. We understood that these studies might not benefit him directly, but we believed strongly in contributing to the advancement of knowledge for future patients and families. Over the years, there were many opportunities to participate, each requiring significant time, travel, and physical endurance.

My husband underwent multiple MRIs, frequent blood draws, and several lumbar punctures, procedures that were often physically uncomfortable and emotionally taxing. Each study visit required careful coordination, long days at medical centers, and a willingness to tolerate

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uncertainty and risk. As both a patient and a former healthcare professional, Jon approached these experiences with determination and generosity, fully aware of what participation entailed and why it mattered.

As his disease progressed, the physical and cognitive demands of trial participation increased, and eventually Jon no longer met eligibility criteria. This transition was difficult, not only because it marked another loss caused by Huntington's disease, but because research participation had given us a sense of purpose and hope. Through conversations with researchers, we have been reassured that Jon's involvement helped inform current trial design and deepen scientific understanding of Huntington's disease progression. Our experience underscores how FDA decision making—particularly around trial design, regulatory clarity, and benefit risk assessment for rare disease populations—directly determines whether families like ours have meaningful opportunities to participate in research and pursue hope in the face of devastating illness.

As we approach the fifteen year mark since Jon's diagnosis—and nearly twenty years since I first noticed subtle changes in his gait—I am now the one planning our funerals and end of life care. I will turn 65 in a couple of weeks. Retirement, for me, does not mean rest or shared moments of ease. It means providing constant supervision, cleaning up accidents, assisting with feeding, and managing emotional outbursts. This is the daily reality of caregiving for someone with advancing Huntington's disease.

Respectfully submitted,
 Patricia Huffman
 Richmond, Texas
 pahuff01@gmail.com

My name is Karl Miran, and I live in North Plainfield, NJ. I am a family caregiver for my wife, who is living with late-stage Huntington's disease. I am submitting this testimony to share my concerns about current FDA regulatory decisions and their impact on the Huntington disease (HD) community.

My wife (an accomplished librarian and IT director, managing a staff of 10) had her first physical symptoms of HD in 2008, but after 2012, the progression intensified as she lost her

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career, her ability to safely drive a car and became clinically depressed. She became alienated from many friends and family members. Today, she is unable to walk, speak more than 2-3 words at a time. She is dependent on our help for all her Activities of Daily Living, including eating, drinking, dressing, bathing and toileting.

Our children, and to a lesser extent our nephews and nieces, have seen her decline and the loss of her personality. Many of them are at risk. They could get tested for the HD gene, but, if there is no cure, they wonder if it is better to "not know" their status. However, if there was an approved therapy to slow the progression of the disease, they would be more likely to test for the gene. That early knowledge would allow them to start the medication much earlier (before symptoms start), which would result in a better and longer life, since The potential new medications work by slowing the disease's progression.

Respectfully submitted,
Karl Miran
North Plainfield, NJ
kmiran60@gmail.com

My name is Martha Larson, and I live in Durham, NC. I am a family member of someone living with Huntington's disease. I am submitting this testimony to share my concerns about current FDA regulatory decisions and their impact on the Huntington disease (HD) community.

Huntington Disease does not discriminate; it affects people of all races, socioeconomic groups, and communities. This disease is deeply personal to me. Both my husband and son are living with HD. My husband was diagnosed 3 years ago after several years of a misdiagnosis of Alzheimer's disease. Our son tested before having a second child. His life and those of his wife and young son has been turned upside down. Our daughter and grandson are considered At Risk meaning they have not tested but have a parent who is positive. He is a successful entrepreneur however that means he relies on the marketplace for health insurance. You can only imagine the anxiety around whether the marketplace will continue. My husband and I are both Navy veterans. We do not have concerns related to health or dental insurance. However the tetrabenazaprine my husband takes costs over \$10,000/mo. We worry how our son will be able to afford that if or when chorea movements begin. We are not alone in this fight but this can be a very isolating disease. Social engagement is vital but requires planning for contingencies like coughing outbursts, bowel issues, and access to restaurants and other public places.

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When UniQure's AMT-130 was looking like it would be approved our 10 year old granddaughter said "When Papa is better we can go on another camper van trip."

Because of Eric's age, he is not eligible to participate in clinical trials. But can you imagine how it felt to complete paperwork donating my husband's brain to the Harvard brain bank.

Respectfully submitted,
Martha Larson
Durham, NC
mlarson102@gmail.com

My name is Amy Turner LaDow and I live in Valparaiso, Indiana. I have and care for other family members living with Huntington's disease. I am submitting this testimony to share my concerns about current FDA regulatory decisions and their impact on the Huntington disease (HD) community.

This hereditary disease has already eliminated many members of my family (6) and is destroying many others (20+). Since 1974, for 51 years, this hereditary disease has been the constant that informed every decision of my life. And today in very quick fashion it is trying to take the lives of two more nieces after already claiming their mothers, three of my sisters total, my father, grandmother, and a nephew. Five more are actively living with it, me included, two are nearing end of life, and 20 more are at-risk across four generations. I don't write about this horror story impact for shock value; I write this because it is my rare disease story, and it is slowly killing us. It is imperative that Huntington's disease receive the attention it was promised by the FDA to review AMT130 to allow my family to regain some of the hope it once had.

A little about HD, there is no treatment or cure, no way to slow it down, and minimal symptomatic medications (at \$10,000/month). Basically the brain is slowly dying bringing cognitive, psychological, and physical impairment to all motor skills affecting basic skills like thinking, sitting up, and eating. In 1993 the gene marker was found, and we believed a cure was "just around the corner". That has proven false trial after trial, year after year. My family alone has participated in over 20 medical trials, some observational, but many invasive. Many of the trials can be brutal, specifically, our most recent trial for a niece requires lumbar punctures and significant walking, testing, EKGs, MRIs, all of which are embarrassingly difficult, exhausting, and some painful. Sadly, we believe she is in the placebo group because she is no longer able walk without assistance. For Christmas she got a walker and just this week we almost lost her to associated complication, choking, which resolved through use of the Heimlich. This marks the second time and four years that her 25+ trips to the city are for naught. And, given that her brain is degrading, her executive function, mental health, and physical health, is significantly

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deteriorating, she can no longer motivate herself to participate only for the good of others. Were it not constant reminders of her at-risk kids and grandkids, she would have ended her participation.

But she, my 47-year-old niece, is just one example, of many who have already lost or are caring for their ill parents, and cannot drive to the city for trial visits. Luckily she has me to sponsor her and get her to the city for her visits. But this is not sustainable given that this fatal disease is hereditary; your parents die and cannot lead you in this journey.

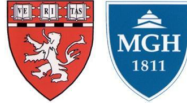
It is essential that we find a faster, better, more humane way to run these necessary human trials. One way, which was the agreed to plan for Amt-130, is to use our very robust database of lived experience as the control group. That would mean, if you are eligible to get in the trial, you would definitely receive the medicine, and if not, we track comparable data from like candidates without them having to face the physical and psychological pain of the placebo trial. They could go on living their shortened life with their annual HD program check-in for blood work and objective symptoms testing.

Further, I implore you to reinstate the science team on the FDA and charge them to earnestly, ethically review the empirical trial data and get this treatment in the hands of doctors so the researchers can move on to discover a version that is less costly and more achievable for the extended families like mine that have hope that they can receive ten or more in the next decade, to significantly slow the advancing of this cruel disease.

Respectfully submitted,
 Amy Turner LaDow
 Valparaiso, Indiana
 Amyturnerladow@gmail.com

HARVARD MEDICAL SCHOOL

JEREMY D. SCHMAHMANN, M.D.
Professor of Neurology

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October 3rd 2023

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Dear Drs. Freilich and Buracchio,

Re: Troriluzole in spinocerebellar ataxia

We, the undersigned neurologists, subspecialty ataxiologists, clinical trialists and researchers who have for decades studied and treated patients suffering from Spinocerebellar Ataxia (SCA), have been exceedingly frustrated by the lack of meaningful options for our patients.

SCA is a rare, genetic neurodegenerative disease that consists of multiple genetic subtypes. The most common subtype, SCA3, is estimated to affect up to 5,000 people in the U.S., though the number of people who are currently diagnosed is much fewer. SCA3 usually strikes patients in mid-adulthood but it can manifest in the teenage years. It is characterized clinically by a range of debilitating symptoms. These

include loss of coordination and balance leading to falls, self-injury and loss of independence; dysarthria making speech unintelligible; dysphagia leading to aspiration pneumonia; dystonia, spasticity, rigidity, and tremors which can be pain-inducing, embarrassing, and disabling; bulging eyes and visual dysfunction with nystagmus, diplopia and ophthalmoplegia preventing reading, driving and independent living; urinary incontinence and retention predisposing to urosepsis and systemic infection; and cognitive decline characterized by dysexecutive function and personality change. SCA is relentlessly progressive, leading to severe disability and premature death. There are no FDA-approved treatments or available disease-modifying therapies that change the trajectory of this devastating neurodegenerative disease.

Because SCA is inherited in an autosomal dominant pattern, multiple family members (parents, children, aunts, uncles, cousins) are living with SCA, often at the same time. A single caregiver in a family may be taking care of multiple affected relatives. Beyond the physical impact, the emotional and psychological damage is unfathomable and often leads to anxiety, depression, and suicidality. It is unbearable to think about the desperation people with SCA face, with one study finding 65% of people with SCA3 experiencing suicidal ideation.

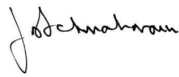
We have reviewed the results of Biohaven's Phase 3 study of troriluzole and, based on these data, we want to have troriluzole available for our patients with SCA3. We note that this is the first prospective study of a SCA therapeutic that has shown clinically meaningful changes in patients with SCA, and we are impressed with the findings. Data from the randomization phase show clear and consistent improvements in troriluzole-treated patients with SCA3, including data showing treatment benefit in the f-SARA and CGI, as well as a greater than 50 percent reduction in falls in treated patients as compared to placebo. While not originally designed to assess efficacy in reducing falls, the importance of morbidity related to falls in this patient population cannot be overstated and is endorsed by patients and their families in the countless interactions that we have all had with our patients over the years. Further supportive to us are: analyses in SCA3 from a composite scale, which reveals a 7-month delay in disease progression in troriluzole-treated patients during the double blind phase; the 3-year long-term data from both the pivotal SCA trial and the earlier proof of concept trial, which demonstrates attenuation of disease progression at years 1, 2, and 3 across the All SCA genotype population; and an exploratory analysis from a quantitative video analysis of gait showing improvement in gait ataxia in the troriluzole-treated arm, as well as quantitative data to support the falls analysis. The consistency of these analyses, despite the lack of a positive finding on the primary endpoint in All SCA in the Phase 3 study, leaves us in no doubt that troriluzole is likely to have meaningful improvements in the disease trajectory in patients with SCA3.

We urge the FDA to minimize any future delays in evaluating the troriluzole clinical data and to exercise maximum flexibility in considering approval of an NDA for troriluzole in SCA3. This drug has proven to be safe and well tolerated, which we find remarkable given the evidence so far in favor of its beneficial impact in the SCA patient population. Since the discovery of the first gene for SCA over three decades ago, we have been waiting for a treatment to offer our patients. The need for an intervention that can delay disease progression and help patients maintain independence is urgent. With every passing month, patients suffer irreversible neuronal cell death and functional decline. The SCA community cannot wait

the years it would take to conduct an additional, appropriately powered trial in SCA, when we believe the available data provide adequate information to inform our prescribing decisions.


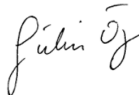

We appreciate the complexity and volume of applications the FDA must contend with. We are nevertheless encouraged by the FDA's own precedence for a path forward, given FDA willingness to approve a number of other drugs that did not fully meet primary endpoints. Approval of these other drugs provided life-changing treatments for patients without other options. We respectfully and urgently request the same consideration for troriluzole for the SCA patient population. We believe troriluzole is a beneficial, clinically meaningful, safe treatment for our patients, we want to have this option to offer our patients and their families, and we respectfully but urgently request that in the spirit of beneficence you honor our plea to help us care for and improve the lives of our SCA patients by an FDA evaluation of the troriluzole clinical data.







Yours sincerely,



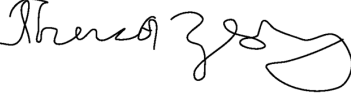

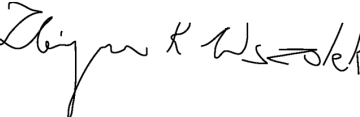


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Together with:

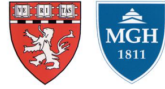
Name	Title	Signature
Burton Scott	Professor of Neurology, Duke University Movement Disorders Center	
Gulin Oz	Professor of Radiology, Center for Magnetic Resonance Research, University of Minnesota	
Laura Ranum	Kitzman Family Professor of Molecular Genetics and Microbiology and Director of the Center for NeuroGenetics	/Laura Ranum/ 

Lauren Seeberger	Clinical Professor Neurology, University of Colorado	/Lauren C. Seeberger, M.D., F.A.A.N./
Liana Rosenthal	Associate Professor of Neurology, Director JHU Ataxia Center	
Matthew Burns	Assistant Professor of Neurology, Director of the University of Florida Center of Excellence in Ataxia	
Patricia Greenstein	Assistant Professor of Neurology, Harvard Medical School and Beth Israel Deaconess Medical Center	/Patricia Greenstein, MB.BCh/
Pravin Khemani	Neurologist, Medical Director, Movement Disorders Section, Swedish Neuroscience Institute, Seattle, WA	
Robert B. Wilson	Professor of Pathology and Laboratory Medicine, Perelman School of Medicine at the University of Pennsylvania	
Sheng-Han Kuo	H. Houston Merritt Associate Professor of Neurology, Columbia University	
Susan Perlman	Clinical Professor of Neurology, David Geffen School of Medicine at UCLA	

Terry D. Fife, MD	<p>Professor of Neurology, University of Arizona College of Medicine – Phoenix Director, Vestibular Neurology & Balance Disorders Program</p> <p>Director, Barrow Ataxia Center, a National Ataxia Foundation Center of Excellence Director, Graduate Medical Education & DIO</p>	
Tetsuo Ashizawa	<p>Professor of Neurology, Weill Cornell Medicine and Houston Methodist Hospital; Director, Neuroscience Research Program, Houston Methodist Research Institute</p>	
Theresa Zesiewicz	<p>Professor of Neurology, Division Chief, USF Ataxia Research Center</p>	
Trevor Hawkins	<p>Assistant Professor of Neurology, University of Colorado Anschutz Medical Campus</p>	
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January 7, 2025

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Dear Drs. Cavazzoni and Stein,

We, the undersigned neurologists, experts in ataxia, clinical trialists and researchers who have taken care of patients suffering from Spinocerebellar Ataxia (SCA), have been waiting decades for a meaningful treatment option for our patients. Troriluzole is the first pharmacotherapy to demonstrate effectiveness in the treatment of patients with SCA.

SCAs are rare, dominantly inherited neurodegenerative diseases that affect approximately 15,000 people in the U.S., though the number of people who are currently diagnosed is much fewer. SCA usually strikes patients in mid-adulthood, but it can manifest in the teenage years. It is characterized clinically by relentless progression in ataxia symptoms, which include loss of coordination and balance leading to falls, self-injury and loss of independence; dysarthria making speech unintelligible; dysphagia leading to aspiration pneumonia; painful neuropathy; visual dysfunction; urinary incontinence and retention predisposing to urosepsis and systemic infection; and cognitive decline characterized by dysexecutive function and personality change. SCA leads to severe disability and premature death. There are no FDA-

approved treatments or available disease-modifying therapies that change the trajectory of this devastating neurodegenerative disease.

Because SCA is inherited in an autosomal dominant pattern, multiple family members (parents, children, aunts, uncles, cousins) are living with SCA, often at the same time. A single caregiver in a family may be taking care of multiple affected relatives. Beyond the physical impact, the emotional and psychological burden to patients and families is unfathomable and often leads to anxiety, depression, and suicidality.

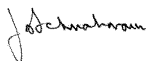
Biohaven's 8-year development program has produced the largest clinical trial dataset in SCA to date. We have been investigators in Biohaven's clinical trials of troriluzole and have reviewed data from Study BHV4157-RWE as well as the earlier studies. Results across these studies show consistent evidence that troriluzole delays disease progression in patients with SCA. In our own clinics, this is exactly what we have observed. Many of us are also investigators in the US natural history study, CRC-SCA. While progression rates vary both across and within genotypes, all SCA patients worsen by year 3. The nonlinear progression observed in the Biohaven trial is consistent with natural history data, and with our own observations of patients. Because predictable progression is reliably seen at year 3, the use of natural history data was necessary to demonstrate disease stability in troriluzole-treated patients across genotypes. The real-world evidence study was designed with the utmost rigor and shows substantial slowing of disease progression in patients treated with troriluzole versus matched patients from three separate control arms. Troriluzole treated patients experienced a 50-70% slowing of progression compared to patients from the natural history studies, representing a 1.5-2.2 year delay in disease progression over the 3 year study period. Supportive data from the randomization phase of Study 206 showed clear and consistent improvements in SCA3 troriluzole-treated patients, the genotype that progressed over one year in the placebo arm, including data showing treatment benefit in the f-SARA and the Clinical Global Impression of change. Results across these studies are consistent with a treatment effect. Additionally, a greater than 50 percent reduction in falls in treated patients across all genotypes compared to placebo was observed. While not originally designed to assess efficacy in reducing falls, the importance of morbidity related to falls in this patient population cannot be overstated and is endorsed by patients and their families in the countless interactions that we have all had with our patients over the years. This is the first and only therapeutic that has shown clinically meaningful changes in patients with SCA, and we are impressed with the findings. The consistency of these analyses, and the compelling positive results from the real-world evidence study across 9 hierarchical primary and secondary endpoints convinces us that troriluzole is likely to have meaningful improvements in disease trajectory in SCA patients.

We urge the FDA to minimize any delays in evaluating the troriluzole clinical data and to exercise maximum flexibility in considering approval of an NDA for troriluzole in SCA. This drug has proven to be safe and well tolerated, which we find remarkable given the evidence so far in favor of its beneficial impact in the SCA patient population. The need for an intervention that can delay disease progression and help patients maintain independence is urgent. With every passing month, patients suffer irreversible neuronal cell death and functional decline. The SCA community cannot wait the many years

it would take to conduct an additional 3-year placebo controlled trial, when we believe the available data provide adequate information to inform our prescribing decisions.

We are encouraged by the regulatory flexibility afforded to rare and fatal diseases and by the FDA's willingness to accept real-world data in other rare disorders. Approval of troriluzole, a safe, once daily pill, has the potential to provide life changing treatments for patients without other options. We believe troriluzole is a beneficial, clinically meaningful, safe treatment for our patients, we want to have this option to offer our patients and their families, and we respectfully but urgently request that in the spirit of beneficence you honor our plea to help us care for and improve the lives of our SCA patients.

Yours sincerely,



Jeremy D. Schmähmann, MD, FAAN, FANA, FANPA

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CC:
 Senator Susan Collins, Chair, Senate Appropriations Committee
 Senator Roger Wicker, Co-Chair, Rare Disease Caucus
 Senator Amy Klobuchar, Co-Chair, Rare Disease Caucus
 Representative Gus Bilirakis, Co-Chair, Rare Disease Caucus
 Representative Doris Matsui, Co-Chair Rare Disease Caucus
 Senator Richard Blumenthal, Member, Rare Disease Caucus
 Representative Ro Khanna, Member, Rare Disease Caucus

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April 29th 2025

Dr. Martin Makary, MD, MPH, Commissioner
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Commissioner@fda.hhs.gov

Martin.Makary@fda.hhs.gov

Dear Dr. Makary,

We, the undersigned neurologists, experts in ataxia, clinical trialists and researchers who have taken care of patients suffering from Spinocerebellar Ataxia (SCA), have been waiting decades for a meaningful treatment option for our patients. Troriluzole is the first pharmacotherapy to demonstrate effectiveness in the treatment of patients with SCA.

SCAs are rare, dominantly inherited neurodegenerative diseases that affect approximately 15,000 people in the U.S., though the number of people who are currently diagnosed is much fewer. SCA usually strikes patients in mid-adulthood, but it can manifest in the teenage years. It is characterized clinically by relentless progression in ataxia symptoms, which include loss of coordination and balance leading to falls, self-injury and loss of independence; dysarthria making speech unintelligible; dysphagia leading to aspiration pneumonia; painful neuropathy; visual dysfunction; urinary incontinence and retention predisposing to urosepsis and systemic infection; and cognitive decline characterized by dysexecutive function and personality change. SCA leads to severe disability and premature death. There are no FDA-approved treatments or available disease-modifying therapies that change the trajectory of this devastating neurodegenerative disease.

Because SCA is inherited in an autosomal dominant pattern, multiple family members (parents, children, aunts, uncles, cousins) are living with SCA, often at the same time. A single caregiver in a family may be taking care of multiple affected relatives. Beyond the physical impact, the emotional and psychological burden to patients and families is unfathomable and often leads to anxiety, depression, and suicidality.

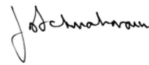
Biohaven's 8-year development program has produced the largest clinical trial dataset in SCA to date. We have been investigators in Biohaven's clinical trials of troriluzole and have reviewed data from Study BHV4157-RWE as well as the earlier studies. Results across these studies show consistent evidence that troriluzole delays disease progression in patients with SCA. In our own clinics, this is exactly what we have observed. Many of us are also investigators in the US natural history study, CRC-SCA. While progression rates vary both across and within genotypes, all SCA patients worsen by year 3. The nonlinear progression observed in the Biohaven trial is consistent with natural history data, and with our own observations of patients. Because predictable progression is reliably seen at year 3, the use of natural history data was necessary to demonstrate disease stability in troriluzole-treated patients across genotypes. The real-world evidence study was designed with the utmost rigor and shows substantial slowing of disease progression in patients treated with troriluzole versus matched patients from three separate control arms. Troriluzole treated patients experienced a 50-70% slowing of progression compared to patients from the natural history studies, representing a 1.5-2.2 year delay in disease progression over the 3 year study period. Supportive data from the randomization phase of Study 206 showed clear and consistent improvements in SCA3 troriluzole-treated patients, the genotype that progressed over one year in the placebo arm, including data showing treatment benefit in the f-SARA and the Clinical Global Impression of change. Results across these studies are consistent with a treatment effect. Additionally, a greater than 50 percent reduction in falls in treated patients across all genotypes compared to placebo was observed. While not originally designed to assess efficacy in reducing falls, the importance of morbidity related to falls in this patient population cannot be overstated and is endorsed by patients and their families in the countless interactions that we have all had with our patients over the years. This is the first and only therapeutic that has shown clinically meaningful changes in patients with SCA, and we are impressed with the findings. The consistency of these analyses, and the compelling positive results from the real-world evidence study across 9 hierarchical primary and secondary endpoints convinces us that troriluzole is likely to have meaningful improvements in disease trajectory in SCA patients.

We urge the FDA to minimize any delays in evaluating the troriluzole clinical data and to exercise maximum flexibility in considering approval of an NDA for troriluzole in SCA. This drug has proven to be safe and well tolerated, which we find remarkable given the evidence so far in favor of its beneficial impact in the SCA patient population. The need for an intervention that can delay disease progression and help patients maintain independence is urgent. With every passing month, patients suffer irreversible neuronal cell death and functional decline. The SCA community cannot wait the many years it would take to conduct an additional 3-year placebo-controlled trial, when we believe the available data provide adequate information to inform our prescribing decisions.

FDA regulations and guidances have established procedures for FDA to appropriately exercise the broadest flexibility in applying the statutory standards of safety and effectiveness for rare, life-threatening and severely debilitating illnesses, especially where no satisfactory alternative therapy exists (21CFR312.80). Moreover, regulations emphasize: "The Food and Drug Administration (FDA) has determined that it is appropriate to exercise the broadest flexibility in applying the statutory standards, while preserving appropriate guarantees for safety and effectiveness. These procedures reflect the recognition that physicians and patients are generally willing to accept greater risks or side effects from products that treat life-threatening and severely debilitating illnesses, than they would accept from products that treat less serious illnesses. These procedures also reflect the recognition that the benefits of the drug need to be evaluated in light of the severity of the disease being treated."

We believe it would stand contrary to FDA policy, legislative mandates to speed treatments for rare diseases and the basic tenets of medical science for the Division to not apply regulatory flexibility to the approval of the troriluzole NDA. Leading SCA experts have directly communicated to FDA their conclusion that troriluzole is the first agent to "bend the arc" of disease trajectory in this neurodegenerative disorder.

Yours sincerely,



Jeremy D. Schmähmann, MD, FAAN, FANA, FANPA

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September 15th, 2025

Dr. Martin Makary, MD, MPH, Commissioner
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Dear Dr. Makary,

We, the undersigned neurologists, experts in ataxia, clinical trialists and researchers, who have collectively taken care of thousands of patients suffering from Spinocerebellar Ataxia (SCA), are writing to reiterate our strongest and most unequivocal support for approval of the New Drug Application (NDA) for troriluzole in SCA, based on our thorough scientific review of the data package as well as our own clinical experience with troriluzole over the near decade long troriluzole development program.

We would like to make very clear that, while any rare disease dataset has its limitations, Biohaven's real-world evidence study is not only interpretable but compelling and convincingly establishes the conclusion that troriluzole is the first effective treatment for patients with SCA—a rare, progressive, severe and life-threatening neurodegenerative disease. There are no FDA-approved treatments or available disease-modifying therapies that change the trajectory of this devastating disease. Accordingly, we urge FDA to act for SCA, as you have publicly emphasized for such rare diseases, employing a customized regulatory process to fit SCA rather than a rigid one-size-fits-all approach. Common-sense, patient-centricity, and maximum regulatory flexibility are needed in considering approval of the NDA for troriluzole.

Patients with SCA and those clinicians who treat them deserve to be heard on this important NDA filing. There is too much at stake for patients if troriluzole is not approved. If needed, we are available to meet directly with you to review the data package that has been submitted to the FDA and provide our expert input.

As we eagerly await word from FDA on the decision of the troriluzole NDA, we would like to highlight what is at stake for SCA patients and their families—life or death and irreversible loss of brain cells and neurological function across generations. Patients with SCA know the devastating course that will transpire in this neurodegenerative disorder with no treatment. Patients are willing to accept some degree of uncertainty

around matters such as statistical approaches and methods based on the safety of troriluzole, biologic plausibility of mechanism of action and the absence of any current treatment options.

FDA leadership and policy has emphasized the importance of incorporating the patient perspective in the benefit-risk assessments for serious conditions and for patients with life-threatening diseases. The FDA must appropriately balance patient access, safety and scientific rigor. Clinicians such as the undersigned have devoted our entire careers to the research and clinical care of SCA. We ask for your help in advancing troriluzole to patients with SCA. The physical and emotional burden of this disease on families is unfathomable. Because SCA is a genetic disease that is inherited in an autosomal dominant pattern, the child of a parent with SCA has a 50% chance of inheriting the disease-causing gene mutation. If that occurs, then succumbing to the disease is inevitable, often with an earlier age of symptom onset compared to their parent (i.e., genetic anticipation). Multiple generations of family members (e.g., grandparents, parents, children, aunts, uncles, and cousins) are often living with SCA at the same time, and a single caregiver within a family may be taking care of multiple affected relatives. This enormous psychological burden, coupled with the lack of any available treatment, is associated with high rates of anxiety, depression, and suicidality.

"I saw my mother. It is like a crystal ball in the future."

— Patient with SCA

SCA strikes in the prime of life, with typical onset between ages 20 and 50, but it can manifest even earlier. SCA is characterized by progressive degeneration of the cerebellum (which is responsible for coordinating movement) as well as the brainstem and spinal cord. SCA causes relentlessly progressive ataxia leading to severe disability, loss of independence requiring a caregiver, and premature death. Symptoms include loss of coordination and balance; frequent falls leading to injury; loss of ambulation (i.e., using a walker, then needing a wheelchair, and eventually becoming bedbound); difficulty speaking leading to loss of ability to communicate; difficulty swallowing leading to loss of ability to safely eat or drink by mouth necessitating use of feeding tube and to risk of choking and aspiration pneumonia and sepsis; visual impairment; urinary incontinence and retention predisposing to urinary tract infection and urosepsis; painful neuropathy; cognitive decline; and personality changes.

The unmet medical need is clear, but SCA is subject to the challenges of rare disease drug development. A traditional, large-scale clinical trial in SCA is not feasible. Based on estimates from published literature and from the troriluzole development program, completing a global randomized placebo controlled trial to show a 50% reduction in disease progression in SCA patients would take a total of approximately 8 years. Not only would such a trial be lengthy, but it would also face other practical challenges that limit its feasibility. It is unlikely that our patients would be willing to commit to such a long-term trial where they have a 50% chance of receiving placebo or that they would not prematurely discontinue from the trial.

SCA firmly fits within FDA's initiatives for rare diseases, for which, conducting a traditional clinical trial is not feasible. Moreover, troriluzole, itself, and the NDA data package have several important and unique features that warrant a customized regulatory process rather than a rigid one-size-fits-all approach. Common-sense, patient-centricity, and maximum regulatory flexibility are needed for these patients.

Troriluzole is a prodrug designed to overcome the significant pharmacology limitations of riluzole (a neuroprotective agent that is FDA-approved), thereby optimizing for efficacy and safety. Riluzole is the first

neuroprotective treatment that was approved by FDA in 1995 for the treatment of amyotrophic lateral sclerosis (ALS), but it exhibits significant pharmacology limitations which restrict its efficacy and safety across other neurodegenerative diseases. Compared to oral riluzole, troiriluzole offers higher oral bioavailability, safely delivering 50% higher exposures of riluzole; lower pharmacokinetic variability, delivering consistent therapeutic exposures of riluzole; and bypasses 1st pass metabolism reducing drug burden on the liver, with superior hepatic safety and no dose-related hepatotoxicity. Notably, ALS is a neurodegenerative disease that has clinical, pathological, mechanistic, and genetic overlap with SCA, suggesting clinical evidence from riluzole in ALS is germane and confirmatory for troiriluzole in SCA.

Troiriluzole acts on a scientifically plausible mechanism directly linked to SCA. Troiriluzole is a glutamate modulator that exerts therapeutic effects in SCA by normalizing synaptic glutamate. Synaptic glutamate dysfunction plays a central role in the pathogenesis of SCA by disrupting the finely tuned excitatory neurotransmission that is critical for cerebellar Purkinje cell function, synaptic activity, and cerebellar circuit integrity. This is supported by incontrovertible evidence from human genetics, molecular, cellular, and animal studies demonstrating altered glutamate receptor signaling, impaired glutamate reuptake by glutamate transporters and subsequent calcium dysregulation in SCA.

Troiriluzole has been remarkably safe and well tolerated to date across all studies, including in SCA patients over the 8 year development program. In fact, the troiriluzole adverse event profile was similar to placebo in SCA clinical trials. Troiriluzole demonstrated favorable overall safety profile compared to that of riluzole with lower rates of liver function test increases and no cases of severe DILI, severe neutropenia, nor interstitial lung disease. The well-characterized safety profile of troiriluzole assures a positive benefit-risk profile for the treatment of SCA.

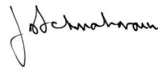
Troiriluzole demonstrates consistent evidence of benefits on SCA disease progression. We have been investigators in clinical trials of troiriluzole and have reviewed data from Study BHV4157-RWE as well as the earlier studies. Results across these studies show consistent evidence that troiriluzole delays disease progression in patients with SCA. In our own clinics, this is exactly what we have observed within the clinical trials and the Expanded Access Program (EAP). Many of us are also investigators in the US natural history study, CRC-SCA. While progression rates vary both across and within genotypes, all SCA patients worsen by year 3. The nonlinear progression observed in the Biohaven trial is consistent with natural history data, and with our own observations of patients. Because progression is reliably seen at year 3, the use of natural history data was necessary to demonstrate disease stability in troiriluzole-treated patients across genotypes. The real-world evidence (RWE) study was designed with the utmost rigor and shows substantial slowing of disease progression in patients treated with troiriluzole versus matched patients from three separate control arms. Troiriluzole treated patients experienced a 50-70% slowing of progression compared to patients from the natural history studies, representing a 1.5-2.2 year delay in disease progression over the 3 year study period. Supportive data from the randomization phase of Study 206 showed clear and consistent improvements in SCA3 troiriluzole-treated patients, the only genotype that progressed over one year in the placebo arm, including data showing treatment benefit in the f-SARA (primary outcome) and the Clinical Global Impression of change. Results across these studies are consistent with a treatment effect. Additionally, a greater than 50% reduction in falls in treated patients across all genotypes compared to placebo was observed. While not originally designed to assess efficacy in reducing falls, the importance of morbidity related to falls in this patient population cannot be overstated and is endorsed by patients and their families in the countless interactions that we have all had with our patients over the years. This is the first and only therapeutic that

has shown clinically meaningful changes in patients with SCA, and we are impressed with the findings. The consistency of these analyses, and the compelling positive results from the RWE study across 9 hierarchical primary and secondary endpoints convinces us that troriluzole is likely to have meaningful improvements in disease trajectory in SCA patients.

Given the FDA's commitment to accelerating patient access to therapies for devastating rare diseases through pragmatic and rigorous evidentiary standards aligned with scientific understanding and patient needs, we urge FDA to apply maximum flexibility and to approve the troriluzole NDA for SCA. FDA regulations and guidances have established procedures for FDA to appropriately exercise the broadest flexibility in applying the statutory standards of safety and effectiveness for rare, life-threatening and severely debilitating illnesses, especially where no satisfactory alternative therapy exists.

We, the leading SCA experts, have directly communicated to you our conclusion that troriluzole is the first agent to "bend the arc" of disease trajectory in this neurodegenerative disorder. Troriluzole has shown a strong safety and tolerability profile, along with clear signals of benefit for patients with this progressive disease. Ongoing post-approval monitoring to ensure continued safety and effectiveness in real-world settings may be reasonable. But the urgent need for patients and families is undeniable. Each day without treatment leads to irreversible neuronal loss and functional decline. The SCA community simply should not have to endure the years required for another years-long randomized placebo controlled trial when the available data already provide sufficient evidence to guide our prescribing decisions.

Yours sincerely,



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WAIVER PETITION UNDER 21 C.F.R. § 10.30; 21 C.F.R. § 314.126(c)

Interested parties including Spinocerebellar Ataxia (“SCA”) patients and family members, SCA treating clinicians, and Biohaven (each individually a “Petitioner” and collectively “Petitioners”) submit this petition under 21 C.F.R. § 10.30, 21 C.F.R. § 314.126(c), section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA), and its implementing regulations to request that the Commissioner of Food and Drugs and the Director of the Center for Drug Evaluation and Research take the actions set forth below in Section A with respect to the approval of Troriluzole to treat for Spinocerebellar Ataxia (SCA) for marketing under section 505(b)(2) of the FDCA pursuant to NDA 210862.

A. Actions Requested

The petitioner requests that the Food and Drug Administration (FDA or Agency):

1. Determine that the criteria for adequate and well controlled studies that requires placebo current control should be waived and instead FDA should recognize real world patients as control subjects for the pivotal clinical trial (Study BHV4157-206-RWE; ClinicalTrials.gov ID#NCT06529146) under which marketing approval has been sought for Troriluzole to treat for SCA. See 21 C.F.R. §314.126(b)(5)(c).
2. Determine that regulatory flexibility should be exercised to recognize real world patients as control subjects for the pivotal clinical trial under which marketing approval has been sought for Troriluzole to treat for SCA. See 21 C.F.R. §312.80.
3. On the basis of either or both of the foregoing determinations, and the fact that Study BHV4157-206-RWE achieved its primary and secondary outcome endpoints ($p < 0.05$), issue approval of NDA 210862 for marketing for treatment of SCA.

B. Statement of Grounds

1. Executive Summary

SCA is a rare, progressive, genetic and debilitating neurodegenerative disorder with no approved therapies currently available in the United States. This utterly unmet need calls for an innovative and flexible approach to approval.



Clinical trials typically include a population that serves as a concurrent control arm with which to compare the effects of the investigational drug to avoid confounding the study with bias. That control arm may consist of study subjects administered a placebo. However, conventionally controlled trials may be problematic due to limited patient populations and the severity of the condition.

The study that served as the primary basis of the NDA for troriluzole to treat SCA used an external control arm consisting of patients who had been treated outside the study in the “real world” rather than internally within the study. Nevertheless, the Study utilized the highly credible Clinical Research Consortium for the Study of Cerebellar Ataxia (CRC-SCA) natural history cohort as the external control arm. The CRC-SCA is supported by the National Ataxia Foundation (NAF) in collaboration with leading academic institutions to generate real-world data on the natural progression of SCAs that could inform clinical trial design, serve as external controls, and support regulatory decision-making. The CRC-SCA is recognized in the SCA research and treatment community to provide high-quality evidence on disease progression and to serve as an ideal external control.

The Study compared outcomes in troriluzole-treated patients against untreated participants from the CRC-SCA cohort using validated measures such as the functional Scale for the Assessment and Rating of Ataxia (f-SARA). The Study design aligns with FDA guidance on the use of RWE in regulatory contexts, particularly for a rare life-threatening disease with no existing treatment, including avoiding the ethical concerns of using placebo in this type of a population. The Study demonstrated meaningful slowing of disease progression over three years.

However, FDA has taken the position, in its November 4, 2025, CRL that the external control was inappropriate and issued a CRL. FDA stated that the Study could not be considered adequate and well controlled because of design flaws and methodological limitations that introduced bias into the study:

Several factors undermined the reliability of the Clinical Research Consortium for the Study of Cerebellar Ataxia natural history study (CRC-SCA) as a control arm in Study 206-RWE. The propensity score matching could not address important factors that could affect disease progression.... The comparison between progression rates at 1 year in subjects randomized to placebo in Study 206 and CRC-SCA controls revealed significant differences favoring placebo (particularly in SCA1 and SCA2 genotypes), providing direct evidence of confounding that undermines confidence in CRC-SCA as a control arm and in the results of Study 206-RWE.

The relevant federal regulations do provide that drug approvals generally should be based on adequate and well controlled studies which may include using placebo control. The same regulations provide that adequate and well controlled studies may use an historical control derived from an adequately documented natural history of the disease or condition. In addition, federal regulations expressly provide that FDA may waive all or any criteria of what may constitute an adequate and well-controlled study:

The Director of the Center for Drug Evaluation and Research may, on the Director's own initiative or on the petition of an interested person, waive in whole or in part any of the criteria in paragraph (b) of this section with respect to a specific clinical investigation, either prior to the investigation or in the evaluation of a completed study (21 C.F.R. 314.126(c)).

Further, federal regulations provide that while uncontrolled or partially controlled studies may not be the sole basis for approval they “may provide corroborative support ... regarding efficacy.” Even more specifically, federal



regulations state that in determining the approvability of new therapies for a rare life-threatening disease for which no treatment exists FDA should use maximum flexibility:

*The Food and Drug Administration (FDA) has determined that it is appropriate to exercise the **broadest flexibility** in applying the statutory standards, while preserving appropriate guarantees for safety and effectiveness. These procedures reflect the recognition that physicians and **patients are generally willing to accept greater risks or side effects** from products that treat life-threatening and severely-debilitating illnesses, than they would accept from products that treat less serious illnesses. These procedures also reflect the recognition that the **benefits** of the drug need to be **evaluated in light of the severity** of the disease being treated (21 C.F.R.312.80).*

In the present case, the external control arm was not problematic because the comparability between trial subjects and external controls was addressed by using rigorous Propensity Score Matching (PSM) and leveraging the US Natural History Study (CRC-SCA).

Ultimately, in these circumstances FDA should exercise regulatory flexibility, waive any purported requirement regarding placebo control in this instance, and approve the NDA.

2. Factual Background

a. Overview of Investigational Product and Regulatory History

This petition addresses NDA 210862 (the NDA) which is a 505(b)(2) application currently under review before the Center for Drug Evaluation and Research (CDER) and the subject of a Complete Response Letter issued on November 4, 2025 (the CRL). The sponsor of the NDA is Biohaven, which is a global clinical-stage biopharmaceutical company focused on the discovery, development, and commercialization of life-changing therapies to treat rare and common diseases. The NDA seeks marketing approval for troriluzole (BHV-4157) to treat for the treatment of adult patients with spinocerebellar ataxia (SCA).

SCA is a rare, progressive, genetic, and debilitating neurodegenerative disorder with no approved symptomatic or disease-modifying therapies currently available in the United States. Patients with SCA face significant unmet medical needs, including relentless motor impairment, loss of independence, injuries due to falls, loss of ambulation and reduced quality of life, often leading to premature disability and mortality. SCA3 is the most common genotype of SCA affecting over 40% of SCA patients. The high unmet need in this patient population underscores the urgency for innovative approaches to drug development and approval, particularly for rare diseases where traditional randomized controlled trials may be ethically and practically challenging due to small patient populations and the progressive nature of the condition.

The investigational drug product troriluzole is a tripeptide prodrug conjugate of riluzole designed to deliver consistent drug exposures and improve the safety profile of the active metabolite. Troriluzole has been developed as a formulated oral capsule in 3 dose strengths, 60 mg, 100 mg, and 140 mg. Troriluzole was investigated in a Phase 2b/3 study as treatment for SCA using the 140 mg capsule strength and a dosing regimen of 140 mg QD. In addition, a pivotal Phase 3 study investigated troriluzole 140 mg and 60 mg capsule strengths and a dosing regimen of 200 mg QD for treatment of SCA.



FDA has granted Orphan Designation, Fast Track Designation, and Priority Review, although FDA designed a Major Amendment that extended the action date by three months before issuing the CRL.

b. Chronology of Key Regulatory Submissions and Sponsor Correspondence

The key regulatory submissions and correspondence between FDA and the sponsor are as follows:

May 18, 2016 – Orphan designation

May 31, 2016 – IND 129397 submitted

April 27, 2017 – Fast Track designation

April 2017-November 2018 – Sponsor develops and validates f-SARA scale

- For use as primary outcome measure in clinical trials
- Working closely with SCA experts and FDA

December 2017 – FDA written recommendations from Type C Meeting

- FDA stated change from SARA scale to f-SARA

August 2018-March 2021 – FDA meetings and correspondence on Primary Outcome

2022 – Sponsor generates data from clinical trial in SCA3

- 1-year double-blind placebo-controlled trial shows signal for efficacy of troriluzole in the SCA3 genotype, which comprises >40% of all SCA genotypes. The placebo-adjusted difference on the primary outcome measure, the f-SARA, met a nominal p-value < 0.05. In addition, treatment with troriluzole was associated with favorable response on a clinician reported assessment (CGI-I) and risk reduction for falls (both < 0.05).

May 26, 2023 – NDA submission for SCA3

July 25, 2023 – Division issued a Refusal to file despite submission of a complete submission

August 16, 2023 – Type A Meeting request

October 5, 2023 – Type A Meeting

- Discussion with FDA, sponsor, NAF, SSCA patients, and SCA clinicians to discuss path forward for SCA treatment development

November 21, 2023 – Type C Meeting Request

- Sponsor spoke with leading SCA experts and considered new controlled study based on the 8 years of clinical trial experience and largest clinical trial dataset in SCA. Sponsor and leading ataxia experts concluded the only way to study treatment effect is to use real world evidence to develop a rigorous analysis of the data collected with troriluzole over several years and use an external control as the comparator.

February 8, 2024 – Type C Meeting



- Discussion focused on challenges of variable disease progression across SCA genotypes, and necessity of 3-year follow-up to assess for treatment effects across all genotypes.
- Conducting an adequately powered, placebo-controlled trial of this extended duration would not be feasible or ethical in this rare and fatal disease.
- Biohaven therefore proposed leveraging the 3-year data from troriluzole-treated subjects in Study BHV4157-206 and using a rigorously matched untreated external control derived from patient-level natural history data to fully assess treatment benefits in troriluzole-treated SCA patients.
- Division had no recommendations for a path forward, but referred sponsor to the FDA Guidance for Industry, Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision Making for Drug and Biological Products.
- Division requested sponsor to submit proposed SAP for the 3-year efficacy analysis compared to an external control natural history cohort for review.

March 7, 2024 – SAP submitted to IND

March 8, 2024 – FDA Type C Meeting Minutes

- Minutes requested additional information to be included in Biohaven's SAP
- Agency noted challenges to RWE approach, indicating that in light of the limitations, a large and robust treatment effect would be needed to overcome the biases of an externally controlled trial, in order for it to be used as the primary basis for substantial evidence for effectiveness
- FDA emphasized need for data transparency and traceability of real world data and referred to the FDA guidance Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision Making for Drug and Biological Products.

March 19, 2024 – SAP re-submitted to IND per FDA's comments

May 8, 2024 – Division reviewed SAP and provided comments

- Division's response again referenced FDA Guidance for Industry, Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision Making for Drug and Biological Products, which recommends providing both the draft protocol and SAP to the Division for review and comment prior to conducting analyses and stated that only a draft SAP was provided.

May 20, 2024 – Sponsor submitted BHV4157 SAP protocol and updated SAP

- SAP addressed FDA's May 8, 2024 comments

July 25, 2024 – FDA final feedback on protocol BHV4157-206-RWE and SAP to sponsor

August 29, 2024 – Sponsor submits final protocol and SAP incorporating FDA's comments

September 20, 2024 – Topline data from BHV4157-206-RWE

- Large robust treatment effect in SCA with troriluzole showing a 50-70% slowing of disease progression after 3 years of therapy ($p < 0.05$).
- Study achieved prespecified primary and 8 prespecified consecutive secondary outcome objectives



September 22, 2024 – Sponsor notifies Division of data

September 26, 2024 – FDA responds to sponsor

- FDA recommends Type B meeting to discuss the content, format, and data analysis methods to be included in resubmission to support determination of effectiveness.

October 1, 2024 – Type B Meeting Request

November 22, 2024 – Type B Meeting

February 12, 2025 – NDA 210862 for SCA re-submission accepted

- 505(b)(2) NDA
- Indication submitted for all SCA and not limited to SCA3
- Priority review granted
- PDUFA date August 10, 2025

March 27, 2025 – Mid-Cycle Meeting

- Sponsor asks if any supplemental data or analyses needed
- Division responds that any requests would be provided by information requests

May 14, 2025 – FDA notifies sponsor of Major Amendment designation

- FDA states designation due to sponsor responses to 3 IRs and Sponsor objects that responding to IRs should not be designated a Major Amendment
- IR responses directed FDA to data already in FDA's possession
- New PDUFA date delayed until November 10, 2025

May 14, 2025 – Sponsor request to FDA for meeting with Division

- Sponsor states IR responses do not meet standard for Major Amendment
- Sponsor requested FDA rescind designation and reinstate original PDUFA date

May 14, 2025 – Division holds 15-minute meeting

- Sponsor emphasizes 3-month delay effectively negates priority review and Fast Track
- Both designations reflective of unmet need, no current approved therapies, life-threatening condition

August 8, 2025 – FDA schedules Late Cycle Meeting for September 16, 2025

August 21, 2025 – FDA reschedules Late Cycle Meeting to September 18, 2025

- FDA states after further internal discussion advisory committee meeting not needed

September 18, 2025 – Late Cycle Meeting

- Sponsor states that if the Division disagrees with approvability of NDA using RWE that external expert opinion should be obtained by FDA and requests Advisory Committee meeting to resolve uncertainties or differences of opinion regarding 206-RWE data



- Sponsor notes when Division communicated after mid-cycle that planned Advisory Committee was cancelled
- Sponsor interpreted it to mean any internal FDA difference of opinion on the data had been resolved
- Sponsor suggested if Division continued to believe 206-RWE could not serve as basis of approval then an Advisory Committee should be held for further external expert opinion on the data.
- Division suggests that prior knowledge of data could have biased 206-RWE study,
- Sponsor responds by noting that open label data is routinely used in RWE studies but that information did not bias the design of the external control and the rigorous statistical approach suggested by the Division.
- Sponsor noted that prior to database analysis Division had directed that primary outcome measure at 3 years would be f-SARA and external comparison would be CRC-SCA
- Division did not want the external control to be the Global or EUROSACA natural history cohort, despite lower rates of missing data in the Global or EUROSACA natural history cohort. Division criticized the study for higher rates of missing data at Year 3 but the Sponsor noted that it was the Division that limited the dataset to CRC-SCA and that the Sponsor wanted to include the EUROSACA as rates of missing data were lower.
- Sponsor included EUROSACA and GLOBAL as secondary outcome measures in 206-RWE.
- Division provided feedback that sponsor should not use MAIC comparison but instead PSM approach should be taken with regard to the statistical analysis.
- Division speculation that sponsor used prior knowledge to bias results is unfounded and does not reflect the actual design of 206-RWE. The Division's criticism about prior knowledge does not reflect the facts that the SAP and protocol design were modified to incorporate all of the Division's feedback, thus reducing any bias that the Sponsor might have had on the study design and statistical analysis.
- 206-RWE design had been prespecified after incorporating Division's preferred approach to RWE design in both the SAP and study protocol.

September 29, 2025 – FDA notification to sponsor

- FDA has not identified any post-marketing requirements

September 30, 2025 – Amendment to NDA

- Sponsor provides additional data and analysis in support of ongoing review

October 17, 2025 – Sponsor requests correction to FDA Late Cycle Meeting Minutes

- Sponsor requests clarification that it did not oppose holding an advisory committee but had thought Advisory Committee was not warranted given the strength of the data and safety profile of trilorazole supporting approval
- Sponsor also requested notation that if FDA has residual concerns Division should convene Advisory Committee as the appropriate forum to resolve uncertainties or differences regarding the interpretation of 206-RWE.

October 24, 2025 – FDA response to sponsor

- FDA acknowledges sponsor's request but denies requested revisions since leadership has determined not to convene Advisory Committee so correction was not warranted.

November 4, 2025 – FDA issues CRL

- FDA finds 206-RWE is not adequate and well controlled due to design flaws and methodological limitations that have introduced bias including:



- Limited comparability between trial subjects and external controls and residual biases
- Site overlap, selection and expectations biases
- Substantial Missing Data
- Systematic Timing Bias
- Measurement Methodology Differences
- Lack of Pre-specification
- FDA also finds methodological issues preclude using secondary efficacy analyses of 206-RWE and post hoc analyses of 206 as confirmatory evidence including:
 - Secondary efficacy analyses of Study 206-RWE suffer same limitations as primary efficacy analysis
 - Post hoc SCA genotype 3 subgroup analyses of Study 206 not prespecified
 - Fall Risk Analysis of Study 206 not prespecified and suffers from multiple limitations
- FDA also finds nonclinical issue that major circulating metabolite DKP was not adequately assessed

November 9, 2025 – Sponsor responds to each item of the CRL and requests Type A Meeting

December 17, 2025 – Post CRL Type A Meeting

- Sponsor presented multiple paths forward based upon 8 year dataset that has been generated to date.
- The Division did not agree on any path forward based upon the current dataset but acknowledged that a new data doesn't necessarily need to be placebo-controlled.
- The Division suggested a randomized control study to take a subset of compassionate use patients off treatment and monitor for decline which could provide further evidence of a drug effect. An SCA expert at the meeting and the Sponsor both raised significant ethical issues about the FDA suggested randomized withdrawal design, as SCA is a progressive, neurodegenerative disorder and if patients worsened they would not recover as such worsening.
- FDA stated that a hard endpoint would need to be developed, and that prospective, fresh data from a new trial would be needed for a resubmission.
- Biohaven stated that there are no resources to do another 8 year study to gather data, but if there was an accelerated path forward that Biohaven and FDA could work on in a collaborative way, then that could be a possibility to continue the program. Biohaven will not be able to continue the program without a path forward.
- FDA stated that it did not see a path forward with this data and new data, new patients and a new trial is needed. FDA stated no resubmission could be based on data from -206 since the agency has exhausted all options with the current data.

c. Chronology of Key Submissions to FDA From Patients and Clinicians

Patients and their clinicians are passionately interested in the approval of the NDA because SCA is so debilitating and there are no approved therapies currently available in the United States. They recognize that this utterly unmet need calls for an innovative and flexible approach to approval and they have been active and vocal with FDA in their support. The following is a chronology of submissions to FDA made by patients and their clinicians:

September 14, 2023 – NAF Letter to FDA



- NAF CEO Andrew Rosen sends letter to Dr. Emily Freilich, MD, Director, Division of Neurology 1 and Teresa Buracchio, MD, Director, Office of Neuroscience

September 15, 2023 – NAF Publication Regarding FDA

- NAF publishes Community Response: FDA Review of Troriluzole NDA signed by over 3k patients

September 29, 2023 – Clinician-Researcher Letter to FDA

- Dr. Jeremy Schmähmann and clinician experts send letter to Dr. Emily Freilich, MD, Director, Division of Neurology 1 and Teresa Buracchio, MD, Director, Office of Neuroscience

November 19, 2024 – NAF Congressional Briefing

- NAF Hosts Congressional Briefing on importance of approving new treatments for rare diseases, especially those with no FDA-approved treatment options like SCA

January 6, 2025 – NAF and Ataxia UK Letter to FDA

- NAF and Ataxia UK send joint letter to CDER Director Dr. Patrizia Cavazzoni and Office of New Drugs Director, Dr. Peter Stein

January 7, 2025 – Clinician-Researcher Group Letter to FDA

- Dr. Jeremy Schmähmann and 17 clinician experts send letter to CDER Director Dr. Patrizia Cavazzoni and Office of New Drugs Director, Dr. Peter Stein

January 30, 2025 – Clinician-Researcher Group Letter to FDA

- Dr. Jeremy Schmähmann and 17 clinician experts send letter to Acting Director, CDER, Dr. Jacqueline Corrigan-Curay and Office of New Drugs Director, Dr. Peter Stein

April 29, 2025 – Clinician-Researcher Group Letter to FDA

- Dr. Jeremy Schmähmann and 17 clinician experts send letter to Commissioner Makary,

May 9, 2025 – NAF Petition For FDA Prioritization

- NAF launches Change.org petition calling on FDA to prioritize treatment options for rare diseases with urgent unmet needs including SCA

September 13, 2025 – NAF Posting Regarding SCA Patient

- NAF posts Cameryn's Story: this is what happens when hope takes too long

September 15, 2025 – Clinician-Researcher Group Letter to FDA

- Dr. Jeremy Schmähmann and 17 clinician experts send letter to Commissioner Makary, entitled: "Ataxia specialists around the USA urgently request the FDA to use its Congressionally mandated regulatory flexibility to approve troriluzole to improve the lives of patients with spinocerebellar ataxia"

3. Statutory and Regulatory Framework

The FDCA requires that drugs must be shown to be safe and effective. Effectiveness must be established by:



substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling.

21 U.S.C. § 355(d). "Substantial evidence" is defined as:

evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

21 U.S.C. § 355(d). FDA may base this finding on a single adequate and well-controlled study:

If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence.

21 U.S.C. § 355(d). To that end, federal regulations define "adequate and well controlled studies" to have the following characteristics:

- (2) The study uses a design that permits a valid comparison with a control to provide a quantitative assessment of drug effect. The protocol for the study and report of results should describe the study design precisely; for example, duration of treatment periods, whether treatments are parallel, sequential, or crossover, and whether the sample size is predetermined or based upon some interim analysis.

21 C.F.R. §314.126(b)(2). The regulations recognize various types of control:

- (i) *Placebo concurrent control.*
- (ii) *Dose-comparison concurrent control.*
- (iii) *No treatment concurrent control.*
- (iv) *Active treatment concurrent control.*
- (v) *Historical control.*

21 C.F.R. §314.126(b)(2). The regulation further requires that:

Adequate measures are taken to minimize bias on the part of the subjects, observers, and analysts of the data.

21 C.F.R. §314.126(b)(5). After stating these statements of parameters, the regulation includes a section that specifies that FDA may waive any of these requirements in appropriate circumstances:

- (c) The Director of the Center for Drug Evaluation and Research may, on the Director's own initiative or on the petition of an interested person, waive in whole or in part any of the criteria in paragraph (b) of this section with respect to a specific clinical investigation, either prior to the investigation or in the



evaluation of a completed study. A petition for a waiver is required to set forth clearly and concisely the specific criteria from which waiver is sought, why the criteria are not reasonably applicable to the particular clinical investigation, what alternative procedures, if any, are to be, or have been employed, and what results have been obtained. The petition is also required to state why the clinical investigations so conducted will yield, or have yielded, substantial evidence of effectiveness, notwithstanding nonconformance with the criteria for which waiver is requested.

21 C.F.R. §314.126(c). The regulation contains additional language concerning study control:

- (e) Uncontrolled studies or partially controlled studies are not acceptable as the sole basis for the approval of claims of effectiveness. Such studies carefully conducted and documented, may provide corroborative support of well-controlled studies regarding efficacy and may yield valuable data regarding safety of the test drug. Such studies will be considered on their merits in the light of the principles listed here, with the exception of the requirement for the comparison of the treated subjects with controls. Isolated case reports, random experience, and reports lacking the details which permit scientific evaluation will not be considered.

21 C.F.R. §314.126(e).

In addition, federal regulations provide that in determining the approvability of new therapies for rare life-threatening disease for which no treatment exists FDA should use maximum flexibility:

The Food and Drug Administration (FDA) has determined that it is appropriate to exercise the broadest flexibility in applying the statutory standards, while preserving appropriate guarantees for safety and effectiveness. These procedures reflect the recognition that physicians and patients are generally willing to accept greater risks or side effects from products that treat life-threatening and severely-debilitating illnesses, than they would accept from products that treat less serious illnesses. These procedures also reflect the recognition that the benefits of the drug need to be evaluated in light of the severity of the disease being treated.

21 C.F.R. §312.80.

The present petition seeks such a waiver as authorized by this regulation "on the petition of an interested person." 21 C.F.R. §314.126(c). The petition also seeks the exercise of the "broadest flexibility" to determine that the studies conducted by the sponsor are sufficient basis to approve the NDA in the prevailing circumstances. 21 C.F.R. §312.80.

4. Discussion

In the circumstances as described above and based on the authorities as cited above, this petition seeks:

- a finding by FDA that its legitimate exercise of regulatory flexibility to applications for treatments of rare and debilitating conditions for which there is an absolutely unmet need requires approval of the NDA; and/or



- to the extent deemed necessary for approval of the NDA, a waiver of the requirements of control as applied to Study 206-RWE sufficient for FDA to determine that the study has provided substantial evidence of efficacy and to grant approval of the NDA.

Both grounds for approval of the NDA are supported by the historical data as well as the data generated by 206-RWE.

a. Historical Data

In accordance with the 505(b)(2) pathway, Biohaven is relying in part upon FDA's findings of safety and effectiveness for Rilutek (riluzole), including its 30-year, well-established safety profile. In addition, Biohaven has developed significant evidence of safety and efficacy of troriluzole.

i. Safety

Biohaven has developed considerable evidence documenting the safety of troriluzole. Troriluzole has been studied in 10 Phase 1 studies, two Phase 2/3 studies in SCA, and six Phase 2/3 studies in a number of additional indications. The safety data to date thus represents troriluzole exposure to over 2,000 subjects. Across these studies, troriluzole not only demonstrated an acceptable and comparable safety and tolerability profile in subjects with SCA, but also demonstrated some safety advantages to riluzole. For instance, there were no instances of severe drug-induced liver injury, severe neutropenia, or interstitial lung disease. Thus, the data submitted in NDA 210,862 in support of troriluzole's safety is robust.

ii. Efficacy

Biohaven has also developed considerable evidence documenting the efficacy of troriluzole. The troriluzole development program has generated the largest clinical trial dataset in SCA, served as the basis for the development and validation of the f-SARA rating scale, provided clinical trial data confirming that different SCA genotypes vary in disease progression rates over time, and showed that troriluzole slows disease progression by at least 50% as measured by the f-SARA over a 3-year period. The troriluzole NDA has provided substantial clinical evidence of benefit supporting the use of troriluzole 200 mg QD for the treatment of adults with SCA across all genotypes.

b. Clinical Data Provided by 206-RWE

The primary evidence of effectiveness relied on in NDA 210,862 is the long-term RWE study (BHV4157-206-RWE), designed based on dialogue with the FDA, to assess the benefit of troriluzole treatment in SCA patients over a 3-year period. Confirmatory and supportive evidence were also provided from data generated in Studies BHV4157-206-RWE, BHV4157-206, and BHV4157-201. The following data demonstrate the consistent treatment effect observed with troriluzole:

- Study 206-RWE represents an adequate and well-controlled study where the prespecified primary endpoint, change from baseline in total f-SARA[®] at Year 3 in All SCA genotypes, was met favoring troriluzole with a robust treatment effect that was statistically significant (p=0.03).



- Troriluzole met prespecified endpoints, change from baseline in total f-SARA® at Years 1, 2, and 3 in All SCA genotypes, compared to a second independent external control natural history cohort from Europe (EUROSCA; $p < 0.0001$ at Year 3) in Study 206-RWE.
- Troriluzole met prespecified endpoints, change from baseline in total f-SARA® at Years 1, 2, and 3 in All SCA genotypes, compared to a third independently matched external control global cohort (CRC-SCA + EUROSCA; $p < 0.01$ at Year 3) in Study 206-RWE.
- A Kaplan-Meier analysis demonstrated that the risk of progression to a wheelchair was 4 times greater in the untreated external control cohort as compared to troriluzole-treated SCA patients. These results provide further confirmatory evidence that troriluzole delays disease progression in the SCA patient population.
- Long-term Year 4 analysis from Study 206-RWE demonstrate continued disease stability in troriluzole-treated SCA patients and serves as additional confirmatory evidence of the Year 3 primary analysis.
- Troriluzole demonstrated reduction in risk of falls in All SCA genotypes compared to placebo over 48 weeks in Study 206, the first agent to provide such benefit in SCA.
- Efficacy (f-SARA®, CGI-I, and falls) in SCA3 genotype compared to placebo at Week 48 was observed in Study 206.
- SCA3 analyses from BHV4157-206-RWE demonstrated continuity of the troriluzole treatment benefits observed at Year 1 in SCA3 patients from the double-blind phase of Study 206.
- Gap dosing/restart in All SCA genotypes during OLE administrative gap in dosing in Study 201 showed that patients worsen when off troriluzole and stabilize when treatment is reinitiated. Furthermore, worsening in SARA scores during gaps in dosing correlated directly with duration off troriluzole.
- 7 years of clinical data from Study 201 OLE demonstrated long-term benefits of troriluzole treatment
- LOWESS supportive analysis of data from both Studies 201 and 206 demonstrated a change in trajectory of disease progression associated with troriluzole.

Ultimately, the consistent treatment effect shown by troriluzole across the SCA program in NDA 210,862 could not have been observed unless troriluzole is an effective treatment. SCA is a neurodegenerative, genetic disease that is not known to spontaneously improve or demonstrate long-term stability without treatment. Further, the mechanism of action supports the view that troriluzole is effective, as troriluzole modulates glutamate in motor neurons in the brainstem and spinal cord, thereby preventing their degeneration.

c. Immense and Critical Unmet Need

In addition to the historical data and clinical data provided by 206-RWE, the historical and current circumstances of the Expanded Access Program as applied to troriluzole demonstrate the most dire need for immediate approval of the product.

Biohaven's expanded access program currently has over 300 patients enrolled in the troriluzole EAP, 241 treated with troriluzole, and with another 100 SCA patients and treating clinicians requesting access to troriluzole under the program and the federal Right to Try Act. Further, Biohaven regularly receives additional EAP and Right to Try requests, highlighting the immense unmet need in this patient population. These facts undeniably demonstrate that there is a tragically high unmet need with a corresponding favorable benefit and risk profile for this life-threatening disease with no current approved therapy. This is precisely the situation contemplated by FDA when it promulgated regulations to specifying the application of regulatory flexibility because:



[P]hysicians and patients are generally *willing to accept greater risks or side effects* from products that treat life-threatening and severely-debilitating illnesses, than they would accept from products that treat less serious illnesses

and

[T]he benefits of the drug need to be *evaluated in light of the severity of the disease* being treated.

21 C.F.R. § 312.80.

Ultimately, a small biotechnology company such as Biohaven has finite resources which in addition have been negatively affected by the CRL as well as the previous 3-month PDUFA delay by FDA and the prior NDA refusal to file. Without a timely path forward, sponsors like Biohaven faces significant challenges in sustaining operations, including the potential inability to manufacture drug product and support ongoing patient access programs or Right to Try requests. Immediate relief from FDA is necessary to ensure that patients who have been receiving treatment may continue, and more importantly patients who have not been receiving treatment may have the benefit of tiriluzole.

C. Environmental Impact

The actions requested herein are subject to categorical exclusion under 21 C.F.R. §§ 25.30 and 25.31.

D. Economic Impact

Pursuant to 21 C.F.R. § 10.30(b), an economic impact statement will be submitted only upon the request of the Commissioner.

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E. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, it includes representative data and information known to the petitioner which are unfavorable to the petition, the undersigned has taken reasonable steps to ensure that any representative data and/or information which are unfavorable to the petition were disclosed to the undersigned, and the information upon which the action requested herein is based first became known to the party on whose behalf this petition is submitted on or about November 4, 2025.

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January 30, 2026¹

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WAIVER PETITION UNDER 21 C.F.R. § 10.30; 21 C.F.R. § 314.126(e)

Interested parties including Spinocerebellar Ataxia ("SCA") patients and family members, SCA treating clinicians, and Biohaven (each individually a "Petitioner" and collectively "Petitioners") submit this petition under 21 C.F.R. § 10.30, 21 C.F.R. § 314.126(c), section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA), and its implementing regulations to request that the Commissioner of Food and Drugs and the Director of the Center for Drug Evaluation and Research take the actions set forth below in Section A with respect to the approval of Troriluzole to treat for Spinocerebellar Ataxia (SCA) for marketing under section 505(b)(2) of the FDCA pursuant to NDA 210862.

A. Actions Requested

The petitioner requests that the Food and Drug Administration (FDA or Agency):

1. Determine that the criteria for adequate and well controlled studies that requires placebo current control should be waived and instead FDA should recognize real world patients as control subjects for the pivotal clinical trial (Study BHV4157-206-RWE; ClinicalTrials.gov ID#NCT06529146) under which marketing approval has been sought for Troriluzole to treat for SCA. See 21 C.F.R. §314.126(b)(5)(c).
2. Determine that regulatory flexibility should be exercised to recognize real world patients as control subjects for the pivotal clinical trial under which marketing approval has been sought for Troriluzole to treat for SCA. See 21 C.F.R. §312.80.
3. On the basis of either or both of the foregoing determinations, and the fact that Study BHV4157-206-RWE achieved its primary and secondary outcome endpoints ($p < 0.05$), issue approval of NDA 210862 for marketing for treatment of SCA.

B. Statement of Grounds

1. Executive Summary

SCA is a rare, progressive, genetic and debilitating neurodegenerative disorder with no approved therapies currently available in the United States. This utterly unmet need calls for an innovative and flexible approach to approval.

¹ Other Interested Parties have been added from date of original communication to CDER, December 19, 2025, to present, January 30, 2026.



Clinical trials typically include a population that serves as a concurrent control arm with which to compare the effects of the investigational drug to avoid confounding the study with bias. That control arm may consist of study subjects administered a placebo. However, conventionally controlled trials may be problematic due to limited patient populations and the severity of the condition.

The study that served as the primary basis of the NDA for troriluzole to treat SCA used an external control arm consisting of patients who had been treated outside the study in the “real world” rather than internally within the study. Nevertheless, the Study utilized the highly credible Clinical Research Consortium for the Study of Cerebellar Ataxia (CRC-SCA) natural history cohort as the external control arm. The CRC-SCA is supported by the National Ataxia Foundation (NAF) in collaboration with leading academic institutions to generate real-world data on the natural progression of SCAs that could inform clinical trial design, serve as external controls, and support regulatory decision-making. The CRC-SCA is recognized in the SCA research and treatment community to provide high-quality evidence on disease progression and to serve as an ideal external control.

The Study compared outcomes in troriluzole-treated patients against untreated participants from the CRC-SCA cohort using validated measures such as the functional Scale for the Assessment and Rating of Ataxia (f-SARA). The Study design aligns with FDA guidance on the use of RWE in regulatory contexts, particularly for a rare life-threatening disease with no existing treatment, including avoiding the ethical concerns of using placebo in this type of a population. The Study demonstrated meaningful slowing of disease progression over three years.

However, FDA has taken the position, in its November 4, 2025, CRL that the external control was inappropriate and issued a CRL. FDA stated that the Study could not be considered adequate and well controlled because of design flaws and methodological limitations that introduced bias into the study:

Several factors undermined the reliability of the Clinical Research Consortium for the Study of Cerebellar Ataxia natural history study (CRC-SCA) as a control arm in Study 206-RWE. The propensity score matching could not address important factors that could affect disease progression.... The comparison between progression rates at 1 year in subjects randomized to placebo in Study 206 and CRC-SCA controls revealed significant differences favoring placebo (particularly in SCA1 and SCA2 genotypes), providing direct evidence of confounding that undermines confidence in CRC-SCA as a control arm and in the results of Study 206-RWE.

The relevant federal regulations do provide that drug approvals generally should be based on adequate and well controlled studies which may include using placebo control. The same regulations provide that adequate and well controlled studies may use an historical control derived from an adequately documented natural history of the disease or condition. In addition, federal regulations expressly provide that FDA may waive all or any criteria of what may constitute an adequate and well-controlled study:

*The Director of the Center for Drug Evaluation and Research may, on the Director's own initiative or on the petition of an interested person, **waive** in whole or in part **any of the criteria** in paragraph (b) of this section with respect to a specific clinical investigation, either prior to the investigation or in the **evaluation** of a **completed** study (21 C.F.R. 314.126(c)).*

Further, federal regulations provide that while uncontrolled or partially controlled studies may not be the sole basis for approval they “may provide corroborative support ... regarding efficacy.” Even more specifically, federal



regulations state that in determining the approvability of new therapies for a rare life-threatening disease for which no treatment exists FDA should use maximum flexibility:

*The Food and Drug Administration (FDA) has determined that it is appropriate to exercise the **broadest flexibility** in applying the statutory standards, while preserving appropriate guarantees for safety and effectiveness. These procedures reflect the recognition that physicians and **patients are generally willing to accept greater risks or side effects** from products that treat life-threatening and severely-debilitating illnesses, than they would accept from products that treat less serious illnesses. These procedures also reflect the recognition that the **benefits** of the drug need to be **evaluated in light of the severity** of the disease being treated (21 C.F.R.312.80).*

In the present case, the external control arm was not problematic because the comparability between trial subjects and external controls was addressed by using rigorous Propensity Score Matching (PSM) and leveraging the US Natural History Study (CRC-SCA).

Ultimately, in these circumstances FDA should exercise regulatory flexibility, waive any purported requirement regarding placebo control in this instance, and approve the NDA.

2. Factual Background

a. Overview of Investigational Product and Regulatory History

This petition addresses NDA 210862 (the NDA) which is a 505(b)(2) application currently under review before the Center for Drug Evaluation and Research (CDER) and the subject of a Complete Response Letter issued on November 4, 2025 (the CRL). The sponsor of the NDA is Biohaven, which is a global clinical-stage biopharmaceutical company focused on the discovery, development, and commercialization of life-changing therapies to treat rare and common diseases. The NDA seeks marketing approval for troriluzole (BHV-4157) to treat for the treatment of adult patients with spinocerebellar ataxia (SCA).

SCA is a rare, progressive, genetic, and debilitating neurodegenerative disorder with no approved symptomatic or disease-modifying therapies currently available in the United States. Patients with SCA face significant unmet medical needs, including relentless motor impairment, loss of independence, injuries due to falls, loss of ambulation and reduced quality of life, often leading to premature disability and mortality. SCA3 is the most common genotype of SCA affecting over 40% of SCA patients. The high unmet need in this patient population underscores the urgency for innovative approaches to drug development and approval, particularly for rare diseases where traditional randomized controlled trials may be ethically and practically challenging due to small patient populations and the progressive nature of the condition.

The investigational drug product troriluzole is a tripeptide prodrug conjugate of riluzole designed to deliver consistent drug exposures and improve the safety profile of the active metabolite. Troriluzole has been developed as a formulated oral capsule in 3 dose strengths, 60 mg, 100 mg, and 140 mg. Troriluzole was investigated in a Phase 2b/3 study as treatment for SCA using the 140 mg capsule strength and a dosing regimen of 140 mg QD. In addition, a pivotal Phase 3 study investigated troriluzole 140 mg and 60 mg capsule strengths and a dosing regimen of 200 mg QD for treatment of SCA.



FDA has granted Orphan Designation, Fast Track Designation, and Priority Review, although FDA designed a Major Amendment that extended the action date by three months before issuing the CRL.

b. Chronology of Key Regulatory Submissions and Sponsor Correspondence

The key regulatory submissions and correspondence between FDA and the sponsor are as follows:

May 18, 2016 – Orphan designation

May 31, 2016 – IND 129397 submitted

April 27, 2017 – Fast Track designation

April 2017-November 2018 – Sponsor develops and validates f-SARA scale

- For use as primary outcome measure in clinical trials
- Working closely with SCA experts and FDA

December 2017 – FDA written recommendations from Type C Meeting

- FDA stated change from SARA scale to f-SARA

August 2018-March 2021 – FDA meetings and correspondence on Primary Outcome

2022 – Sponsor generates data from clinical trial in SCA3

- 1-year double-blind placebo-controlled trial shows signal for efficacy of troriluzole in the SCA3 genotype, which comprises >40% of all SCA genotypes. The placebo-adjusted difference on the primary outcome measure, the f-SARA, met a nominal p-value < 0.05. In addition, treatment with troriluzole was associated with favorable response on a clinician reported assessment (CGI-I) and risk reduction for falls (both < 0.05).

May 26, 2023 – NDA submission for SCA3

July 25, 2023 – Division issued a Refusal to file despite submission of a complete submission

August 16, 2023 – Type A Meeting request

October 5, 2023 – Type A Meeting

- Discussion with FDA, sponsor, NAF, SSCA patients, and SCA clinicians to discuss path forward for SCA treatment development

November 21, 2023 – Type C Meeting Request

- Sponsor spoke with leading SCA experts and considered new controlled study based on the 8 years of clinical trial experience and largest clinical trial dataset in SCA. Sponsor and leading ataxia experts concluded the only way to study treatment effect is to use real world evidence to develop a rigorous analysis of the data collected with troriluzole over several years and use an external control as the comparator.

February 8, 2024 – Type C Meeting



- Discussion focused on challenges of variable disease progression across SCA genotypes, and necessity of 3-year follow-up to assess for treatment effects across all genotypes.
- Conducting an adequately powered, placebo-controlled trial of this extended duration would not be feasible or ethical in this rare and fatal disease.
- Biohaven therefore proposed leveraging the 3-year data from troriluzole-treated subjects in Study BHV4157-206 and using a rigorously matched untreated external control derived from patient-level natural history data to fully assess treatment benefits in troriluzole-treated SCA patients.
- Division had no recommendations for a path forward, but referred sponsor to the FDA Guidance for Industry, Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision Making for Drug and Biological Products.
- Division requested sponsor to submit proposed SAP for the 3-year efficacy analysis compared to an external control natural history cohort for review.

March 7, 2024 – SAP submitted to IND

March 8, 2024 – FDA Type C Meeting Minutes

- Minutes requested additional information to be included in Biohaven's SAP
- Agency noted challenges to RWE approach, indicating that in light of the limitations, a large and robust treatment effect would be needed to overcome the biases of an externally controlled trial, in order for it to be used as the primary basis for substantial evidence for effectiveness
- FDA emphasized need for data transparency and traceability of real world data and referred to the FDA guidance Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision Making for Drug and Biological Products.

March 19, 2024 – SAP re-submitted to IND per FDA's comments

May 8, 2024 – Division reviewed SAP and provided comments

- Division's response again referenced FDA Guidance for Industry, Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision Making for Drug and Biological Products, which recommends providing both the draft protocol and SAP to the Division for review and comment prior to conducting analyses and stated that only a draft SAP was provided.

May 20, 2024 – Sponsor submitted BHV4157 SAP protocol and updated SAP

- SAP addressed FDA's May 8, 2024 comments

July 25, 2024 – FDA final feedback on protocol BHV4157-206-RWE and SAP to sponsor

August 29, 2024 – Sponsor submits final protocol and SAP incorporating FDA's comments

September 20, 2024 – Topline data from BHV4157-206-RWE

- Large robust treatment effect in SCA with troriluzole showing a 50-70% slowing of disease progression after 3 years of therapy ($p < 0.05$).
- Study achieved prespecified primary and 8 prespecified consecutive secondary outcome objectives



September 22, 2024 – Sponsor notifies Division of data

September 26, 2024 – FDA responds to sponsor

- FDA recommends Type B meeting to discuss the content, format, and data analysis methods to be included in resubmission to support determination of effectiveness.

October 1, 2024 – Type B Meeting Request

November 22, 2024 – Type B Meeting

February 12, 2025 – NDA 210862 for SCA re-submission accepted

- 505(b)(2) NDA
- Indication submitted for all SCA and not limited to SCA3
- Priority review granted
- PDUFA date August 10, 2025

March 27, 2025 – Mid-Cycle Meeting

- Sponsor asks if any supplemental data or analyses needed
- Division responds that any requests would be provided by information requests

May 14, 2025 – FDA notifies sponsor of Major Amendment designation

- FDA states designation due to sponsor responses to 3 IRs and Sponsor objects that responding to IRs should not be designated a Major Amendment
- IR responses directed FDA to data already in FDA's possession
- New PDUFA date delayed until November 10, 2025

May 14, 2025 – Sponsor request to FDA for meeting with Division

- Sponsor states IR responses do not meet standard for Major Amendment
- Sponsor requested FDA rescind designation and reinstate original PDUFA date

May 14, 2025 – Division holds 15-minute meeting

- Sponsor emphasizes 3-month delay effectively negates priority review and Fast Track
- Both designations reflective of unmet need, no current approved therapies, life-threatening condition

August 8, 2025 – FDA schedules Late Cycle Meeting for September 16, 2025

August 21, 2025 – FDA reschedules Late Cycle Meeting to September 18, 2025

- FDA states after further internal discussion advisory committee meeting not needed

September 18, 2025 – Late Cycle Meeting

- Sponsor states that if the Division disagrees with approvability of NDA using RWE that external expert opinion should be obtained by FDA and requests Advisory Committee meeting to resolve uncertainties or differences of opinion regarding 206-RWE data



- Sponsor notes when Division communicated after mid-cycle that planned Advisory Committee was cancelled. Sponsor interpreted it to mean any internal FDA difference of opinion on the data had been resolved.
- Sponsor suggested if Division continued to believe 206-RWE could not serve as basis of approval then an Advisory Committee should be held for further external expert opinion on the data.
- Division suggests that prior knowledge of data could have biased 206-RWE study.
- Sponsor responds by noting that open label data is routinely used in RWE studies but that information did not bias the design of the external control and the rigorous statistical approach suggested by the Division.
- Sponsor noted that prior to database analysis Division had directed that primary outcome measure at 3 years would be f-SARA and external comparison would be CRC-SCA.
- Division did not want the external control to be the Global or EUROSCA natural history cohort, despite lower rates of missing data in the Global or EUROSCA natural history cohort. Division criticized the study for higher rates of missing data at Year 3 but the Sponsor noted that it was the Division that limited the dataset to CRC-SCA and that the Sponsor wanted to include the EUROSCA as rates of missing data were lower.
- Sponsor included EUROSCA and GLOBAL as secondary outcome measures in 206-RWE.
- Division provided feedback that sponsor should not use MAIC comparison but instead PSM approach should be taken with regard to the statistical analysis.
- Division speculation that sponsor used prior knowledge to bias results is unfounded and does not reflect the actual design of 206-RWE. The Division's criticism about prior knowledge does not reflect the facts that the SAP and protocol design were modified to incorporate all of the Division's feedback, thus reducing any bias that the Sponsor might have had on the study design and statistical analysis.
- 206-RWE design had been prespecified after incorporating Division's preferred approach to RWE design in both the SAP and study protocol.

September 29, 2025 – FDA notification to sponsor

- FDA has not identified any post-marketing requirements

September 30, 2025 – Amendment to NDA

- Sponsor provides additional data and analysis in support of ongoing review

October 17, 2025 – Sponsor requests correction to FDA Late Cycle Meeting Minutes

- Sponsor requests clarification that it did not oppose holding an advisory committee but had thought Advisory Committee was not warranted given the strength of the data and safety profile of trilorazole supporting approval
- Sponsor also requested notation that if FDA has residual concerns Division should convene Advisory Committee as the appropriate forum to resolve uncertainties or differences regarding the interpretation of 206-RWE.

October 24, 2025 – FDA response to sponsor

- FDA acknowledges sponsor's request but denies requested revisions since leadership has determined not to convene Advisory Committee so correction was not warranted.

November 4, 2025 – FDA issues CRL

- FDA finds 206-RWE is not adequate and well controlled due to design flaws and methodological limitations that have introduced bias including:



- Limited comparability between trial subjects and external controls and residual biases
- Site overlap, selection and expectations biases
- Substantial Missing Data
- Systematic Timing Bias
- Measurement Methodology Differences
- Lack of Pre-specification
- FDA also finds methodological issues preclude using secondary efficacy analyses of 206-RWE and post hoc analyses of 206 as confirmatory evidence including:
 - Secondary efficacy analyses of Study 206-RWE suffer same limitations as primary efficacy analysis
 - Post hoc SCA genotype 3 subgroup analyses of Study 206 not prespecified
 - Fall Risk Analysis of Study 206 not prespecified and suffers from multiple limitations
- FDA also finds nonclinical issue that major circulating metabolite DKP was not adequately assessed

November 9, 2025 – Sponsor responds to each item of the CRL and requests Type A Meeting

December 17, 2025 – Post CRL Type A Meeting

- Sponsor presented multiple paths forward based upon 8 year dataset that has been generated to date.
- The Division did not agree on any path forward based upon the current dataset but acknowledged that a new data doesn't necessarily need to be placebo-controlled.
- The Division suggested a randomized control study to take a subset of compassionate use patients off treatment and monitor for decline which could provide further evidence of a drug effect. An SCA expert at the meeting and the Sponsor both raised significant ethical issues about the FDA suggested randomized withdrawal design, as SCA is a progressive, neurodegenerative disorder and if patients worsened they would not recover as such worsening.
- FDA stated that a hard endpoint would need to be developed, and that prospective, fresh data from a new trial would be needed for a resubmission.
- Biohaven stated that there are no resources to do another 8 year study to gather data, but if there was an accelerated path forward that Biohaven and FDA could work on in a collaborative way, then that could be a possibility to continue the program. Biohaven will not be able to continue the program without a path forward.
- FDA stated that it did not see a path forward with this data and new data, new patients and a new trial is needed. FDA stated no resubmission could be based on data from -206 since the agency has exhausted all options with the current data.

c. Chronology of Key Submissions to FDA From Patients and Clinicians

Patients and their clinicians are passionately interested in the approval of the NDA because SCA is so debilitating and there are no approved therapies currently available in the United States. They recognize that this utterly unmet need calls for an innovative and flexible approach to approval and they have been active and vocal with FDA in their support. The following is a chronology of submissions to FDA made by patients and their clinicians:

September 14, 2023 – NAF Letter to FDA



- NAF CEO Andrew Rosen sends letter to Dr. Emily Freilich, MD, Director, Division of Neurology 1 and Teresa Buracchio, MD, Director, Office of Neuroscience

September 15, 2023 – NAF Publication Regarding FDA

- NAF publishes Community Response: FDA Review of Troriluzole NDA signed by over 3k patients

September 29, 2023 – Clinician-Researcher Letter to FDA

- Dr. Jeremy Schmahmann and clinician experts send letter to Dr. Emily Freilich, MD, Director, Division of Neurology 1 and Teresa Buracchio, MD, Director, Office of Neuroscience

November 19, 2024 – NAF Congressional Briefing

- NAF Hosts Congressional Briefing on importance of approving new treatments for rare diseases, especially those with no FDA-approved treatment options like SCA

January 6, 2025 – NAF and Ataxia UK Letter to FDA

- NAF and Ataxia UK send joint letter to CDER Director Dr. Patrizia Cavazzoni and Office of New Drugs Director, Dr. Peter Stein

January 7, 2025 – Clinician-Researcher Group Letter to FDA

- Dr. Jeremy Schmahmann and 17 clinician experts send letter to CDER Director Dr. Patrizia Cavazzoni and Office of New Drugs Director, Dr. Peter Stein

January 30, 2025 – Clinician-Researcher Group Letter to FDA

- Dr. Jeremy Schmahmann and 17 clinician experts send letter to Acting Director, CDER, Dr. Jacqueline Corrigan-Curay and Office of New Drugs Director, Dr. Peter Stein

April 29, 2025 – Clinician-Researcher Group Letter to FDA

- Dr. Jeremy Schmahmann and 17 clinician experts send letter to Commissioner Makary,

May 9, 2025 – NAF Petition For FDA Prioritization

- NAF launches Change.org petition calling on FDA to prioritize treatment options for rare diseases with urgent unmet needs including SCA

September 13, 2025 – NAF Posting Regarding SCA Patient

- NAF posts Cameryn's Story: this is what happens when hope takes too long

September 15, 2025 – Clinician-Researcher Group Letter to FDA

- Dr. Jeremy Schmahmann and 17 clinician experts send letter to Commissioner Makary, entitled: "Ataxia specialists around the USA urgently request the FDA to use its Congressionally mandated regulatory flexibility to approve troriluzole to improve the lives of patients with spinocerebellar ataxia"

3. Statutory and Regulatory Framework

The FDCA requires that drugs must be shown to be safe and effective. Effectiveness must be established by:



substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling.

21 U.S.C. § 355(d). “Substantial evidence” is defined as:

evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

21 U.S.C. § 355(d). FDA may base this finding on a single adequate and well-controlled study:

If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence.

21 U.S.C. § 355(d). To that end, federal regulations define “adequate and well controlled studies” to have the following characteristics:

- (2) The study uses a design that permits a valid comparison with a control to provide a quantitative assessment of drug effect. The protocol for the study and report of results should describe the study design precisely; for example, duration of treatment periods, whether treatments are parallel, sequential, or crossover, and whether the sample size is predetermined or based upon some interim analysis.

21 C.F.R. §314.126(b)(2). The regulations recognize various types of control:

- (i) *Placebo concurrent control.*
- (ii) *Dose-comparison concurrent control.*
- (iii) *No treatment concurrent control.*
- (iv) *Active treatment concurrent control.*
- (v) *Historical control.*

21 C.F.R. §314.126(b)(2). The regulation further requires that:

Adequate measures are taken to minimize bias on the part of the subjects, observers, and analysts of the data.

21 C.F.R. §314.126(b)(5). After stating these statements of parameters, the regulation includes a section that specifies that FDA may waive any of these requirements in appropriate circumstances:

- (c) The Director of the Center for Drug Evaluation and Research may, on the Director's own initiative or on the petition of an interested person, waive in whole or in part any of the criteria in paragraph (b) of this section with respect to a specific clinical investigation, either prior to the investigation or in the



evaluation of a completed study. A petition for a waiver is required to set forth clearly and concisely the specific criteria from which waiver is sought, why the criteria are not reasonably applicable to the particular clinical investigation, what alternative procedures, if any, are to be, or have been employed, and what results have been obtained. The petition is also required to state why the clinical investigations so conducted will yield, or have yielded, substantial evidence of effectiveness, notwithstanding nonconformance with the criteria for which waiver is requested.

21 C.F.R. §314.126(c). The regulation contains additional language concerning study control:

- (e) Uncontrolled studies or partially controlled studies are not acceptable as the sole basis for the approval of claims of effectiveness. Such studies carefully conducted and documented, may provide corroborative support of well-controlled studies regarding efficacy and may yield valuable data regarding safety of the test drug. Such studies will be considered on their merits in the light of the principles listed here, with the exception of the requirement for the comparison of the treated subjects with controls. Isolated case reports, random experience, and reports lacking the details which permit scientific evaluation will not be considered.

21 C.F.R. §314.126(e).

In addition, federal regulations provide that in determining the approvability of new therapies for rare life-threatening disease for which no treatment exists FDA should use maximum flexibility:

The Food and Drug Administration (FDA) has determined that it is appropriate to exercise the broadest flexibility in applying the statutory standards, while preserving appropriate guarantees for safety and effectiveness. These procedures reflect the recognition that physicians and patients are generally willing to accept greater risks or side effects from products that treat life-threatening and severely-debilitating illnesses, than they would accept from products that treat less serious illnesses. These procedures also reflect the recognition that the benefits of the drug need to be evaluated in light of the severity of the disease being treated.

21 C.F.R. §312.80.

The present petition seeks such a waiver as authorized by this regulation "on the petition of an interested person." 21 C.F.R. §314.126(c). The petition also seeks the exercise of the "broadest flexibility" to determine that the studies conducted by the sponsor are sufficient basis to approve the NDA in the prevailing circumstances. 21 C.F.R. §312.80.

4. Discussion

In the circumstances as described above and based on the authorities as cited above, this petition seeks:

- a finding by FDA that its legitimate exercise of regulatory flexibility to applications for treatments of rare and debilitating conditions for which there is an absolutely unmet need requires approval of the NDA; and/or



- to the extent deemed necessary for approval of the NDA, a waiver of the requirements of control as applied to Study 206-RWE sufficient for FDA to determine that the study has provided substantial evidence of efficacy and to grant approval of the NDA.

Both grounds for approval of the NDA are supported by the historical data as well as the data generated by 206-RWE.

a. Historical Data

In accordance with the 505(b)(2) pathway, Biohaven is relying in part upon FDA's findings of safety and effectiveness for Rilutek (riluzole), including its 30-year, well-established safety profile. In addition, Biohaven has developed significant evidence of safety and efficacy of triloriluzole.

i. Safety

Biohaven has developed considerable evidence documenting the safety of triloriluzole. Triloriluzole has been studied in 10 Phase 1 studies, two Phase 2/3 studies in SCA, and six Phase 2/3 studies in a number of additional indications. The safety data to date thus represents triloriluzole exposure to over 2,000 subjects. Across these studies, triloriluzole not only demonstrated an acceptable and comparable safety and tolerability profile in subjects with SCA, but also demonstrated some safety advantages to riluzole. For instance, there were no instances of severe drug-induced liver injury, severe neutropenia, or interstitial lung disease. Thus, the data submitted in NDA 210,862 in support of triloriluzole's safety is robust.

ii. Efficacy

Biohaven has also developed considerable evidence documenting the efficacy of triloriluzole. The triloriluzole development program has generated the largest clinical trial dataset in SCA, served as the basis for the development and validation of the f-SARA rating scale, provided clinical trial data confirming that different SCA genotypes vary in disease progression rates over time, and showed that triloriluzole slows disease progression by at least 50% as measured by the f-SARA over a 3-year period. The triloriluzole NDA has provided substantial clinical evidence of benefit supporting the use of triloriluzole 200 mg QD for the treatment of adults with SCA across all genotypes.

b. Clinical Data Provided by 206-RWE

The primary evidence of effectiveness relied on in NDA 210,862 is the long-term RWE study (BHV4157-206-RWE), designed based on dialogue with the FDA, to assess the benefit of triloriluzole treatment in SCA patients over a 3-year period. Confirmatory and supportive evidence were also provided from data generated in Studies BHV4157-206-RWE, BHV4157-206, and BHV4157-201. The following data demonstrate the consistent treatment effect observed with triloriluzole:

- Study 206-RWE represents an adequate and well-controlled study where the prespecified primary endpoint, change from baseline in total f-SARA[®] at Year 3 in All SCA genotypes, was met favoring triloriluzole with a robust treatment effect that was statistically significant (p=0.03).



- Troriluzole met prespecified endpoints, change from baseline in total f-SARA[®] at Years 1, 2, and 3 in All SCA genotypes, compared to a second independent external control natural history cohort from Europe (EUROSCA; $p < 0.0001$ at Year 3) in Study 206-RWE.
- Troriluzole met prespecified endpoints, change from baseline in total f-SARA[®] at Years 1, 2, and 3 in All SCA genotypes, compared to a third independently matched external control global cohort (CRC-SCA + EUROSCA; $p < 0.01$ at Year 3) in Study 206-RWE.
- A Kaplan-Meier analysis demonstrated that the risk of progression to a wheelchair was 4 times greater in the untreated external control cohort as compared to troriluzole-treated SCA patients. These results provide further confirmatory evidence that troriluzole delays disease progression in the SCA patient population.
- Long-term Year 4 analysis from Study 206-RWE demonstrate continued disease stability in troriluzole-treated SCA patients and serves as additional confirmatory evidence of the Year 3 primary analysis.
- Troriluzole demonstrated reduction in risk of falls in All SCA genotypes compared to placebo over 48 weeks in Study 206, the first agent to provide such benefit in SCA.
- Efficacy (f-SARA[®], CGI-I, and falls) in SCA3 genotype compared to placebo at Week 48 was observed in Study 206.
- SCA3 analyses from BHV4157-206-RWE demonstrated continuity of the troriluzole treatment benefits observed at Year 1 in SCA3 patients from the double-blind phase of Study 206.
- Gap dosing/restart in All SCA genotypes during OLE administrative gap in dosing in Study 201 showed that patients worsen when off troriluzole and stabilize when treatment is reinitiated. Furthermore, worsening in SARA scores during gaps in dosing correlated directly with duration off troriluzole.
- 7 years of clinical data from Study 201 OLE demonstrated long-term benefits of troriluzole treatment
- LOWESS supportive analysis of data from both Studies 201 and 206 demonstrated a change in trajectory of disease progression associated with troriluzole.

Ultimately, the consistent treatment effect shown by troriluzole across the SCA program in NDA 210,862 could not have been observed unless troriluzole is an effective treatment. SCA is a neurodegenerative, genetic disease that is not known to spontaneously improve or demonstrate long-term stability without treatment. Further, the mechanism of action supports the view that troriluzole is effective, as troriluzole modulates glutamate in motor neurons in the brainstem and spinal cord, thereby preventing their degeneration.

c. Immense and Critical Unmet Need

In addition to the historical data and clinical data provided by 206-RWE, the historical and current circumstances of the Expanded Access Program as applied to troriluzole demonstrate the most dire need for immediate approval of the product.

Biohaven's expanded access program currently has over 300 patients enrolled in the troriluzole EAP, 241 treated with troriluzole, and with another 100 SCA patients and treating clinicians requesting access to troriluzole under the program and the federal Right to Try Act. Further, Biohaven regularly receives additional EAP and Right to Try requests, highlighting the immense unmet need in this patient population. These facts undeniably demonstrate that there is a tragically high unmet need with a corresponding favorable benefit and risk profile for this life-threatening disease with no current approved therapy. This is precisely the situation contemplated by FDA when it promulgated regulations to specifying the application of regulatory flexibility because:



[P]hysicians and patients are generally *willing to accept greater risks or side effects* from products that treat life-threatening and severely-debilitating illnesses, than they would accept from products that treat less serious illnesses

and

[T]he benefits of the drug need to be *evaluated in light of the severity of the disease* being treated.

21 C.F.R. § 312.80.

Ultimately, a small biotechnology company such as Biohaven has finite resources which in addition have been negatively affected by the CRL as well as the previous 3-month PDUFA delay by FDA and the prior NDA refusal to file. Without a timely path forward, sponsors like Biohaven faces significant challenges in sustaining operations, including the potential inability to manufacture drug product and support ongoing patient access programs or Right to Try requests. Immediate relief from FDA is necessary to ensure that patients who have been receiving treatment may continue, and more importantly patients who have not been receiving treatment may have the benefit of troriluzole.

C. Environmental Impact

The actions requested herein are subject to categorical exclusion under 21 C.F.R. §§ 25.30 and 25.31.

D. Economic Impact

Pursuant to 21 C.F.R. § 10.30(b), an economic impact statement will be submitted only upon the request of the Commissioner.

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**E. Certification**

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, it includes representative data and information known to the petitioner which are unfavorable to the petition, the undersigned has taken reasonable steps to ensure that any representative data and/or information which are unfavorable to the petition were disclosed to the undersigned, and the information upon which the action requested herein is based first became known to the party on whose behalf this petition is submitted on or about November 4, 2025.

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**United States Senate Special Committee on Aging
Written Testimony from The Little Hercules Foundation Regarding Hearing: "From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation"**

March 2, 2026

Dear Chairman Scott, Ranking Member Gillibrand, and Members of the Committee,

The Little Hercules Foundation (LHF) appreciates the Senate Committee on Aging's focus on FDA regulatory processes and the critical barriers that prevent patients from accessing life-saving innovations. We submit this testimony on behalf of families fighting Duchenne muscular dystrophy (DMD) and other rare genetic diseases to highlight a paradox at the heart of our healthcare system, one that is central to LHF's mission: the FDA and HHS have made historic progress in expediting the approval of rare disease therapies, yet patients still cannot access these approved treatments.

The missing link we wish to highlight is not FDA approval; it is payer access. Without private insurance and Medicaid coverage, FDA approval becomes a cruel promise—a therapy that has made it through the scientific goalposts but remains out of reach for patients and families. We would like to take this opportunity to underscore the payer barriers that prevent the FDA's innovation efforts from fully benefitting patients, and highlight how state policy choices leave patients behind, even as science moves forward.

Along with other rare disease advocates, we applaud FDA efforts to more urgently bring desperately needed therapies to waiting patients, including the Framework for Accelerating Development of Individualized Therapies announced just this week. At the same time, we urge this committee to recognize that expedited FDA approval is only the first step. Congress and HHS must work in partnership to ensure that payer policies—particularly at the state Medicaid level—do not become the new regulatory bottleneck that defeats the purpose of innovation.

FDA Progress Only Matters if Patients Can Access Treatments

The FDA deserves credit for advancing rare disease policy and for utilizing pathways such as Breakthrough Designation, Fast Track Review, and Accelerated Approval to bring life-saving therapies to patients faster. In recent years the Accelerated Approval pathway has helped to increase the number of approved DMD therapies to eight. One of those therapies is Elevidys, the first gene therapy for DMD, which was approved under the Accelerated Approval in 2023.

For Duchenne families, this was a watershed moment, as evidence has shown that Elevidys can meaningfully slow disease progression. DMD is a uniformly devastating, 100 percent fatal disease that robs patients (mostly male) of their ability to walk in their teens; ultimately, it robs them of their lives in young adulthood. After decades of watching their children lose muscle and independence, with Elevidys' approval families finally had hope that science could rewrite a devastating disease trajectory.

This hope rapidly collided with reality. Immediately following FDA approval, both state Medicaid programs and private insurers began denying coverage. The barrier was not efficacy, not safety, not the rigor of the clinical trial, but payer policy, which continues to put families—who vary widely in their health literacy and access to resources—in endless cycles of denials and appeals. These policies and determinations put these families in lopsided David-and-Goliath battles with commercial insurance behemoths and state-run agencies in order to access therapies determined by FDA to be safe and effective.

New York's Elevidys Denial: When FDA Approval Meets Medicaid Roadblocks

In October 2025, the New York Department of Health made a decision that exemplifies this payer-access crisis: it recommended against coverage for Elevidys under Medicaid, despite the FDA's expanded approval of the therapy for all patients ages 4 and older who are able to walk. This life-altering determination was not made by the FDA or by treating physicians. It was made by a state payer, proxied by a Drug Utilization Review Board (DURB), a state payer body with no clinical expertise in rare genetic disease. It threatens to deny access to the only FDA-approved gene therapy for DMD patients in New York State receiving Medicaid.

The FDA's expansion of Elevidys approval to patients 4 and older was based on rigorous review of clinical data demonstrating the therapy's ability to stabilize or improve motor function and slow irreversible disease progression. The FDA determined that the benefits—including prevention of mobility loss in boys at critical developmental ages—outweigh the risks based on the well-characterized safety and efficacy profile. This represented the FDA's expert judgment that the clinical evidence was sufficiently robust to expand access.

Yet the New York DURB recommended against coverage, disregarding the FDA's expert judgment and the clinical evidence the agency weighed. This position directly contradicts New York's stated commitment to healthcare innovation and patient-centered policy. The DURB's recommendation fails to acknowledge that Elevidys is not experimental—it is an FDA-approved therapy, the first and only approved treatment of its kind for Duchenne. By allowing a state advisory board to second-guess the FDA's clinical determination, New York has effectively converted FDA approval into a payer recommendation, not a guarantee of access.

The result is a crisis of access. New York families testified before the DURB with candor about their lived experience—the relentless progression of Duchenne, the daily challenges their children face, and their profound need for access to FDA-approved treatments. Yet the DURB's recommendation disregards those patient voices and the clinical evidence alike. A boy born with DMD in New York today cannot access Elevidys through Medicaid. A boy born blocks away in New Jersey can. For Duchenne families, timely access to approved therapies is not a matter of convenience—it is essential. Every month of delay, while disease irreversibly progresses, is a month lost. The window for intervention closes and the opportunity for this child is gone forever.

The DURB's recommendation also represents an inappropriate exercise of state authority under federal law. The Social Security Act Section 1927 (SSA 1927) requires states to cover FDA-approved drugs with rebate agreements for their medically accepted uses. Elevidys has an FDA-approved label for ambulatory children 4 and older with Duchenne. A state Medicaid program's pause or denial of coverage directly violates this federal requirement. New York's DURB recommendation, if it is upheld, would place the state in violation of federal law—not merely a policy disagreement with the FDA, but a violation of the Medicaid statute itself.

Accelerated Approval Is Weaponized Against Access

New York's Elevidys denial is not an isolated incident. Across the country, payers are using Accelerated Approval status as a blanket rationale to deny coverage, label therapies as experimental, and refuse reimbursement until confirmatory trials are complete. This represents a fundamental misunderstanding—in some cases, deliberate misuse—of FDA policy.

The FDA's Accelerated Approval program exists precisely because some patients cannot wait for traditional approval timelines. For fatal genetic diseases like DMD, waiting 5-10 years for confirmatory trial data while the disease progresses means losing the biological window for intervention. Early-stage boys who could benefit from gene therapy will be too advanced in disease when confirmatory data arrives. Accelerated Approval was created to solve this problem.

When payers use Accelerated Approval as grounds to deny access, they nullify the FDA's clinical judgment and impose their own additional gatekeeping layer. For DMD specifically, this is unconscionable. Once a boy reaches his mid-teens, the window for therapeutic efficacy begins to close. Disease progression becomes

irreversible. Every month of delay—not due to science, but due to payer denials—costs families irreplaceable time. In recent years, FDA has moved with appropriate urgency. Payers are moving in the opposite direction.

The Structural Problem: Payer Coverage Gaps in Rare Disease

The Elevidys denial in New York illustrates a broader structural problem: there is no coordinated mechanism to ensure that payer policies align with FDA's innovation objectives for rare diseases. State Medicaid programs make independent coverage decisions with no requirement to consider the clinical urgency of a condition, the rarity of alternatives, or the time-sensitive nature of early intervention.

In rare diseases, the stakes are high: Patients have no alternatives. They cannot switch to a competitor product or try a different treatment. For DMD, if a boy misses the window for gene therapy because his state Medicaid program denied coverage, that opportunity is lost forever. Unlike common diseases where delayed access to one drug still leaves other options, rare disease patients often have access to one therapy alone.

Additionally, payers cite cost as a rationale to deny rare disease therapies—therapies with one-time or limited treatment populations. Yet the cost of a gene therapy that may halt disease progression is economically justified when compared to decades of supportive care, wheelchair use, ventilator dependency, and cardiac monitoring. Payers are making these determinations without transparent health economic analysis or patient input.

The committee should understand: FDA approval means nothing to a patient if their payer denies coverage. The FDA cannot compel coverage, but HHS can.

Recommendations to Congress and HHS

To address the payer-access crisis in rare disease, we urge the Congress and HHS to take the following steps:

1. Establish clear federal guidance that Accelerated Approval does not justify coverage denial.

CMS should issue guidance explicitly prohibiting state Medicaid programs and private insurers from using FDA Accelerated Approval status as grounds to deny or delay coverage. Accelerated Approval reflects FDA's clinical judgment that benefits outweigh risks based on available evidence. Payers should defer to that judgment, especially in life-threatening rare diseases where delays are irreversible.

2. Require state Medicaid programs to align payer policy with FDA orphan drug and rare disease designations.

When a drug receives FDA Breakthrough Designation or Orphan Drug designation for a rare disease, state Medicaid programs should have a presumption of coverage unless there is compelling clinical evidence of harm or inefficacy. Payer coverage policies should not impose a higher standard of evidence than the FDA itself requires. This would ensure that FDA and HHS policy objectives are not undermined by state-level gatekeeping.

3. Establish a federal review mechanism for state Medicaid denials of rare disease therapies.

A CMS pathway for patients and providers to appeal state Medicaid coverage denials of FDA-approved rare disease therapies could prevent a patchwork of coverage across states and ensure that a child's access to treatment does not depend on their geography. New York's Elevidys denial should trigger federal review; such a consequential decision about patient access to a rare disease therapy should not rest with a single state payer without federal oversight.

4. Include patient representatives in state Medicaid coverage decisions for rare diseases.

Coverage decisions that affect whether children with life-threatening rare diseases can access the only available therapy should not be made by actuaries and administrators alone. State Medicaid programs should be required to convene patient and clinician input in coverage deliberations for orphan drugs and rare disease therapies. These voices understand the clinical urgency and stakes in ways that generic payer reviews cannot.

The FDA and HHS have earned credit for advancing rare disease policy and expediting access to promising new therapies. But that progress is being undermined by payer coverage denials that occur after FDA approval and with no federal oversight. When a state Medicaid program can deny access to an FDA-approved gene therapy for a fatal disease of childhood, the payer system has become the new regulatory bottleneck.

New York's denial of Elevidys coverage demonstrates the urgency of this problem. But it is not unique. Across the country, families face similar barriers. A child's access to a life-saving therapy should not depend on whether their state's Medicaid program agrees with the FDA's clinical judgment.

Congress has the authority and responsibility to act. We urge this committee to pursue the recommendations outlined above to align payer policy with FDA innovation efforts and ensure that expedited approval translates into expedited patient access. For children with rare genetic diseases, time is not an abstract policy concern—time is life itself.

Thank you for this opportunity to contribute to the record.

Sincerely,

A handwritten signature in blue ink, appearing to read 'K Maynard', with a stylized flourish at the end.

Kelly Maynard, President
Little Hercules Foundation

Kathryn Bryant Knudson – February 6th, 2026

Dear Chairman Scott, Ranking Member Gillibrand, and Members of the Committee:

My name is Kathryn Bryant Knudson, and I live with a rare, devastating, progressive neuromuscular disease called Limb-Girdle Muscular Dystrophy (LGMD). Thank you for taking the time to hold this incredibly important hearing on rare diseases and the Food and Drug Administration's (FDA) role in ensuring treatments get to the patients who need them, like me, expediently. LGMD is a progressive, genetic disease that causes severe muscle wasting, loss of complete mobility and increasing medical complexity over time, often leading to death. Currently, there is no cure, and there are no FDA-approved treatments.

I am the founder and president of The Speak Foundation, the largest patient-led organization dedicated to individuals and families living with LGMD. The Speak Foundation serves as a critical voice for patients living with LGMD and all rare diseases. Through my experience living as an LGMD patient and my role at The Speak Foundation, I have learned first-hand that living with a rare disease is frightening – not just because of my diagnosis, but because the health system is not set up to support us, and the landscape looks stark for the development of treatments that will stop our disease progression. Aging with a lifelong disability does not follow a traditional aging trajectory, yet our healthcare, regulatory, and social support systems are not designed to reflect that reality. We have lost something fundamental: the ability to truly care for patients.

For those of us living with a rare disease, this apparent brokenness in our health care system is magnified. As a patient with LGMD, I remember when the disease began to take away my ability to walk. Walking became difficult and exhausting. I started stumbling and falling, and eventually, I made the decision to use a wheelchair to avoid serious injury. The loss of independence – and the need to rely on others for so much – is deeply difficult, both emotionally and practically. This is especially true for adult rare disease patients who are often left to fend for themselves. My organization, The Speak Foundation, founded the LGMD Centers of Excellence because the standard local healthcare system does not have capacity to manage rare, progressive diseases. Patients should not be burdened with having to travel long distances to receive care.

Creating and nurturing a regulatory environment that serves rare disease patients and works to get them needed treatments faster is urgently needed. The incredible scientific advances we have seen in rare disease drug development in the past decade serve as a glimmer of hope for our patients in an otherwise extremely challenging environment. It is incumbent on the FDA to do everything in its power to help get new, safe and effective treatments to patients.

The FDA has the tools and authorities to bring effective treatments to LGMD patients efficiently, but the agency must use the tools with which it has been empowered. For rare and ultra rare diseases, randomized controlled clinical trials are often not possible. Congress acknowledged this when drafting the 21st Century Cures Act (P.L. 114-255),

and, within that legislation, empowered the FDA with certain flexibilities to review and approve treatments for rare disease patients, including the use of biomarkers, natural history comparators, patient experience data, and real-world evidence. As an example, LGMD alone has 30 subtypes, with some forms being rarer than others.

Many of our subtypes have very few patients, and in some cases, fewer than 10 affected individuals in the United States. When trials cost over \$10,000,000, change will never happen if we don't think differently. Clinical trials must look different to work for ultra rare diseases.

Our current system is not patient- centered and often sets up trials that are burdensome or invasive for patients, which can often inhibit the ability for them to participate.

An example of this came from a researcher I recently spoke with who has a treatment with the potential to regenerate muscle tissue. It is an exciting development, but she was given guidance by the FDA that was so archaic that no patient would ever want to participate in the trial. The phase one trial design that the FDA requested involved injecting the cells into a toe muscle, then removing the muscle from the patient's body to see if the cells were still working. This type of medieval guidance in which we butcher bodies with endless muscle biopsies or ridiculous hurdles fails patients.

We must allow for decentralized or hybrid trials where patients are not forced to travel for routine blood work that can be done at home.

It is challenging and not practical that the current clinical trial system uses a centralized system. A sick person in a wheelchair with tons of medical equipment must travel to a location often very far away from home to receive experimental treatments. Then, this system wears patients out with endless visits, multiple invasive procedures, missing school and work. These are very burdensome requirements for both patients and caregivers in addition to managing their illnesses.

It is essential to maintain flexibility to combine subtypes of a disease to test treatments with platform approaches and basket trials.

The Speak Foundation has worked with the FDA on the issue of basket trials in the past. In order to approve treatments for conditions with incredibly small populations, it will be imperative that FDA rely on these novel approaches. Basket trials will allow FDA to assess the efficacy of a therapy against different subtypes of LGMD that are grouped together. This model makes it feasible to test treatments for some of our incredibly small subtypes that would not have a chance to receive an approval for a treatment otherwise.

FDA must accept natural history comparators.

For ultra rare diseases, placebo-controlled trials are not feasible and often unethical. Many rare conditions, including LGMD, have a very robust, known, and documented natural history. Where this exists, the FDA must allow trials to rely on natural history comparators in order to best serve patients.

We must support and strengthen the Accelerated Approval pathway.

The Accelerated Approval (AA) pathway was established in 1992 in response to the HIV/AIDS crisis – it allows the FDA to use a surrogate endpoint, or biomarkers, to evaluate the safety and efficacy of therapies for serious conditions with unmet need. Therapies approved through the AA pathway are held to the same rigorous standards as the FDA's traditional pathway and should not be viewed any differently. In recent years, AA has come under attack with some policymakers questioning its utility and some payers declining to cover products approved via AA. Protecting and strengthening this pathway is critically important for the rare disease community.

In addition to these seminally important topics, it would be beneficial for FDA to look for novel solutions to trials when plausible genetic mechanisms are in place, simplify trials into a proof of concept when a small molecule drug for one subtype of disease is likely to work for another subtype, and allow adaptation of a trial when it hits an issue versus requiring an entirely new trial when the population size does not support that.

Despite the laws on the books, there is a pervasive and growing belief in rare disease communities that the voices of people with lived experience no longer matter in the drug development process. Patients have repeatedly asked for feasible and affordable trial designs. Those requests are routinely overridden by rigid regulatory expectations that do not reflect the realities of small patient populations. Ultimately, patients must be at the center of drug development. The risk-benefit analysis for rare diseases is unique, and patients must be at the table informing regulators' decision-making. LGMD patients themselves are the only ones who can provide context on risks, benefits, and uncertainty. Of note, Patient-Focused Drug Development (PFDD) is a critical tool for diseases like LGMD that progress irreversibly and lack any treatment options. In the 118th Congress, a bill was introduced that would have been helpful to expand on PFDD and ensure patient experience was accurately reflected in drug development - the Better Empowerment Now to Enhance Framework and Improve Treatments (BENEFIT) Act. I would urge Congress to continue pursuing this piece of legislation.

Rare disease clinical trials are long, burdensome, and dominated by paperwork and outdated methodology. Patients want to participate, but many are pushed to the breaking point. For rare diseases, clinical trials often involve as few as six or seven participants. In that context, when the FDA requires a trial to be redone, redesigned, or expanded, it effectively ends the program. There is no additional patient pool. There is no financial runway. There is no time to start over. When this happens, treatments do not fail—they are abandoned.

Trials for rare diseases now routinely escalate into the tens of millions of dollars. Every additional demand from the FDA brings extraordinary cost to companies operating with limited capital. As a result, development programs are being shuttered—not because the science failed, but because the economics became impossible. Reauthorizing the Rare Pediatric Priority Review Voucher program (PRV) was an important step forward in making these economics more sustainable. I applaud Congress for taking decisive action on this and making a real difference for rare disease patients. As many as half of

the individuals living with rare diseases are children. The PRV program offers a crucial incentive to develop therapies for children with devastating and often life-threatening rare conditions. With its recent reauthorization, the program will help address the substantial unmet medical needs maintained in pediatric rare disease communities. PRV is a tool that has and will continue to keep American rare disease innovation viable and anchored drug development in the United States.

Because drug development has become so difficult and inflexible in the United States, sponsors and patients are openly and regularly considering early-stage trials outside the country, including in nations such as China, where costs are lower and regulatory pathways are more predictable. Other countries are actively funding drug development so that their healthcare systems—not ours—will benefit first from future therapies. This pulls researchers, capital, innovation, and hope away from the United States. Also troubling, patients and families are now beginning to self-fund trials—raising money or paying out of pocket for experimental treatments. If we don't create a pathway for approval for everyone that is flexible, trial access will rapidly become inaccessible to the average person.

In the LGMD community today, we have treatments sitting on the shelf—not because it lacks promise, but because prolonged negotiations and inflexible trial expectations have stalled progress. While this continues, patients are losing function and independence. These are losses over time that can never be recovered. For patients living with rare diseases, this reality is not theoretical. It is daily life. It is exhausting. And it is unsustainable.

I have focused on FDA given the focus of today's hearing, but I would be remiss not to mention that rare disease patients face many additional challenges, including a lack of access to long-term home care. Despite having worked for many years, Medicare provides no meaningful coverage for long-term or in-home care for disabled workers like me. I am not on Medicaid. There are not enough systems to support people who worked, paid into the system, and then became disabled. Families are forced to absorb enormous financial and emotional strain because personal care services are unavailable.

I submit this statement not as an abstraction, but as a warning. If we do not re-center healthcare and rare disease drug development around the patient experience, especially for adults living with rare and complex diseases, this system will continue to fail the very people it exists to serve. Thank you for the opportunity to provide testimony. I look forward to engaging with the committee toward solutions for rare disease patients.

Sincerely,

Kathryn Bryant Knudson
Founder and President
The Speak Foundation

Christina DeGryse – February 17th, 2026

Written Testimony

Huntington's disease (HD) is a hereditary, progressive, and uniformly fatal neurodegenerative disorder that causes the relentless loss of cognitive, psychiatric, and physical function. It slowly robs individuals of their ability to think, reason, walk, speak, swallow, and live independently. Symptoms typically begin between the ages of 30 and 50 and worsen over 10 to 20 years, though some individuals develop symptoms in childhood. If one parent carries the faulty gene, each child has a 50% chance of inheriting the disease.

An estimated 50,000 Americans are currently symptomatic, and more than 200,000 Americans are living with or at risk for Huntington's disease. There is no cure, no approved disease-modifying treatment, and no gene therapy available today.

For families like mine, this disease is not theoretical, it is deeply personal. We have watched loved ones deteriorate year by year, knowing there is nothing available to slow or stop the progression of this devastating illness.

That is why the gene therapy AMT-130 has generated unprecedented hope in the HD community.

AMT-130 is the first therapy ever to demonstrate a meaningful slowing of Huntington's disease progression. In the high-dose group, it has shown approximately a 75% reduction in disease decline over three years when compared with Enroll-HD natural history data. In a uniformly fatal, relentlessly progressive disease, this magnitude of effect is extraordinary and represents the first genuine promise of altering the course of Huntington's disease.

In November 2024, nearly 100 HD patients, caregivers, and advocates met directly with the FDA and the Center for Biologics Evaluation and Research (CBER) to urge timely access to therapies for Huntington's disease. Following these discussions, the FDA aligned with the sponsor on the use of Enroll-HD external natural-history controls as a potential pathway toward Accelerated Approval. This alignment, supported by data from more than 30,000 participants, gave families real and reasonable hope that meaningful clinical benefit could translate into earlier patient access.

The recent reversal of that regulatory position has been devastating to the HD community. Shifting expectations, lack of transparency, and regulatory unpredictability threaten to stall progress for years—time that HD families simply do not have.

FDA leadership has repeatedly emphasized that the central regulatory question should be: does it work? In the case of AMT-130, the answer is yes. The therapy has demonstrated the strongest effect signals ever recorded in Huntington's disease. Yet evolving regulatory standards now place this progress in jeopardy.

AMT-130 has received both Breakthrough Therapy and Regenerative Medicine Advanced Therapy (RMAT) designations, reflecting the FDA's own recognition that this therapy has the potential to address a serious unmet medical need and fundamentally

alter the course of a fatal neurodegenerative disease. However, these designations lose meaning if regulatory expectations continue to shift after alignment has been established.

Huntington's disease presents a regulatory context in which traditional randomized, placebo-controlled trials are often infeasible, unethical, or both. The FDA has long recognized the value of external natural-history controls in rare, rapidly progressive, and fatal diseases. Enroll-HD is the largest and most comprehensive HD observational study in the world and was explicitly accepted by the agency during prior alignment.

The HD community is not asking for shortcuts. We are asking for consistency, transparency, and regulatory integrity. We urge the FDA to honor prior commitments, uphold the intent of the Accelerated Approval program, and ensure that patient experience, urgency, and risk tolerance remain central to regulatory decision-making.

The collective response from the Huntington's disease community underscores the urgency of this moment:

- Nearly 50,000 individuals have signed petitions urging FDA action
- More than 10,000 emails and letters have been sent to Members of Congress

This engagement reflects not only desperation, but deep understanding. Families living with Huntington's disease know that time is the one thing we do not have.

We respectfully ask this Committee to continue its oversight of FDA regulatory processes, particularly regarding:

- The agency's evaluation and acceptance of external natural-history controls in rare, fatal neurodegenerative diseases
- The viability of Accelerated Approval pathways for gene therapies in conditions such as Huntington's disease
- The need for consistency, transparency, and predictability in regulatory decision-making

Public clarification at the policy level would meaningfully reduce uncertainty for patients, families, and innovators alike.

For families facing Huntington's disease, regulatory delays are not abstract. Every month lost means irreversible decline. Every year lost means more lives are devastated. We urgently need a regulatory framework that aligns scientific rigor with compassion, urgency, and the realities of living with a fatal rare disease.

Thank you for your leadership, your attention to this critical issue, and your commitment to ensuring that patients remain at the center of FDA decision-making.

Respectfully,

Christina DeGryse

Huntington's Disease Family Member

Demi Sellers – February 17th, 2026

Written Testimony

My aunt lost her independence to Huntington's disease in 2021, but our journey with this disease began long before that. She lived with my family for over a decade after her husband filed for divorce and gained custody of their children. My parents stepped in and took her in — something that was easier said than done.

As many know, Huntington's disease can cause personality changes and, at times, aggression. As a child, that was frightening. I didn't fully understand that some behaviors were the result of a medical condition, not the person I loved. As her disease progressed, my family did everything we could — attending every fundraiser, every clinic appointment, and meeting with every specialist in hopes of finding treatments that could even slightly improve her condition.

My cousins had to watch their mother go through every stage of this illness. One of the hardest parts of Huntington's disease is that it is hereditary. They live with the knowledge that they may one day face the same diagnosis — that they could be watching their possible future unfold before them.

What brings this community together is hope. Hope that our children will not inherit this disease. Hope that there will be a cure. And hope that if there is a promising treatment, it will be given a fair opportunity — not delayed or denied.

For families like mine, access to treatment represents more than medicine. It represents dignity, time, and possibility. I want my cousins — and every child in a Huntington's family — to never feel as though a diagnosis means their life has no purpose. Promising treatments offer hope, and hope is everything to this community.

Please ensure that this drug receives a fair review so families who are able to access it have the opportunity to receive the treatment they desperately need.

Katie Jackson – February 17th 2026

Written Testimony

Chairman Scott, Ranking Member Casey, and distinguished members of the Committee, thank you for the opportunity to submit my testimony. My name is Katie Jackson. I am the President and CEO of Help 4 HD International, a nonprofit organization serving the Huntington's disease community and I am an HD family member.

My late husband was diagnosed with Huntington's Disease at 24 years old. After a long, 14-year battle, he passed away six years ago. I have children who are at risk. For nearly 20 years, I have been an advocate for the Huntington's Disease community — and what I have learned from thousands of families across this nation is that for us, time is both precious and a source of constant fear.

I am writing today because the Huntington's Disease community feels let down by the very agency that is supposed to protect us.

The Unmet Need: A Disease Without Hope

Huntington's Disease is a fatal, genetic neurological illness that causes the progressive breakdown of nerve cells in the brain. It destroys a person physically, cognitively, and psychiatrically — robbing them of every ability until death. There is no cure. There is no disease-modifying therapy. There is nothing approved that slows, stops, or reverses the progression of this disease.

Let me say that plainly for the record: in the year 2026, there is not a single FDA-approved treatment that changes the course of Huntington's Disease. Not one.

HD does not just take away everything from the person who is living with HD, it does the whole family. It is a family disease. Every child of an affected parent has a 50 percent chance of inheriting it. I have spoken to mothers who are gene-positive, caring for a dying parent, while wondering when their own symptoms will begin — and whether their children will face the same fate. I have spoken to young adults who serve as 24-hour caregivers for a parent, knowing the disease may hit them even younger. We see generational trauma in a way that is hard to comprehend. Sometimes, their own symptoms begin almost as soon as their loved one's battle ends.

When we surveyed our community and asked, "what is the number one thing you would like to see in drug development?" the answer was overwhelming and unified: something — anything — in their lifetime that will slow down the progression of HD.

You might ask, "what amount of slowing progression is meaningful?" The answer is: *any* amount of time. Our lives are defined by moments. A slowing of progression means people can work longer, drive longer, share more holidays with their families. It means more time before the person living with HD feels like they are a burden on the ones they love the most.

The Urgency: A Community Running Out of Time

The urgency of this moment cannot be overstated. For years, the HD community has had no viable treatment options — until now. The gene therapy AMT-130, developed by uniQure, has shown significant promise in slowing disease progression. The FDA itself

acknowledged this potential by granting AMT-130 both Regenerative Medicine Advanced Therapy (RMAT) and Breakthrough Therapy designations — designations reserved for drugs that may demonstrate substantial improvement over available therapy for serious conditions.

The FDA and uniQure had previously agreed on an accelerated approval pathway. This was not a casual suggestion. It was a framework built on collaboration, regulatory science, and precedent. Accelerated approval exists specifically for devastating diseases like HD — diseases that are fatal, irreversible, and have no alternatives.

Yet the FDA reversed course.

To give this Committee a sense of how our community responded, We started a petition alongside four sister HD organizations — Help 4 HD, the Huntington's Disease Society of America, HD Reach, the Huntington's Disease Foundation, and the Huntington's Disease Youth Organization. As of today, that petition has over 40,000 verified signatures and nearly 200 supporter voices. We analyzed the sentiment and common themes of the comments. Eighty-one percent expressed urgency and the need for regulatory flexibility.

I want to share some of their words directly, because these are the people whose lives hang in the balance:

"A delay of a few years is literally the difference between life and death for me and others. Knowing there are drugs like AMT-130 that have gone through two trial phases and shown slowing of progression and are safe — and then not following through with accelerated approvals — is heartbreaking. I'm watching HD slowly take my dad. Please don't be a reason for that same fate for me." — gene-positive for HD

"My husband qualifies for this treatment right now — but if the FDA delays approval, he likely won't by the time they revisit it. We have three boys that want their dad around 75% longer as this treatment can offer them." — HD caregiver

"For many of these people, another long clinical trial does not just delay access — it eliminates it completely."

"We aren't asking for a cure without evidence. We are asking you to use regulatory flexibility which you possess. Do not let 'perfect' data be the enemy of the good when time is a luxury that HD families do not have." — HD family member

"I have lived with this devastating disease for over 40 years as I've watched it slowly but surely destroy my family. First, it killed my husband and two of his three brothers, one by suicide, in 2000, 2001, and 2002. We were told there would be a cure in 10 years. Our son, my only child, tested positive in 2001... To rip away the only hope we have is unconscionable." — 24/7 caregiver

These are not abstract policy concerns. These are parents, spouses, and children who are watching the people they love die — slowly, irreversibly — while a promising therapy sits in regulatory limbo.

Do Not Move the Goalposts

Members of the Committee, I want to be very direct about what happened. The FDA agreed to an accelerated approval pathway for AMT-130. The HD community organized around that agreement. Families participated in clinical trials. They endured brain surgery, MRIs, and invasive procedures. They traveled long distances. They also contributed to one of the most robust natural history databases in all of rare disease — the Enroll-HD study, with data from over 30,000 individuals mapping the natural progression of this disease.

Then the FDA changed its position. The Agency began reconsidering its acceptance of natural history data as an external control — a scientifically valid and widely accepted method for rare diseases where using a placebo is unethical. This is not a new or untested approach. It has strong precedent. And it was previously agreed upon.

The FDA is now signaling that it may not allow a BLA submission. This may mean more clinical long trials needed.

Let me be clear about AMT 130 specifically: the science has not changed. The data has not changed. What changed was the FDA's stance. When a regulatory agency moves the goalposts after families have already organized their lives, their hope, and their participation around an agreed-upon framework, it does more than delay a drug. It breaks trust. It discourages pharmaceutical investment in rare disease. And it sends a devastating message to families who have given everything they have to support research.

As one petition signer wrote:

"Changing the rules in the middle of the game sows nothing but distrust. The US government should honor its agreements." — HD community member

"The FDA's current reluctance isn't about saving people — because those of us who have HD are already dying. I urge the FDA to follow through on its previous commitments and give people the chance to fight for their lives." — gene-positive for HD

Our Ask

The Huntington's Disease community is not asking for corners to be cut. We are not asking for approval without evidence. We understand that accelerated approval comes with continued data collection and responsibility — and we accept that, because the alternative is having no chance at all.

We are asking for three things:

First, honor previous guidance. The FDA should fully uphold the previously agreed-upon accelerated approval pathway for AMT-130 and any future therapies that are granted accelerated approval, including the use of external control data from natural history studies. Agreements matter. Consistency matters. Predictability in the regulatory process is essential — not just for HD, but for every rare disease community watching this unfold.

Second, recognize the urgency. Huntington's Disease is fatal, irreversible, and has zero disease-modifying therapies.

Third, expedite review. Make the review and approval of AMT-130, and any future HD therapies, a top priority. Every day of delay is a day that someone loses function they will never get back. Every month of delay is a month where a patient may progress past the point of eligibility. For a community that has waited decades with no options, the clock is not metaphorical. It is real.

Closing

I want to close with this. Over 40,000 people signed our petition. Families from across the United States raised their voices because this is the first real hope the HD community has ever had. Many of them may not have time to submit their testimony because they are home caring for a loved one who can no longer speak, walk, or feed themselves.

One of our petition signers, a young woman wrote:

"Everyone who did not pass this through that sits on the FDA board, I want you to sit on the fact that your delays not only taking my future away — you are senselessly killing me, and you are killing others like me. Real human beings, not stats on your board."

Senators, I am asking you to hold the FDA accountable. Do not allow procedural hesitation to become a death sentence. The HD community has done its part. We have participated in research, contributed data, and organized with an urgency that reflects the stakes of our lives. We are asking the FDA — and now we are asking you — to do the same.

Thank you.

Susan Harris – February 18th, 2026

Written Testimony

Chapter 1: In the beginning I wasn't always this way. Growing up the daughter of a military man I can honestly say red, white and blue run through my veins. I love America and my family for years has fought vehemently for this glorious country. Allow me to say here how conservative my financial values are and have always been and always will be. Socially, not so much. But that's a story for later. I never regarded my family as special. But now I know that's not true. Yes, every cousin and aunt and uncle is successful. Not Microsoft successful but we are happy.

As a descendant of Abraham Lincoln what makes my family "special" indeed is that SCA5 is running through our DNA (thanks Bathsheba, his granny). My brother decided not to have kids because his symptoms started to emerge way too young—19. I had no symptoms so I went along my merry way and had two children which are the biggest blessing to my family. The stress about did me in but I can't even imagine my sweet mother having no grandkids to spoil rotten. My background was that of a pre-Olympic swimmer, so teaching swim lessons and water aerobics was a no brainer. I did it for the income and so I could stay-at-home with my children but little did I know how therapeutic water really was.

Chapter 2: The benefits of water exercise

Do I really need to say a lot here? The benefits are well documented. Water helps with balance, strength and conditioning. Plus, there is a lot we can't do (gosh, I'd love to go for a run or a speeding bike ride to feel the warm air blow onto my face...). I love my adult tricycle. It really entertains the neighbors with my doggie in the basket as I try to pedal FAST! Whoa, watch the feet as they slip off the pedals and I bruise ankles constantly. Bruising is not possible in the pool unless you run into the sidewalls. Please don't do that. Trust me, it hurts. But do get in the pool. It doesn't matter, instructor or not, just MOVE. Jumping rope, cross-country skiing, or simply walking back and forth (which are movements you may or may not be able to do on land). Doing the exercises recommended by the Arthritis Foundation™ will benefit each and every person out there. It doesn't matter what issues. Unless you are dead and if you are reading this you most definitely are NOT dead yet. Get out there and MOVE!! I am competing in master's meets although I am now unable to dive off the starting block. I just start off the side and swim as fast as I can. At least I'm out there.

Chapter 3: Focus on what you can do

I never wanted to lament over the lost abilities. I am thankful for the abilities I do still have. So this swimming adventure is my own mental exercise. I also enjoy traveling and meeting new people. It is another gift from God. I will also be embarking on that adventure and cherishing each moment! Might be in a wheelchair, who cares. The finale is coming!

Chapter 4: Ataxia Sucks

We all have problems. Yes, that's true. But ours are something we must confront every single day. It's very personal to each of us. We are a gift from God and what we do with that is our gift back to God. Always look up. Get out there and move each and every

day. Thanks for taking your valuable time to read this. You are kind and you are beautiful. Each in his or her own way PERIOD.

Susan is loving life and thankful for God's many blessings in her life. Proud American.

"I never wanted to lament over the lost abilities. I am thankful for the abilities I do still have."

Jennifer Medina – February 18th, 2026

Written Testimony

I'm reaching out as a constituent from Texas and someone whose family is being devastated by Huntington's disease (HD). My mother and uncle both died from it, and I've inherited the same risk, as have three of my cousins and my 3 year old son. I'm 44 years old, and for the first time in history, there is a real treatment that could change the future for people like me, uniQure's AMT-130 gene therapy.

Unfortunately, the FDA just indicated that they may not allow the program to move forward based on the existing Phase I/II data, even though it showed a 75% slowing of disease progression and has Breakthrough and RMAT designations. This setback threatens to delay or derail the only therapy showing real hope for HD families. Every delay costs lives, and time is something our families simply don't have.

I'm pleading for your help. We need attention from federal leadership, from both parties, to ensure the FDA and other agencies take seriously the urgency of neurodegenerative diseases like Huntington's. What can we do to get this back on track, and to get in front of decision-makers in Washington, D.C., including the administration and campaign offices who could use their influence to prioritize this issue?

I would be deeply grateful for your guidance or help in arranging meetings with the relevant federal health or policy staff. Families like mine are dying from HD, and many of us are running out of time. Please help us keep this treatment alive.

Gloria Dennard – February 19th, 2026

Written Testimony

Thank you for allowing me to share my story with this distinguished body of leaders and decision makers.

"In 2022, at the age of 66, my blood pressure suddenly became treatment resistant after a decade of blood pressure being controlled by one medicine. I also developed constant pulsatile tinnitus. After several months of trying different medicine combinations, a combination of 4 medicines stabilized my blood pressure. I had undergone a multitude of tests to determine cause and an MRA showed bilateral renal artery stenosis. The goal was to keep my blood pressure in a healthy range and monitor kidney function via bloodwork.

Prior to 2022, I had always been a physically active person. I am a 3rd degree Black Belt in Taekwon Do and won a World Championship in weapons at age 51. When my blood pressure went haywire, I became extremely fatigued and lost almost 20 pounds of muscle mass because my appetite simply vanished.

I worked at regaining healthy weight and tried to stay active but I would have drops in blood pressure during any kind of excursion. Loss of physical activity was and still is a daily mental challenge.

This year, 2025, I began retaining a lot of fluid and had a sharp uptick in shortness of breath and fatigue. My cardiologist referred me to a vascular surgeon who did a Doppler ultrasound on the renal arteries which showed significant stenosis and it was determined stenting was required. On February 17, the procedure was started and when the camera approached the left renal artery, the giant monitor showed the classic string of beads associated with Fibromuscular Dysplasia. The right artery presented the same structure. The vascular surgeon let me know that he preferred not to stent until he could consult with the nephrologist.

As it turns out, none of my local physicians have had any FMD patients so I reached out to FMDSA to find a medical team that could help me. They told me about Dr Bryan Wells at Emory University in Atlanta, GA. I live in the Middle Georgia area and scheduled an appointment in July and met with Dr Bryan Wells and his team at Emory University Hospital. Dr Wells ordered additional scans and discovered FMD in my iliac, coronary, and carotid arteries in addition to the renal arteries. He also had me added to the FMDSA registry which is an important tool for gathering detailed information for use by researchers.

I have added a therapist to my medical team to help me learn new coping mechanisms for the anxiety I have about living with FMD. My old coping mechanism of a good, hard workout in the gym is a thing of the past. 24/7 pulsatile tinnitus is also hard to live with. I miss silence. Therapy is helping and I am so grateful for FMDSA."

Dr. Victoria Manax-Rutson – February 19th, 2026

Written Testimony

Chairman Scott, Ranking Member Gillibrand and Committee Members:

Thank you for the opportunity to testify today on an issue that has defined my professional life and, more importantly, affects millions of American families living with rare and life-threatening diseases.

My name is Victoria Manax-Rutson. I have spent decades in healthcare, overseeing clinical trials across rare oncology, neurology, metabolic disease, and genetic disorders, and helping guide therapies from early development through regulatory approval and into patient care. I have worked alongside clinicians, researchers, regulators, academic medical centers, and patient advocates. I have seen the extraordinary promise of modern biomedical science—and I have also seen how our current regulatory system too often prevents that promise from reaching patients in time.

I appear before you today not as a critic of science or safety, but as someone deeply concerned that the United States is allowing regulatory inefficiency, not scientific limitation, to dictate who receives treatment, who is forced to wait, and who never receives care at all. Rare disease patients and their families live on a different clock than regulators. For many conditions, there is no approved therapy, no meaningful alternative, and no second chance if a drug is delayed or abandoned. Disease progression does not pause while an application sits under review. Children age out of eligibility. Patients decline beyond treatable stages. Families watch hope turn into irreversible loss.

I have overseen pediatric neurodegenerative trials where children lost motor function month by month while regulatory questions remained unresolved. In these cases, therapies demonstrated measurable stabilization using validated biomarkers, yet approval timelines stretched as additional data was requested—data that could only be generated as untreated patients continued to decline.

In rare oncology, I have managed trials for ultra-rare cancers where enrollment populations number in the dozens nationwide. In these settings, surrogate endpoints are widely accepted internationally, yet U.S. sponsors are often asked to expand trials beyond feasible enrollment pools or delay submission until outcomes mature—despite no alternative therapies existing. In rare metabolic and genetic disorders, early intervention can prevent irreversible organ and neurologic damage. Yet I have seen approvals arrive only after patients aged out of eligibility, transplant windows closed, or permanent harm had already occurred. Despite extraordinary advances in genomics, biologics, and precision medicine, our regulatory timelines increasingly resemble those of a bygone era—designed for common diseases, large populations, and decades-long development cycles.

In rare disease, these assumptions simply do not hold. The FDA's mission is to protect patients. But today, process has overtaken purpose. Sponsors routinely face prolonged review timelines that extend well beyond statutory targets, shifting evidentiary standards mid-review, requests for additional trials where patient populations are vanishingly small, and inconsistent application of surrogate endpoints and real-world evidence.

These delays do not merely slow innovation—they kill it.

Small and mid-size biotech companies, which drive the vast majority of rare-disease innovation, often cannot survive repeated regulatory resets. Programs are shelved. Investors walk away. Promising therapies die not because they failed patients, but because they failed to navigate an opaque and unpredictable system.

Increasingly, sponsors respond by moving trials overseas.

I have overseen programs where U.S. academic medical centers were ready to enroll patients, investigators were funded, and infrastructure was in place—yet trials launched abroad first because foreign regulators provided faster, more predictable authorization. When trials move overseas, American patients lose access to cutting-edge therapies that were often discovered by American scientists. Families are told to wait—or to travel abroad if they can afford it. Access becomes a function of geography, not need.

This shift also sidelines America's world-class research institutions. When trials leave the United States, U.S. investigators lose first-in-human experience, research infrastructure atrophies as funding follows trials abroad, and the next generation of clinicians and scientists lose hands-on exposure to emerging modalities such as gene therapy, RNA therapeutics, and precision oncology. Once this erosion occurs, it is extraordinarily difficult to reverse.

While we debate incremental reforms, China is moving with speed and strategic clarity. China has streamlined clinical trial approvals, aggressively accepted foreign data and real-world evidence, aligned regulatory review with national industrial policy, and treated biotech leadership as a matter of economic and national security. As a result, clinical trials, manufacturing capacity, and scientific talent are increasingly flowing overseas. The United States, for now, is the world leader in biomedical innovation and drug discovery – but we cannot and should not accept a future where American patients are among the last to get access to breakthrough clinical trials or life-saving treatments. This is not just a healthcare failure—it is a strategic one.

Biotechnology underpins economic growth, military readiness, supply-chain resilience, and pandemic preparedness. A regulatory system that discourages domestic development actively undermines U.S. competitiveness. I want to be clear: patients do not want unsafe drugs. I have never met a rare disease family asking regulators to abandon rigor. What they ask for is proportionality, transparency, and urgency. We already have tools that can achieve this, including conditional and accelerated approvals, expanded use of surrogate endpoints, adaptive trial designs, international regulatory reliance, and robust post-market surveillance. What is missing is consistent application and cultural commitment. A system that demands perfection before access, while knowing perfection may never be achievable, is not protecting patients. It is denying them agency.

Congress has a critical role to play. Oversight is needed to ensure that FDA decision-making prioritizes patient access where unmet need is severe, applies flexible standards consistently and predictably, embraces global data rather than duplicating effort, and recognizes biotech leadership as a strategic national asset. Rare disease patients cannot advocate with numbers. They rely on leadership.

If we fail to modernize our regulatory approach, the consequences will be measured not only in lost lives, but in lost leadership—and once ceded, that leadership will be extraordinarily difficult to reclaim. I have spent my career helping bring therapies from the lab to the bedside. I know what is possible when science, policy, and urgency align.

The question before us is not whether we can do better. It is whether we will.

On behalf of patients who cannot afford delay, I urge this Committee to act.

Respectfully submitted,

Dr. Victoria Manax-Rutson, M.D.

Christy Dearien – February 19th, 2026

Written Testimony

Hope on hold: FDA decision will have detrimental impact on families with Huntington's disease

Originally posted as a LinkedIn article in January 2026

The genetic mutation that causes [Huntington's disease \(HD\)](#) was discovered in 1993, and yet HD families, including my own, are still waiting for something – anything – to slow disease progression and extend the amount of quality time we have with our loved ones. We are eager to hold onto hope that a disease-modifying treatment could be available soon, but that has been difficult in recent months due to a decision by the US Food and Drug Administration (FDA) to [shift the goalposts](#) on a promising gene therapy.

Huntington's is a rare neurodegenerative disease that affects 41,000 Americans, with another 200,000 being at-risk. It is characterized by physical and cognitive decline paired with a laundry list of potential psychiatric symptoms; it gradually takes away the ability to walk, talk, and participate in daily life. Symptoms typically appear in middle age but can appear in childhood or old age. Every child of a parent with HD has a 50-50 chance of inheriting the disease.

My own family was surprised to learn my brother had HD in 2014 because we didn't know we were an HD family; my dad and grandpa both had HD but never received the correct diagnosis. We had hoped that finding answers for my brother would help him get better. Instead, his diagnosis meant that 10 family members, including me and my kids, might have inherited HD. We were all overwhelmed by what we were up against as we adjusted to this new life.

My brother has changed a lot in the last ten years. He now relies on others for all aspects of care, and communication is challenging. I tested negative in 2019, but I continue to worry about my family. I also care deeply for those I have come to know in the HD community. I've attended many community events, volunteered at a [youth camp](#), and worked with a small group of [community advocates](#). I've also interviewed dozens of people to write [a book about HD](#). What I have found is a community that welcomes anyone impacted by HD as family – a chosen family that works tirelessly to support and advocate for each other.

Research holds promise for my friends and family to have a brighter future. On September 24th, 2025, [uniQure](#) announced [unprecedented results](#) of a combined Phase I/II clinical trial for their investigational medicine, AMT-130, a one-time gene therapy. At the three-year mark, patients in the high-dose cohort showed a 75% slower decline in motor and cognitive function, and the therapy had a strong safety profile. This is the first-ever treatment to show HD progression can be slowed. There was immediate buzz within the HD community as we dared to hope for a better future.

Unfortunately, our hope was short-lived.

Just weeks later, the FDA indicated it [no longer agrees](#) that natural history data can be used as a comparator arm in uniQure's application for accelerated approval. Using a natural history dataset is an [accepted method to measure disease progression](#) in rare diseases without subjecting patients to risky procedures. In this case, it is the most ethical choice, given that delivery of this gene therapy involves an approximately 10-hour brain surgery. Using a placebo arm instead would require patients to undergo a

sham procedure (i.e., undergoing anesthesia without receiving treatment). This is invasive, and patients are likely to experience too much neurodegeneration to qualify for treatment by the time they become eligible.

The FDA's announcement came as a surprise because uniQure and the FDA consulted with each other throughout the clinical trial process and agreed on conditions for moving AMT-130 through that process. The FDA even awarded AMT-130 [Breakthrough Therapy and other designations](#). Despite indicating they were on board throughout, the FDA has now changed course. Accelerated approval is on hold, and next steps are uncertain.

The HD community knows to be cautious about placing too much hope in research, because we've been here before. Other promising clinical trials have been halted or paused due to [safety issues or unmet endpoints](#). This time, however, the issue isn't safety or efficacy; the issue is the FDA backtracking on its commitment to allow natural history data as a control. Their reversal is astonishing and has serious consequences for tens of thousands of families like mine.

HD progresses slowly, so it would be easy to think that the HD community has time. However, HD's long disease progression means our families endure loss after loss, generation after generation. Once neurodegeneration begins, [long before symptoms appear](#), it is very difficult to halt or slow it down. We don't have time to wait years for uniQure to gather more data for a placebo arm. Each year of delay means more of our family members will experience too much neurodegeneration to be eligible for treatment, setting them up for decades of decline. Our loved ones deserve better; they deserve the chance to look forward to a longer and healthier future – a future that seemed within reach when uniQure first announced its AMT-130 clinical trial results.

The FDA's actions have introduced unpredictability into the drug approval process, which has consequences beyond HD. The potential to treat rare diseases is at stake as [other rare disease communities face similar challenges](#). Please join me and more than 38,000 others who have signed at least [one](#) of [two](#) petitions calling on the FDA to uphold its previous commitment to an accelerated pathway for AMT-130. In addition, please [contact your members of Congress](#) to urge them to support a fair review of AMT-130.

Jill Gassman Zullo – February 19th, 2026

Written Testimony

I am living with stage IV sinonasal mucosal melanoma — a rare and aggressive cancer that develops in the mucous membranes rather than on the skin.

It began as a sinus infection.

Then, perhaps, a polyp.

Finally, a referral to an ENT: hypertrophy of the inferior turbinate, they thought.

Still, there was no definitive diagnosis.

A PET scan was ordered. It revealed a mass, but no one could say how big or how deep it was. Surgery was scheduled for October 2024. It was expected to last thirty minutes.

Once inside, the tissue did not look right. A sample was sent to the lab.

It came back cancer.

The approach changed in real time. What was meant to be brief became a three-hour surgery.

When I woke up, I was the only one who did not know. Everyone else — my husband, the nurses, the surgeon — had already learned the truth.

My husband was standing by the recovery room door. The nurse went through the usual questions — how are you feeling, are you in pain, do you need anything?

I was ecstatic. I closed one nostril with my finger and said, "Look — I can breathe." I was almost giddy, amazed at how extraordinary something so ordinary could feel.

The nurse asked if I needed pain medication. I said no. There was mild pain, but it didn't matter. I had grown so used to the obstruction that I hadn't realized how much it had altered something as basic as breathing. I kept inhaling, exhaling, quietly testing it, only then beginning to understand how much it had affected me.

I knew the nurse was finishing her checks, but I was so absorbed in my ability of breathing without difficulty that I barely noticed her glance at my husband before she left the room and closed the door softly behind her.

My husband walked toward me.

And the language changed.

Cancer.

Stage IV sinonasal mucosal melanoma.

That was the moment I was inducted into the "rare disease club"—a club no one chooses and I didn't know existed until that day.

After surgery, after hearing the name, I searched for solid ground. I looked up everything: large survival curves, established treatment pathways, definitive guidance. What I found was how limited the evidence base remains. Studies are small because the community is small. Many physicians will never encounter a single case in their careers. Research is progressing — I am alive because of it. But the science is still catching up to the urgency of the disease.

Mucosal melanoma accounts for about one percent of melanoma diagnoses. It can arise in areas such as the sinuses, nasal passages, oral cavity, vagina, or anus — places that are not easily visible, where symptoms can resemble common conditions. Because it hides, it is often diagnosed at advanced stages.

The five-year survival rate is often cited around twenty to twenty-five percent. For advanced disease, it is lower.

There are no FDA-approved treatments specifically for mucosal melanoma.

Treatment often relies on therapies developed for other cancers or participation in clinical trials. Access depends on eligibility criteria — prior treatments, lab values, organ function, and timing. Not everyone qualifies. And eligibility can change as the disease progresses.

For patients with mucosal melanoma, time is not abstract. It is measured in scan intervals. In treatment response. In whether options remain available.

Delay is not theoretical. It can mean progression. It can mean losing eligibility. It can mean an option exists — just not in time.

What I long for is simple: ordinary years. Unremarkable years. To witness vows, to hold imagined grandchildren, to rise into morning, and another, and another, until a lifetime has been lived.

Time bends differently for me. You count in seasons; I count in fragments — a week without pain, a month until the next scan, an hour when hope feels steady enough to carry.

Mucosal melanoma is rare. I may be one of few. Rare describes the disease. It does not diminish the life being lived.

I respectfully ask the Committee to consider how regulatory timelines and evidentiary standards affect ultra-rare, aggressive diseases like mucosal melanoma — where no FDA-approved treatments exist, where data is limited, and where this disease does not pause while decisions are made.

Thank you for allowing my experience to be included in the record.

Brigitte Bontems – February 19th, 2026

Written Testimony

When I was 15 years old, I watched my 13 year old brother take his last breath and be taken away from our home in a hearse. He had Hunter Syndrome (MPS II). The weeks leading up to that moment started with trips to the hospital, watching him flatline and be revived, bringing him home on life support, and eventually watching my parents make the decision to remove him from life support. Awesome God still rings in my head and brings me to tears as we sang it to him as he breathed his last. The faces of my family members etched in my brain as a deafening silence crushed us. I watched my dad disappear while he tried to find distractions. My siblings fell into their own bad habits to cope. I stayed home from school for a week trying to plan my brother's funeral while my mom crumbled in despair.

Now I am 32, and my only child was just diagnosed with the same disease that took my brother's life. He's not yet 2 years old, and I see the delays beginning. This sweet, energetic toddler has to go to the hospital once every single week for the rest of his life to be poked with a needle and sit still in a room for 4-7 hours while the medication is pumped into his body. A medication that can't stop the disease from getting worse and it can't fix the damage that's already done. All it can do is slow the progression of physical ailments. The medication does not cross the blood brain barrier, so it does nothing to preserve his cognitive ability. He's 19 months old. Any word he once said, he no longer says. I may never hear my son say "I love you". We gave up our hobby of off roading at the dunes because it's not safe for him. He may never have a hobby of his own, or a job, or a girlfriend, wife, or kids. He may never even see adulthood.

The life expectancy in severe cases is 10-20 years old. Every time I look at my son, I see him dying in my arms like my brother did. We need better treatments and we need them now. My son is 19 months old, has been on the current available treatment for 6 months, and I'm seeing decline. Japan has a treatment that crosses the blood brain barrier and a one time gene therapy has been created and shown to be successful in clinical trials but was denied by the FDA. We don't have time to wait. I'm already watching my son move closer to death every day.

Mary Nuernberger – February 19th, 2026

Written Testimony

Hello,

My 17 month old son has recently been diagnosed with Hunter Syndrome, or mucopolysaccharoidosis (MPS) type 2. Most simply put, MPS diseases are the results of a missing enzyme in the body resulting in toxic product build up that causes irreversible damage. Nothing can prepare a parent to learn their child has a rare, genetic, progressive, and terminal disease.

He is a very sweet little boy with an infectious laugh; he is walking, getting into everything, and finding his voice. However, he also has chronic respiratory infections, ear problems, asthma, an enlarged liver and spleen, and developing skeletal changes. We know what we are facing moving forward – worsening of all of these symptoms he already has along with cardiac changes, eye changes, loss of the ability to walk and other motor skills, loss of speech, developmental regression, and other neurological changes. The average life expectancy of a child with Hunter syndrome is 10-20 years.

There is only one available treatment for Hunter Syndrome right now, weekly infusions of a replacement enzyme that can improve some, but not all symptoms. It is unable to cross into the brain to help with neurological symptoms, a very impactful part of Hunter Syndrome. There are promising new clinical trials and studies recently performed that target the disease in 2 ways – gene therapy that can help the body produce the enzyme on its own and enzymes that can cross into the brain. Both of these therapies can slow the progression of disease, improve quality of life, retain skills, and make a very positive impact on lives and families of these children.

Unfortunately, I have learned that many treatments submitted through the FDA accelerated approval program for many rare diseases, not just MPS, have been denied. I am a veterinarian, thus with strong understanding of science and medicine. Reasonings for denial have included wanting longer follow up data, larger sample sizes, placebo or control groups, and rejection of the parameters set up to determine efficacy of the drug. Time is not on our side with rare genetic diseases; longer follow up before approval is devastating to the families waiting for this treatment. When you are facing a lifespan of 10-20 years, research following response for a few years showing improved quality of life is impactful. Rare diseases are just that, rare. It can be difficult to find larger numbers of study participants in such a small population, especially with how specific the parameters for trial patients can be. A specific placebo or control group is not necessary when we already know what happens to children without treatment. Finally, parameters set up to show efficacy aside from seeing clinical improvement, are often measuring these toxic build ups and showing significant decrease in values, used in a variety of research historically for the disease. How can there be an argument that this is not an appropriate measurement?

No one knows more about what delay of treatment means than the children and the families with these diseases like ours. The time for treatment for my son is now, at the time of diagnosis. Not in 1 year, not in 5 years. As his body is undergoing irreversible changes, every delay or denied treatment moves us closer to a life without our sweet, laughing boy. I struggle to understand a world where treatments are being developed

that could keep my son happier, more comfortable, able to do more for himself, and give him a longer lifespan, but those treatments are being denied for unnecessary reasons. Do not let that hope and progress be removed by delay or denial of treatment. Look at the children in these studies, hear from their families on how much of a positive impact it made in the symptoms of their disease, and look at what future we see without treatment. There is no worse option than where we are now without them.

Thank you for your care and attention to this letter. I do hope you will take this information and our story into careful consideration when evaluating the role of the FDA in the rare disease community.

Thank you again.
Mary, mother of a MPS type 2 child

Mallory Carter – February 19th, 2026

Written Testimony

Hello,

This month I received a diagnosis that could eventually change my life, but it doesn't have to be my future.

Over the past decade, my father has had symptoms that were hard to pinpoint. Last summer, he was diagnosed with Spinocerebellar Ataxia 6 - SCA6 - a rare neurodegenerative disorder that impairs his ability to complete routine tasks like walking. Seeing my father go through this has been devastating, as any child seeing their parent struggle with an Ataxia I'm sure would agree.

Around the same time that my dad was diagnosed, my family hosted my husband and I's wedding. What was a joyous time also had a nagging feeling in the back of my brain - my future may look different. In an effort to stop this disease in my lineage, I went through genetic testing. Unfortunately, the test came back positive, I have SCA6.

Over the coming years, the cerebellum in my brain will continue to shrink - making every day tasks like walking, talking, and eating increasingly difficult. Once this part of my brain degrades, there is no getting it back. I'm in my 30s, I still have so much life to live and I want to seize every moment of it. If the FDA takes action now to authorize promising breakthrough treatments, myself, my family members, and the thousands of other people in the United States who have SCA6 could live out the rest of their lives not trapped as a prisoner in our own body. My hope is to one day be an old woman who gets up every morning to power walk around my neighborhood and be able to pick up my grandchildren. Please help me make this dream a reality.

Best,
Mallory Carter

Poornima Durgam – February 19th, 2026

Written Testimony

My husband is suffering from SCA, and it has been a challenge every day taking care of him. I would like to urge the government to support and release funds for the studies and Medicines Poornima.

Rosie Acuna – February 19th, 2026

Written Testimony

My family has been bravely battling Huntington's Disease since the early 90s, a time when knowledge about HD was scarce.

My grandfather passed away courageously navigating the challenges of Huntington's Disease with limited insight.

Fast forward years later, my loving mother, my brother, 3 uncles, 1 aunt, 8 cousins (and counting) and myself have bravely faced, are currently battling, or await our turn with courage and strength against this relentless disease as it unfolds.

One of my cousins unfortunately committed suicide because he did not want to live with horrendous disease. Yes, he rather take his own life!

I've witnessed my mother's vibrant spirit slip away, and now my brother's journey with the disease has my heart. Both were once full of life and joy, before the disease took its toll.

My family remains hopeful, holding onto the promise of a brighter future where a cure or more effective treatments will be available for those we love. May we persist in prayer for a miraculous cure and groundbreaking medicines.

Rosie Acuna

Alexandra McNeley – February 19th, 2026

Written Testimony

My name is Alex McNeley and the way I found out I may have this disease was saying good bye to a “father” who didn’t want to be a dad. He didn’t ever communicate with me (his only child) that I could have this disease he died from. So there I am, 24, and just realizing my life could literally be over before it begins. As soon as I got back home from Arizona to Texas, I went to get tested and it turns out that bad father of mine did in fact give me this genetic disease. This was 10 years ago and now I sit here hearing “no” after “no” for anything that might even be able to work for this terrible thing, Huntingtons. Then one shining light of hope, which I’m sure you’re hearing a lot about lately, AMT-130, comes to us! We’re all floored and can’t wait to give this amazing new treatment a try! Then for whatever reason, it seems to basically get swept under the rug by the FDA as because of a “control group issue”? You have no idea how devastating it is to actually have such a beacon come into your life just to have it taken away in the matter of a month. This is why the FDA needs this hearing. For those of us with this disease have been so used to hearing “no” that it would be really nice to hear a “yes” for this one. We have to get the FDA to understand how much of a road block they’ve created for those of us with the disease and all other rare disease. It’s quite literally a matter of life and death.

Thanks for your consideration to help save people’s lives and to make sure the FDA starts to take these kinds of treatments seriously,

Alexandra McNeley

Rouf Banday – February 20th, 2026

Written Testimony

Headline: Life with SCA1: My Journey – Rouf Banday

Hello everyone,

My name is Rouf Banday. I am a Branch Post Master, a husband to a dedicated advocate, and a father to two wonderful sons, Ahil and Moiz.

Today, I am sharing a personal part of my life to help raise awareness: I am living with SCA1 (Spinocerebellar Ataxia Type 1).

Living with SCA1 means facing daily challenges with balance and coordination, but it does not define who I am. I continue to work, care for my family, and cherish every moment with my boys. I am sharing my story because awareness is the first step toward understanding and, ultimately, a cure.

To those fighting similar battles: you are not alone. Our strength lies in our resilience and our community.

Rouf Banday – February 20th, 2026

Written Testimony

My name is Rouf Banday, and I am submitting this statement to share my experience living with Spinocerebellar Ataxia Type 1 (SCA1).

As a Branch Post Master and a father of two young sons, Ahil and Moiz, SCA1 presents daily challenges to my balance and coordination. Despite these hurdles, I continue to serve my community and provide for my family.

I am writing to emphasize that for patients like me, time is everything. Rare diseases like SCA1 are progressive, meaning every day that a potential treatment is delayed by regulatory bureaucracy is a day of lost function. We need the FDA to prioritize faster pathways for therapies so that fathers like myself can remain active in our children's lives.

Access to innovation is not just a policy issue for us; it is a matter of our future and our ability to remain resilient for our families. I urge the committee to work toward reducing the roadblocks that stifle medical innovation.

Sincerely,

Rouf Banday

(Patient living with SCA1)

Samir Noori – February 20th, 2026

Written Testimony

Living with ataxia means never fully trusting your own balance. Simple tasks—walking, writing, holding a cup—can require intense focus. It can be frustrating and sometimes isolating when others don't understand.

But it also builds resilience. Every steady step feels like a small victory.

The hope for a cure isn't about changing who you are—it's about wanting freedom: to move without fear, to speak clearly, to live without constant calculation. Until then, living with ataxia is an everyday act of strength.

Samir Noori – February 20th, 2026

Written Testimony

Living with ataxia feels like your body is always a step behind your mind. You know exactly what you want to do, but your movements don't always follow smoothly. Balance can be shaky, hands can tremble, and even speaking can take extra effort.

There are moments of frustration, but also moments of determination. You learn patience. You learn to adapt.

And deep down, there's a strong hope for a cure—not out of weakness, but out of a simple wish to move freely, confidently, and without limits

Regards

Lauren Holder – February 20th, 2026

Written Testimony

Dear Chairman Rick Scott,

My name is Lauren Holder. I am gene-positive for Huntington's disease. I cared for my father as he declined and eventually passed away from this disease in January 2021. I now live knowing that Huntington's disease is progressing inside me. I am also a clinical research participant.

Over the years, I have participated in a therapeutic clinical trial and in several observational studies, including contributing to the natural history research that helps define how Huntington's disease progresses over time. That natural history data is not abstract to me - it represents blood draws, cognitive testing, travel, vulnerability, and time given freely in the hope that it will help build a pathway to treatment.

Patients like me enroll in these studies because we believe in science. We believe in partnership. We believe that if we do our part, the system will work with us.

Huntington's disease is a fatal, inherited neurodegenerative disorder with no disease-modifying treatment. Time is everything. Time is cognitive function. Time is independence. Time is the ability to be present for your children – to help with homework or teach them how to ride a bike.

Recent regulatory decisions affecting rare disease therapies - including incomplete response letters, refusals to file, and shifting expectations for trial design - have had destabilizing consequences across patient communities.

For diseases like Huntington's, traditional placebo-controlled trials are uniquely difficult. Our population is small. Our disease is progressive and irreversible. Natural history data and external controls are not shortcuts; they are tools built from years of patient contribution and scientific rigor.

When regulatory expectations shift late in development, it does more than delay a submission. It calls into question whether the years patients have spent contributing to natural history databases will truly be recognized and utilized as intended.

We are not asking for lower standards or shortcuts. We are asking for:

- Consistent application of accelerated approval pathways
- Transparent and predictable regulatory expectations
- Scientific flexibility appropriate for fatal neurodegenerative disease
- And meaningful incorporation of patient experience into risk-benefit decisions

I have sat in research visits answering memory questions, knowing that one day I may not be able to answer them. I have contributed to natural history studies designed to map the decline of my own disease. That data exists because patients like me were willing to document our progression in the hope that it would shorten the path to treatment, not extend it.

When a delay happens in Huntington's disease, it is not neutral.

Delay is decline.
Delay is an irreversible loss of brain cells.

Patients have done their part. We show up to studies. We give our data. We accept risk.
We build natural history datasets so that innovative trial designs can be possible.

We are asking that the regulatory framework meet us with the same urgency and consistency.

Thank you for holding this hearing and for examining how FDA processes affect real families like mine that are facing progressive, fatal rare diseases.

Sincerely,

Lauren Holder

Heather Thurgood Wilmoth – February 20th, 2026

Written Testimony

Chairman Scott, Ranking Member Casey and Distinguished Members of the Committee,

I am writing to you today as the spouse and stepmother of Huntington's Disease Patients.

I am also writing to you as the mother of another child who is at risk of developing Huntington's Disease.

Our family has been a part of clinical trials, observational studies and so forth. So, we are not afraid of doing whatever it takes to help our loved ones and other families in our HD community.

However, it seems like the FDA and the medical community, those sworn to uphold and help families like ours, couldn't care less.

In case you aren't aware, Huntington's Disease is a terminal neurodegenerative brain disease that's described as having ALS, Parkinson's and Alzheimer's all at the same time.

Do you know what it's like to wait nearly 40 years to finally find the person you're meant to spend the rest of your life with only to watch them die of a terminal disease like HD?

Knowing that you are lucky that you have had only 14 years with him, 12 married and praying you are blessed enough to have more but know that may not happen.

Finally finding that person, only to watch him go from a productive hard-working member of society to having to feed, bathe, clean him when he has accidents? To watch him go from a fun-loving present father to someone who can barely be understood when he speaks.

To go from having a partner for a husband to him being like your third child. A husband who is now 48 years old. Diagnosed with HD 10 years ago this April but dealing with HD his whole life because of his mother's HD.

Do you know the fear as a parent, knowing one of your children is going to follow the same fate and the other child could as well?

Children who are only 20 years old and diagnosed positive for HD, the other only 11 years old and knowing he is at risk.

These are many reasons families like ours had finally had hope that a drug was discovered to have a potential 75% slowing of disease progression.

We also had hope that the Food and Drug Administration was FINALLY listening to our HD community only to back down and totally reverse that help that was once given to us.

Our family and our HD community aren't asking for immediate approval of Uniqure's AMT-130, we are just asking for a fair review as well as for the FDA to not back down on a promise given to us.

My husband and I were on a panel for an Externally Led Patient Listening session with the FDA in November of 2024. At that meeting, we finally had hope that we were being heard. That the FDA truly wanted to help rare diseases like the one we face daily.

I don't think that people outside of the Huntington's community quite understand the lengths many of us are willing to go to help our loved ones.

I would do whatever it takes to help my husband and our children.

My husband is considered late middle stage, even at this point, I would travel to wherever we needed to get him help. To slow his disease, with the dream of stopping it completely. Willing to do whatever it takes to help both of our children before they were to ever see a symptom.

Meaning I would go broke, homeless, travel to other countries if it meant getting them help.

I don't see that the FDA is willing to help us, so I'm asking you to please help.

Again, I'm not asking for you to accept data blindly, I'm asking you to please not make our families wait any longer. I am asking for a Fair Review of the ONLY medication that has ever seemed to help our disease.

I am begging for more time with my husband. I am begging for my children to have fulfilling productive lives before ever seeing a single symptom. I am begging for not just our family, but the families of over 41,000 patients and the more than 200,000 at risk of Huntington's Disease.

My husband and our oldest being a part of the over 41,000, my son being a part of the over 200,000.

Please allow for a fair review and not make our Huntington's families wait years more because the FDA wants the trial to basically start over before being willing to look at the data. Data the FDA promised to look at as well as promised to allow the trial to go as planned.

Our community is seeing other diseases get these similar treatment options, we just want our fair share of being able to help our loved ones, ourselves and our HD community.

Thank you for your time,

Heather Thurgood Wilmoth,
Huntington's Disease Wife, Mother, Advocate

Amirah – February 20th, 2026

Written Testimony

My name is Amirah, and I am writing to you as the daughter of a man living with spinocerebellar ataxia (SCA), a progressive and currently incurable disease.

I am also writing to you as a family member who recently lost an uncle to the same disease at the age of 44.

Though I live in the UK, I find it important to write to the committee because the only possible treatments for SCA are being developed in the USA (for example, Biohaven have developed a drug called tronaluzole) and could potentially help others suffering from the same condition across the globe.

SCA is not widely known by the general public, but for families affected by it, it shapes daily life.

It progressively gets worse, affecting coordination, speech, and independence.

In the case of my father, he has lost the ability to walk and speak properly.

There is no cure, and treatment options are limited to managing symptoms.

SCA can cause early death, and my uncle lost his life 5 months ago due to this disease. His loss still affects all of us.

I understand the role of the FDA in making sure that treatments are safe and supported by strong evidence.

Patient safety must remain paramount.

However, for progressive rare diseases like SCA, traditional regulatory timelines and evidentiary rules can feel especially heavy, considering that time is crucial for patients. When a condition is degenerative and incurable, delay can become quite severe.

While I recognise that regulatory decisions must be evidence-based, I hope that the broader discussion includes communication with patients and families by listening to their concerns to allow for responsible innovations in rare disease treatments.

Families like mine who live with members suffering from progressive diseases are navigating a state of anticipatory loss, not knowing when are loved ones will die but having to live the feeling of how life will be when they have eventually passed.

I follow research closely because it represents a possibility that life could be different from what it currently looks today.

When applications are declined or delayed, what we need most is transparency, urgency and a framework that acknowledges the unique challenges of rare diseases.

I hope that this Committee will be beneficial to Americans suffering from rare diseases, and will provide hope for those across the world.

I greatly appreciate the work of this committee and hope that by sharing my experience, many people with rare diseases like SCA will know that they are not alone.

Thank you for your attention to this issue and for examining opportunities to improve patient access to innovation.

Kind regards,
Amirah

Amy Poff – February 20th, 2026

Written Testimony

The disease gluten ataxia occurs when certain people eat gluten (pastries, cake, etc) and the gluten antibodies "attack" the cerebellum part of the brain. The cerebellum controls balance and coordination of the body.

The United States is FAR behind on even diagnosing this ailment. (Parts of the UK and Germany are WAY ahead of the United States.)

Please consider more funding for research on this disabling disease - gluten ataxia.

Thank you,
Amy Poff

Tony Mackey – February 20th, 2026

Written Testimony

The FDA should be emphasizing the science, rather than "old wives' tales" to give approval of this medicinal treatment for Spinal Cerebellar Ataxia.

Mary Mattison – February 20th, 2026

Written Testimony

Hello: I have a rare neurological condition called idiopathic late onset cerebellar ataxia (ILOCA). No one in my family has had this. Currently there is no medication or treatment that would stop ILOCA or reverse it. There is one medication, Skyclarys, that is helping some folks who have the genetic Friedreichs' Ataxia stop it from getting worse. Cerebellar ataxia is a life-changing condition and, for many of us, it shortens our lives.

Cerebellar ataxia causes vertigo in me and it happened when I was driving. I almost hit a car in the lane beside me so I had to quit driving many years ago. It also causes wobbling about 15 hours a day, stumbling, trouble swallowing (I aspirate many foods and liquids), exhaustion, and other problems. We badly need the FDA to allow other potential drugs to be put on the marketplace to help the rest of us.

Please consider working to help those who have cerebellar ataxia by approving more drugs that would help this condition. I appreciate any help you can give us. Thank you for your consideration.

Anonymous – February 20th, 2026

Written Testimony

I have a rare disease. It doesn't have a cure. It slowly gets worse.
We need more research!

Ridge Rider – February 20th, 2026

Written Testimony

Imagine a day that starts out trying to get out of bed. Then you have to use a walker just to leave the bedroom. You need to take a shower but you need your wife or husband or caregiver to help you. Then you have to have someone cut up your breakfast for you, you tremble so much, that it's hard to just hold your fork. Then, using your walker you go to the chair that helps you to sit and stand up. It's called a lift chair(and they don't come cheap). Then, in their infinite wisdom, they(the almighty FDA) deny the one drug that would help you. You have to depend on your children(if you are lucky enough to have them) to help you in purchasing your lift chair, walker, wheelchair, scooter or something that helps you get around. Welcome to my world, while you just sit there and do lip service. Our future generations are hoping you will do something to help eradicate these rare diseases, or at least make it possible to try out the new drugs that are up for FDA approval.

Marie Phillips – February 21st, 2026

Written Testimony

Dear Senator Scott and Committee Members,

Regarding the scheduled hearing "From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation", I respectfully submit my statement as a person afflicted by a rare disease.

The disease that I suffer from is progressive, incurable and very rare. It is debilitating and makes simple tasks into momentous challenges.

I have been receiving treatment through the expanded access program with a drug which the FDA issued a Complete Response Letter on in November. This treatment has been life changing for me, not only in the management of my symptoms, but in the literal halt of the progression of my disease. People can now understand my speech, rather than being asked continually to repeat what I said and walk without the fear of falling even walking a short distance. It has also produced absolutely no negative side effects.

I beseech decision makers to consider those of us living with serious rare diseases and to find a way to make new treatments available. The prospect of this medication becoming unavailable to myself and my family in the near future is extremely distressing.

Allison and Marc Saulsbury – February 21st, 2026

Written Testimony

Dear Chairman Scott and the U.S. Senate Special Committee on Aging, Thank you for your incredibly important work. Our names are Allison and Marc Saulsbury from Connecticut. We're writing to share our family's story with Ataxia for submission to the record for the upcoming Hearing on February 26th. We are incredibly grateful to know that you've established the Hearing and want to express our full support for any and all efforts to accelerate innovation and patient access to therapies for rare diseases. Our family recently lost Allison's father, Michael, to Spinocerebellar Ataxia, a degenerative disease of the nervous system we became aware of as his symptoms quickly progressed. As a hereditary condition, we are now aware that Allison also has ataxia, and she has begun to show symptoms as well. Ataxia has upended our lives in ways that we could never have anticipated, and as a rare disease, we have found that we and the 15,000-20,000 others afflicted in the US have very limited options for treatment and no (yet) known cure. Allison is a personal trainer who's always prioritized physical fitness, and facing the challenge of a neurological impact to her movement is a tremendous physical and especially mental burden. She struggles daily with speech and motion issues, and these combined with the anxiety about rapid symptom development for her and our children take a tremendous toll. The rarity of the disease and limited progress on treatment can make things feel hopeless, and the disease has had a debilitating effect on our engagement with work, extended family, and community. Thankfully, we've seen some hope from Troriluzole [see NDA210862]. Allison has seen clear benefits and a marked decrease in the rate of advance of her symptoms, with no side effects at all. We've learned from many others that it has also shown them overwhelmingly positive results, slowing progression and even reversing debilitating symptoms. Given the rarity of ataxia and the lack of any other effective therapy, seeing Allison's and others' results gives us much-needed hope for Allison, and for our children's future. Despite all our many blessings, we worry every day about how their lives will play out, especially if they aren't able to see promising new therapies developed extremely soon. Of course, we fully realize that the regulatory landscape and stakeholders for an experimental drug, especially for such a rare but debilitating disease, are remarkably complex. We're desperate for the development and deployment of innovative new therapies, but the potential for these to be impeded by regulatory burdens or standards that don't accommodate sufficient flexibility for rare diseases is heartbreaking for those many of us who are longing for a breakthrough. We nonetheless remain confident that the benefits of these new therapies are so substantial that they will continue to be responsibly reviewed and progressed, and we can't overstate the marked positive experience the results and the hope have had on our lives. We can't stress enough the vital importance of the Hearing's aims - losing the most promising source of hope for managing our symptoms in the short-term, and seeking a cure for our children in the long-term, would be absolutely devastating to us. We want to do our part to connect and advocate for continued treatment progress and availability in any way we can. We're so grateful for your work on the committee and

service of all those at the FDA, and we'd ask for any assistance or intervention you could possibly provide to further the mission of rapid innovation and patient access.

Thank you so much for your time and consideration.

Sincerely,

Allison and Marc Saulsbury

Wanda Smith – February 21st, 2026

Written Testimony

Dear Chairman Scott and Members of the Senate Special Committee on Aging:

Thank you for the opportunity to submit this statement for the hearing "From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation."

Alzheimer's disease and related disorders (ADRD) include several rare, autosomal dominant genetic forms of dementia. Developing treatments for these conditions requires regulatory flexibility, clearer guidance, and a willingness by the FDA to consider innovative therapies—even when they carry higher risk—given the small patient populations and urgent unmet medical need.

Within the ADRD spectrum is FTD-GRN (progranulin deficiency), a genetic form of frontotemporal dementia caused by mutations in the GRN gene. Currently, four companies have promising therapeutics in clinical trials preparing for FDA review; however, there are no FDA-approved treatments available at this time.

Patients are often in their prime earning years, with children still at home, and the disease wreaks financial and social havoc on families. The cost for FTD families is three times that of Alzheimer's Disease. Symptoms vary widely, ranging from personality and behavioral changes to loss of speech and movement difficulties and memory, which makes early and accurate diagnosis particularly challenging as genetic counseling and testing is not covered by insurance.

As individuals age, symptoms of ADRD-FTD-GRN can emerge at widely varying ages—even within the same family—with onset reported between 39 and 89 years. The disease often strikes during the most productive years of life and progresses rapidly, typically leading to death within 6 to 8 years, although in some cases the decline can occur in as little as 3 years.

We would like your committee and the FDA to understand:

1) Clinical trial participation is especially difficult for FTD-GRN patients and families. For example:

- Traveling long distances to clinical trial sites is burdensome, often requiring multiple caregivers to help and increasing the likelihood patients will drop out.
- Common symptoms of FTD-GRN, including apathy, an inability to communicate, poor judgement and disruptive behaviors make comprehensive cognitive testing onerous, highlighting a need for less taxing decentralized trials and biomarker-based readouts.
- Lengthy trial timelines required by cognitive testing mean longer exposures to placebo and, ultimately, delay access to therapeutics. The longer the disease

process continues (particularly in the symptomatic phase) the more severe the disease presentation.

2) Asymptomatic carriers of *GRN* variants are willing to take risks to access approved drugs prior to symptom onset. For example:

- Asymptomatic carriers fear needing to lose brain function and wait for manifest disease before being eligible for therapeutics.
- Asymptomatic carriers would like subclinical changes, such as changes in blood-based biomarkers, to be sufficient to access approved therapeutics.

3) Flexible, patient-centric trial designs are needed to help overcome challenges to clinical trial participation. For example:

- It is difficult to recruit and retain sufficient numbers of participants for pivotal trials with traditional endpoints. The average time from symptom onset to diagnosis is ~3 years, thus newly-diagnosed patients are often too far progressed to participate in clinical trials. Healthcare professionals do not routinely suggest genetic counseling and testing, so many patients do not know they carry a disease-causing *GRN* variant.
- With a fast-progressing, terminal disease, patients do not want to be put in a placebo arm.
- There is a clear scientific rationale that increasing GRN levels is reasonably likely to predict clinical benefit.
- In the absence of any treatments that effectively address FTD-*GRN*, the FTD-*GRN* community is willing to take on additional risk to access clinical trials and therapeutics, once available. Even small, incremental benefits are desired by people diagnosed and their families.

For individuals living with FTD-GRN — and for asymptomatic carriers who know what the future holds — time is brain loss. Even modest, incremental benefit is meaningful, the community is willing to accept reasonable risk in pursuit of hope.

To better enable patient access to promising treatments for FTD-*GRN*, ***I respectfully urge the committee to consider the following. Regulatory consistency, trial design flexibility, reduce enrollment barriers and enhance predictability***

Regulatory clarity and reduced barriers to clinical trial participation are urgent necessities for families confronting devastating neurodegenerative disease. I thank the Committee for its attention to these issues and for its leadership in ensuring that advances in science are matched by an equally responsive and predictable regulatory environment.

Respectfully submitted,

Wanda Smith

Diana and Chris Rodriguez – February 21st, 2026

Written Testimony

We are writing today to tell you about our son Benjamin's experience with Ataluren (Translarna) manufactured by PTC Therapeutics. This oral small-molecule treatment allows for stop-codon read through to produce dystrophin in patients, like our son, with nonsense mutations which leads a diagnosis of Duchenne Muscular Dystrophy. Recently, the FDA was unable to resolve differences in data interpretations with the manufacturer, causing the new drug application to be withdrawn.

Duchenne muscular dystrophy is a genetic disorder that causes progressive muscle weakness and primarily affects boys. It is caused by a mutation in the dystrophin gene, which normally produces a protein that helps protect and strengthen muscle cells. Without sufficient dystrophin, muscle fibers become damaged and are gradually replaced with fat and scar tissue. Diagnosis usually occurs in early childhood, between the ages 2 and 5. As the disease progresses, weakness spreads to more muscles, and many require a wheelchair during their early teenage years. Over time, Duchenne affects the heart and breathing muscles. Although there is currently no cure, treatments such as corticosteroids, heart and respiratory care, and newer gene-targeted therapies can help slow progression and improve quality of life.

Our son Benjamin was diagnosed with Duchenne in November 2013, 4 months after his first birthday. We knew shortly after the time of diagnosis that Ataluren was the medication he needed for his type of mutation. Unfortunately, at the time they were only enrolling boys over the age of 7 for any trials. We were told that an FDA approval was hopefully around the corner. Three years came and went and while there was no approval however, PTC was starting a safety study for children under the age of five. We immediately started researching sites and were selected to enroll. 11 days before his fourth birthday Benjamin received his first dose of Ataluren. Within the first 6 weeks we saw a positive change in his strength and mobility, and haven't looked back since.

Benjamin is still ambulatory at the age of 13.7 years. In the past year his Cardiac MRI, Pulmonary Function tests, and bone density scan results were all within a normal range. All of his physicians marvel at how incredible he is doing compared to his peers of the same age and diagnosis. They are all very encouraged about how Ataluren has delayed the onset of the typical pathology of Duchenne. Other than a medical stroller and mobility scooter (to use for long walking distances, like at an airport or theme park) Benjamin has no assistive devices. Remarkably, Benjamin participates in PE for 60 minutes 5 days a week. While some of the activities are modified for his safety (no pull-ups, push-ups, etc.), he is still able to claim that PE is his favorite time of the day. A few months ago, he came home excited to share that while playing flag football he caught a pass and ran 20 yards to score a touchdown!

When Benjamin was diagnosed in 2013, we were told by one neurologist to go home and give him the best life possible because by the age of 7 his mobility would start to decline. Another neurologist told us to not give up hope that there were so many things in the pipeline for Duchenne, so much more than there had ever been before. During what was one of the most terrifying times in our lives we are grateful for that second neurologist's advice. We knew there was something out there to help slow this terrible disease. Ataluren was that "something" for Benjamin. We have no doubt in our minds

that Ataluren and the age at which he was able to be first dosed is the reason he is still running and jumping today. It is the reason his heart, lungs, and bones are still healthy. The safety profile of Ataluren is also a major benefit of the drug. Benjamin has never suffered any side effects while taking this drug for the last 9 years.

In addition to our own observations and experiences, results from the most recent clinical trial shows a 3.5 year delay in loss of ambulation. Ataluren is also found to be safe and generally well tolerated. The most recently approved gene therapy Elevidys has shown promise biologically but its impact on motor function is still being investigated and safety concerns have led to liver complications and even death. This makes the denial of a new drug application for Ataluren even more confusing and frustrating. Our son does not qualify for Elevidys because his mutation is on exon 9 which is part of the exclusion criteria. Patients receiving Elevidys with mutations in exons 8 or 9 have the risk of severe immune-mediated myositis. This is a severe, life-threatening autoimmune reaction where the body's T cells mistakenly attack skeletal muscle.

Currently, my son's access to a safe drug, Ataluren, is being denied. However, a drug that would potentially have a life threatening outcome is approved. With the FDA's decision, Benjamin is in a lose-lose situation. There are no other options for him besides the standard of care.

Without Ataluren his life will change dramatically. He will require more assistance with every day tasks such as dressing, bathing, and eating. His favorite activities, like playing basketball in our driveway and football with his friends at school will be stolen from him. His easily accessible Middle School for an ambulatory teen will now be faced with daily obstacles. His future depends on a treatment that is safe and helps preserve his function. Ataluren is that treatment. Please help Benjamin stay on Ataluren, his life depends on it.

Thank you
Diana and Chris Rodriguez

Meagan DeRaps – February 21st, 2026

Written Testimony

Dear Members of the Senate Special Committee on Aging,

The sound of a suction machine still stops me in my tracks. To most, it is a steady mechanical hum. To me, it is the sound of my daughter struggling for air.

She lives with a rare neurodegenerative mitochondrial disease, Pyruvate Dehydrogenase Complex Deficiency (PDCD), which impaired her ability to protect her airway and left her frequently choking on her own saliva.

That eight pound, cumbersome suction machine was the only thing standing between her and her last breath. It was always charged. Always within reach.

Car rides were the most frightening. We didn't plan routes for speed — we planned for safe places to pull over. Interstates were not an option. Travel felt impossible.

And yet, for families with medically complex children, travel is not optional. It is required for neurologists, mitochondrial specialists, surgeries, and — if you are fortunate enough — access to clinical trials.

Four years ago, my daughter became one of only 34 children enrolled in a clinical trial for Sodium Dichloroacetate (DCA), a potential treatment for PDCD.

The changes were almost immediate. Some were measurable: her lactic acid levels decreased and she woke less through the night. But the changes that mattered most couldn't be quantified. She had more energy. She laughed more. She cried less.

At three years old, just four months after starting DCA, she took her first independent steps. Within a year, she no longer relied on a feeding tube. The suction machine that once defined our days was pushed to the corner of the room. Then left behind on short walks and eventually began collecting dust.

But access to the DCA clinical trial came at significant cost. There were nightly reports to complete. Medication that required constant refrigeration. There were more appointments, more bloodwork, and the most costly of all, travel.

Traveling from our home in Alaska was so medically risky that we eventually rented a tiny basement apartment near Seattle Children's Hospital. Not a home — just a place to survive between appointments. It wasn't sustainable. So we made a decision no family plans for. We picked up our life and moved.

We chose Philadelphia because it is home to an extraordinary children's hospital and one of only 9 sites in the country that was offering access to the DCA clinical trial.

We left our home, our support system, and our stability; because that is often what access looks like in rare disease.

When regulatory review stretches on, when decisions are deferred, or when resubmissions restart the clock, children do not pause alongside the process. They regress. They are hospitalized. They lose milestones they may never regain.

Families like mine are not asking for shortcuts or compromises in safety. We are asking for rigorous review – but also timely review – so that when science shows promise, the drug review process moves with the urgency these children deserve.

In September 2025, we were devastated to learn that despite a well-established safety profile, DCA would not be approved in its current form. The FDA is requiring more information and potentially an additional clinical trial. It has been more than twelve years since the initial meeting with the FDA to discuss DCA as a potential treatment for PDCD. For many of these children, twelve years is more than a lifetime.

Consistent, timely regulatory pathways do more than approve just one drug. They signal to researchers, to biotech companies, and to investors that rare pediatric diseases are viable areas for innovation. Efficient review processes accelerate not only current treatments, but the development of future cures.

Our suction machine now sits rarely used in a closet. It is still part of our story — but it no longer defines our days. Science changed that. A clinical trial helped make that possible. That's what happens when science is allowed to move forward.

But there are other families still living to the sound of that suction machine. Families that were not as fortunate to get their diagnosis at the perfect time to be included in the clinical trial. Families where travel is not an option.

They are waiting — not for miracles — but for momentum.

Congress has already provided the FDA with tools designed to address the urgency of life-threatening rare diseases. I respectfully urge this Committee to ensure those tools are used consistently, predictably, and without unnecessary delay.

The urgency of this work is not theoretical. Children living with rare disease do not experience time in review cycles.

They experience it in breaths.

Cure GRN, Cure MAPT FTD, and Cure VCP Disease – February 21st, 2026**Written Testimony**

Dear Chairman Scott and Members of the Senate Special Committee on Aging:

Thank you for the opportunity to submit this statement for the hearing “From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation.”

Alzheimer’s disease and related disorders (ADRD) include several rare, autosomal dominant genetic forms of dementia. Developing treatments for these conditions requires regulatory flexibility, clearer guidance, and a willingness by the FDA to consider innovative therapies — even when they carry higher risk — given the small patient populations and urgent unmet medical need.

Cure GRN, Cure MAPT FTD, and Cure VCP Disease are three nonprofit patient advocacy organizations, each representing families affected by a rare, fatal, genetically caused neurodegenerative disease. Though our diseases are unique, they share a common thread: all three cause frontotemporal dementia, ALS, and/or Parkinsonism; all three are inherited through a single dominant gene mutation; and not one has an FDA approved disease-modifying treatment.

Promising therapies are in development for each of our diseases. Our families are not waiting for science — they are waiting for a regulatory environment that can move at the speed science demands. We submit three concrete recommendations that would accelerate patient access not only for our communities, but for rare disease patients across the country.

1. Expand indication labeling to reflect related patient populations.

Narrowly drawn indications cut off access for patients with closely related diseases who have no other options. We urge the FDA to adopt more flexible, scientifically grounded labeling for rare neurological diseases that creates a viable pathway for informed off-label use across overlapping conditions.

2. Reduce enrollment barriers — include presymptomatic carriers and recognize care partners.

Standard trial eligibility criteria were designed for common diseases and do not fit rare genetic ones. Because our diseases are caused by identifiable mutations, we can find individuals who will develop the disease before symptoms appear — yet they are routinely excluded from trials. Allowing presymptomatic carriers enables earlier intervention research and smaller, more feasible trial designs. Additionally, as frontotemporal dementia progresses, patients lose the ability to self-report reliably. Care partners are often the most accurate source of clinical data available and must be formally recognized as valid participants in trial outcome measurement.

3. Accept natural history data as a valid comparator to reduce trial size and reduce reliance on placebo groups.

For ultra-rare diseases, traditional placebo-controlled trials are both practically impossible and ethically untenable. Our patient registries contain longitudinal natural history data that can serve as a scientifically valid external control arm. Clear FDA guidance formally accepting natural history data as an approvable comparator would reduce required trial size, reduce reliance on placebo assignment, and make rare

disease drug development viable for sponsors who otherwise cannot justify the investment.

These three changes are not compromises on scientific rigor — they are common sense adaptations to the realities of rare disease. For our patients, delay is not an inconvenience. It is the difference between treatment and no treatment, between hope and none.

Respectfully submitted,
Cure GRN | Cure MAPT FTD | Cure VCP Disease

Larkin Garbee – February 21st, 2026

Written Testimony

Caregiver to a Veteran Living with Huntington's Disease Richmond, Virginia

Before the U.S. Senate Special Committee on Aging

Hearing: "From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation"
February 26, 2026

Chairman Scott, Ranking Member Casey, and Members of the Committee,

Thank you for the opportunity to submit testimony.

I am the spouse and primary caregiver of a United States veteran living with Huntington's Disease (HD), a fatal, inherited neurodegenerative disorder. I write to you not as a policy expert, but as someone watching neurological function disappear in real time.

Huntington's Disease is progressive and irreversible. Once brain cells die, they do not return. Every regulatory delay is not neutral — it represents permanent loss of motor control, cognitive clarity, speech, and independence.

There are currently no FDA-approved disease-modifying treatments for Huntington's Disease.

For decades, families have had nothing. Today, for the first time, multiple therapeutic approaches are in development:

- Gene therapy programs such as AMT-130
- Splicing modulators such as PTC518
- RNA-targeted therapies and antisense approaches
- SKY-0515, developed by U.S.-based Skyhawk Therapeutics

SKY-0515 is particularly difficult for American families to watch. Skyhawk Therapeutics is a U.S.-based company. Yet the SKY-0515 trial is currently running in Australia and New Zealand — not in the United States.

As American citizens living with this disease, we are watching promising therapies developed by American companies launch internationally while we cannot access them at home. Families are researching international enrollment options while our own medical centers remain on the sidelines.

This dynamic has broader consequences. When early-stage innovation and trials occur overseas, U.S. academic centers and research hospitals lose the opportunity to remain at the forefront of rare neurodegenerative research. Our clinicians lose experience. Our institutions fall behind. And American patients lose first access to therapies developed with American scientific talent.

As a caregiver navigating both the healthcare system and the Veterans Affairs system, I can tell you this: regulatory unpredictability affects real-life planning. We make decisions

about housing modifications, disability status, clinical trial enrollment, financial security, and caregiving intensity based on expected timelines. When regulatory standards shift or timelines stretch without clarity, families are left unable to plan for their own futures.

One of the most concerning aspects from a patient perspective is the lack of clear, predictable guidance around biomarker-based accelerated approval in neurodegenerative diseases. When a therapy demonstrates meaningful biological effect — such as lowering mutant huntingtin protein — families reasonably expect a transparent pathway forward. If regulatory expectations evolve during development, the impact is not academic. It determines who remains eligible long enough to benefit.

For a fatal genetic disease with no disease-modifying options, regulatory predictability matters as much as speed. Pharmaceutical companies invest where pathways are clear. Clinical trials launch where timelines are navigable. When innovation moves abroad, it signals that something in the U.S. system is discouraging early deployment here.

I respectfully ask this Committee to consider:

1. Greater transparency and timeliness in FDA communication regarding rare neurodegenerative drug development.
2. Clear guidance on biomarker use and external control datasets for accelerated approval in fatal genetic diseases.
3. Policies that prioritize U.S.-based early clinical research so American patients are not last in line for American-developed therapies.
4. Oversight ensuring that regulatory evolution does not unintentionally eliminate access for patients who do not have time to wait.

My husband is not a statistic. He is a veteran, a husband, a son, a friend, a brother and a man who deserves the chance — even a small chance — to slow the progression of this disease.

In Huntington's Disease, time is not theoretical. It is neurological tissue. It is the ability to walk. It is the ability to feed and bathe oneself. It is the ability to regulate behaviors and emotions. It is the ability to speak. It is the ability to regulate your body's temperature and to swallow your food without choking.

We are not asking for shortcuts. We are asking for clarity, consistency, and urgency commensurate with a fatal disease.

Thank you for your attention to this matter and for your commitment to patients living with rare and devastating conditions like Huntington's Disease that affects 41,000 Americans with an estimated 200,000 at genetic risk.

Respectfully,
Larkin Garbee

Karen Quandt – February 22nd, 2026

Written Testimony

The Senate Special Committee on Aging:

My son had Niemann-Pick type C (NPC) disease and died at the age of 20. NPC disease is a fatal, genetic, neurodegenerative disease that causes progressive deterioration of the nervous system resulting in dementia, seizures, disrupted sleep patterns, behavioral disturbances, fine and gross motor problems, and learning disabilities. The disease takes away your ability to walk, talk, swallow, eat and breathe.

The NPC1 gene was discovered in 1997 after decades of research. Then it took 27 more years of research before the FDA approved the first treatment for neurological symptoms of NPC disease in September of 2024. There needs to be multiple drugs approved by the FDA to address all the symptoms of NPC disease.

There are multiple challenges and regulatory delays surrounding FDA approved treatments for NPC disease.

1. Drug trials for common diseases like high blood pressure and asthma can include thousands of participants. The size of the trial makes it easier to achieve better randomization and see statistical significance of the drug's efficacy
2. Trials are much more difficult for rare diseases, particularly because symptoms and the rate of disease progression in the patients is often highly variable
3. The cyclodextrin trial for NPC disease (my son was in this trial) included just 56 children and young adults with a broad range of disease symptoms, which limited the interpretation of the results
4. Rare disease drugs need another pathway to approval by the FDA. They cannot follow the same pathway to approval as common diseases
5. We need to modernize clinical trial designs
6. Include natural history controls and natural history comparison groups
7. Rely on surrogate or intermediate endpoints for rare genetic diseases
8. Allow Accelerated approval for ultrarare genetic diseases with primary disease biomarkers based on clear biology for treatments aimed at the underlying cause
9. Issue a guidance in compliance with original FAST bill (FDASIA) to ease the excessive burden on qualification of primary disease cause biomarkers
10. Accelerated approval shortens the time it takes to drug approval, while allowing for longer timeframes to collect confirmational data
11. Randomized placebo controlled trials for a disease with irreversible brain or muscle disease is unethical. No placebo controlled trials for these diseases

Niemann-Pick type C disease relentlessly take away your ability to walk, talk, swallow, eat and breathe as time marches on. Regulatory delays mean your ability to swallow or walk slips away. Having longer timeframes to collect confirmational data after a drug is approved gives patients with neurodegenerative diseases access to medicines that can slow or stop the progression of their disease, and buy them time with their families. Rare disease drugs need another pathway to approval by the FDA. They cannot follow the same pathway to approval as common diseases.

Karen Quandt

Neil Levy – February 22nd, 2026

Written Testimony

I have a form of Spinal Cerebellar Ataxia, specifically SCA5. I have a de-novo mutation of the gene which means that neither of my parents have the disease, but I have passed it to at least two of my children. My two girls now in early adulthood (22 and 24) are experiencing gait and balance issues. My youngest son (21) has not presented at this time, and we have not tested for the gene because there is no cure or trials for this rare disease.

I currently use a walker because this disease causes issues with my balance and gait. I am beginning to experience some slight difficulties with speech as well. I am 54 and am much more concerned with finding a cure that can halt or slow down the progression for my children. My oldest is getting married and I'm concerned with her navigating life as young mom and being able to handle a child.

I am working with a researcher in the disease and am learning how archaic the process is. I have learned a bit about AlphaFold and some of the tremendous benefits AI can have on research and drug development. Especially in reducing the time and more importantly the cost in drug development. However, I am concerned that bottlenecks in the FDA process will negate these benefits. I am very concerned because my disease and the disease that affects my children is progressive and every delay means that they will face some of the things that I am experiencing as an adult. I am not as worried for me as I am for my children and urge the committee to do whatever is necessary to move this forward.

Jonathan – February 22nd, 2026

Written Testimony

Honorable Senator Scott and Senator Gillibrand,

I submit this testimony as an individual living with Duchenne Muscular Dystrophy, a rare muscle-wasting disease, and as a representative voice for countless Americans affected by rare illnesses and chronic conditions. Our community faces unique challenges in accessing life-changing therapies, and we urge policymakers to recognize and address these barriers.

For nearly two decades, I have benefited from Ataluren (Translarna), a drug specifically targeting Duchenne nonsense mutations. I am now in my early thirties. Since participating in the phase 2 trial in 2006, I have continued treatment through subsequent phase 3 safety trials, which ended in December 2025. Without Ataluren being approved, my only avenue to continue to receive the drug is through compassionate use. This medication has enabled me to maintain independence and quality of life well into adulthood—outperforming typical expectations for my condition. I lost ambulation in my early twenties, began nighttime ventilation only at 30, and regained baseline respiratory function within a month after a prolonged ICU stay. I can independently type on the computer and feed myself. I know dozens of families whose sons have experienced similar stability and resilience. Importantly, Ataluren has demonstrated a strong safety profile, with no deaths reported in two decades of trials.

Despite these proven, sustained benefits, the regulatory process for rare disease treatments remains a significant obstacle. The cohorts for clinical studies are inherently small, making it difficult to achieve traditional statistical thresholds for efficacy. As a result, meaningful improvements may be overlooked, and promising trials may be prematurely terminated. Each year, patients like myself wait as our bodies deteriorate, often left behind when crucial Medicaid funding is cut or when private insurers deny coverage for “non-generic” or “not-needed” treatments. Many families cannot afford essential health needs due to prohibitive costs.

Adding to these challenges, the FDA held the Ataluren file for approval for over 18 months and refused to include the STRIDE data in its review. Ultimately, the FDA indicated it would not review the application based on the totality of the data provided, forcing the drug company to withdraw it voluntarily. This decision has left patients and families in limbo, unable to access a therapy that has demonstrated safety and life-changing efficacy.

We are born into a world with the potential to offer us greater opportunities, yet we are too often marginalized. If the FDA is truly committed to supporting Americans with rare diseases, it must adapt its policies to recognize the unique realities of our population. Specifically, the agency should reconsider how it evaluates drug efficacy for rare diseases, acknowledging that small cohort studies can still yield significant, life-changing results.

Without FDA approval or continued compassionate use, patients will face rapid decline, loss of essential abilities, and preventable suffering and deaths. I urge the FDA and lawmakers to act swiftly to secure ongoing access to Ataluren and similar therapies for

all who need them. Hope for a better life should not be a fleeting platitude—it must be a tangible promise, backed by responsive policy and regulatory action.

Thank you for your attention and commitment to improving the lives of Americans with rare diseases.

Sincerely,
Jonathan

Gretchen Egner – February 23rd, 2026

Written Testimony

Dear Committee members,

My 26 year-old son Nick has Duchenne muscular dystrophy. When he was diagnosed at age 2, life expectancy was mid-to-late teens, but advancements in the standard of care allowed Nick to attend and graduate from college and survive well into his twenties.

Duchenne is all-encompassing, continuing to rob Nick of his independence and agency. He lost his ability to walk at age 12. He uses a bipap machine to help him breathe at night. He wakes multiple times nightly and calls me to reposition him. He lost his ability to raise his elbows and arms last year so is no longer able to feed himself. Recently, his hands have become weaker, making it difficult for him to use his wheelchair joystick for too long and interfering with using his computer mouse.

Although Nick earned a Bachelor's Degree in computer science, he is unable to obtain consistent employment because he is easily fatigued and needs to take frequent breaks to reposition in his chair. Nick's ongoing, compounding losses in his physical abilities has led to much anxiety and depression—living at home with his mother, completely reliant on her for all daily cares—as his peers are thriving in careers, getting engaged and married, etc.

Since Nick was diagnosed in 2001, many therapies have entered the pipeline that potentially could benefit him. The most significant is Ataluren (originally named PTC-124 and later named Translarna when conditionally approved in Europe), developed by PTC Therapeutics. Ataluren was the first drug for Duchenne that saw clinical trials with Duchenne patients. Nick was in that trial in 2006. Participation required many 7 hour drives to Cincinnati, countless blood draws and clinical testing, as well as two muscle biopsies.

Because of Duchenne's complexities and progressive nature—it affects ALL muscle groups and systems in the body—identifying data points to show the drug's efficacy has proved difficult. After FDA's initial denial, PTC continued to hone its trial design and allowed Nick to enter into an extension study, requiring additional invasive muscle biopsies and blood draws. FDA denied again. PTC continued to offer the drug to patients in an extension study for two decades as they worked to develop the necessary data for the FDA. However, after 20 years, the FDA is still not persuaded, so PTC has ended its pursuit for approval.

Ataluren is not a miracle drug. It doesn't "cure" Duchenne. But I believe it has played a role in Nick's pulmonary function. Yes, he does use a bipap and his cough strength has weakened; however, his rate of decline seems significantly delayed compared to others his age with Duchenne. Stopping Ataluren is devastating for him.

Obviously, PTC's struggle with approval for Ataluren is an extreme case in terms of time delay. But all time is precious with a disease like Duchenne that daily robs patients of their mobility, independence and self-direction. Clearing hurdles to drug approval is essential for ensuring maximum quality of life for our community.

Thank you for your help.

Gretchen Egner

Linda Carter – February 23rd, 2026

Written Testimony

Hello,

I am writing as a caregiver for my husband who has been recently diagnosed with Spinocerebellar Ataxia 6. It is a rare genetic progressive disease which has changed his life over the past 7 years, having first noticed symptoms at the age of 63. It has been difficult to see him change and experience worse symptoms every day related to his balance, walking gait and extremity pain. He has gone from a very active, athletic person to a person who must use a rollator to walk. We have four children who very well may be impacted by this terrible disease, one who has just discovered she has SCA6.

I hope you will consider how the regulatory delays of drugs that may help with the symptoms my husband experiences and the impact of the lack of funding for rare diseases affect people each day. Every day my husband does not have access to a helpful and effective drug is a day this disease progressively gets worse. I imagine he may be confined to a wheelchair in the next year. I am worried for my children, grandchildren and so many others who may be affected by rare diseases which have no cure but can be hopefully helped with drug treatments that are being researched and approved. I hope you consider the impact of regulatory drug delays and lack of funding for research and do something to change the trajectory of the decisions being made for the betterment of those affected by rare diseases.

Best regards,
Linda Carter

James Hoyne – February 23rd, 2026

Written Testimony

My name is James Hoyne, I am representing the Esophageal Atresia/Tracheoesophageal Fistula (EA/TEF) & VACTERL Association rare disease community.

I was born with two rare & complex congenital conditions that have affected multiple organ systems since the day I entered this world.

I was born with Esophageal Atresia & Tracheoesophageal Fistula, EA/TEF, which means my esophagus was not properly connected to my stomach & there was an abnormal connection between my trachea & esophagus. Simply put, I could not swallow safely & without immediate surgery, I would not have survived. My life began in an operating room.

I was also diagnosed with VACTERL Association. VACTERL is a cluster of congenital anomalies that can affect multiple parts of the body. The acronym stands for:

- V: Vertebral anomalies
 - A: Anal atresia
 - C: Cardiac defects
- TE: Tracheoesophageal fistula with Esophageal Atresia
 - R: Renal (kidney) abnormalities
 - L: Limb abnormalities

In my case, I was specifically diagnosed with V, T & E, vertebral anomalies, tracheoesophageal fistula & esophageal atresia. Those three letters have defined much of my medical journey.

As a result of my vertebral anomalies, I required major spinal intervention. Today, I live with four (4) rods & thirty-five (35) screws in my spine. That hardware is not temporary. It stabilizes my spine. It is part of my everyday reality.

As a result of my EA/TEF, I have endured lifelong gastrointestinal & airway complications. Today, I also utilize a feeding tube to maintain adequate nutrition. Eating is not automatic for me. It requires planning, monitoring & medical support.

Since that first lifesaving surgery as a newborn, I have undergone fifty-eight (58) surgeries.

Fifty-eight (58) times under anesthesia. Fifty-eight (58) recoveries. Fifty-eight (58) moments of uncertainty for me & for my family. Rare disease has not been a phase of my life, it has been the constant.

EA/TEF is not something that can simply be "fixed." Surgery reconnects the esophagus, but it does not restore normal anatomy or function. I have faced recurrent strictures requiring repeated dilations, severe reflux, swallowing difficulties, airway vulnerability & chronic gastrointestinal complications.

Living with spinal hardware means ongoing monitoring & managing pain & mobility. Living with a feeding tube means navigating medical equipment, supplies, as well as the social & emotional weight that can come with visible medical dependence.

Hospitalizations interrupted childhood milestones. Recovery replaced normal routines.
Chronic pain & medical trauma have been recurring realities, not isolated events.

Medical advances have dramatically improved survival rates for babies born with
EA/TEF & VACTERL. That progress matters. I am alive because of it.

But survival is not the same as lifelong, coordinated care.

There is no cure for EA/TEF or VACTERL Association. Treatment is surgical &
supportive. Early interventions save lives, but they do not eliminate long-term
complications. Many adults like me live with dysmotility, aspiration risks, chronic GERD,
feeding challenges, spinal complications & the need for long-term surveillance, including
increased cancer risk due to chronic esophageal damage.

One of the most difficult & overlooked challenges we face is the transition from pediatric
to adult medical care.

As children, many of us are treated by specialized pediatric teams who understand
congenital anatomy and complex surgical histories. But when we age out of that
system, we enter an adult healthcare world that often has little familiarity with conditions
like EA/TEF & VACTERL.

I have lived that transition. I have had to explain my anatomy to new providers. I have
had to condense decades of surgical history into brief appointments. There are no
widely adopted national standards guiding long-term adult surveillance for patients like
me. Continuity of care becomes fragile at the exact moment it should be strengthened.

Our healthcare system has improved survival, but it has not fully prepared for survivors.

Our patient population is small, research is limited. Long-term adult outcome data is
sparse. Rare congenital conditions are often viewed as pediatric issues, leaving adult
complications underfunded & understudied.

But congenital disease does not disappear at 18.

In six months, strictures can worsen. In a year, reflux can cause progressive damage.
Scar tissue builds. Hardware must be monitored. Feeding access must be maintained.
Complications continue whether research funding moves quickly or not.

When research is delayed, guidance is delayed.
When guidance is delayed, diagnoses are delayed.
When diagnoses are delayed, outcomes worsen.

Time is tissue.
Time is mobility.
Time is quality of life.

I live with four (4) rods & thirty-five (35) screws in my spine.
I live with a feeding tube.
I have endured fifty-eight (58) surgeries.

I have learned resilience, but resilience should not be a requirement for survival.

What I am asking for is not extraordinary. It is equitable.

We need greater investment in rare congenital disease research across the lifespan.

We need long-term adult outcome studies. We need structured transition-of-care models from pediatric to adult medicine. We need adult providers educated about congenital rare diseases.

I am one person. But there are children being born today with VACTERL, with EA/TEF, who will grow into adults navigating the same systems I have.

What we prioritize now will determine whether their futures are defined by coordinated care & research, or by fragmentation & preventable complications.

For me, time has meant 58 surgeries.

For the next generation, time could mean fewer surgeries, stronger systems & better outcomes, if we act with urgency.

Thank you for the opportunity to share my story

Shirley Cabral – February 23rd, 2026

Written Testimony

First of all, I would like to thank Drs. Khurana and Schmahmann for their research, dedication, and support of the Ataxia community. We are very grateful.

My sister was diagnosed with SCA8, an inherited form of ataxia from our mother, who is deceased). Our family had no idea! This ataxia was diagnosed through recommended genetic testing 10+years ago in Dr. Vikram Khurana's clinic. Currently, my sister is stable. As my sister's caregiver, it is painful to watch this once vibrant woman, decline. It's even more painful to know there are drugs that could help her, make life easier, and maybe extend her life. All we need is your approval!

Consider this, Senators: please don't delay approval of these drugs any longer. And please stop, think for a moment, and walk a mile in my caregiver shoes. Don't we all want the best available treatments for all of our family members?!

Mariah Adin, Ph.D. – February 23, 2026

Written Testimony

Dear Esteemed Members of the U. S. Senate Special Committee on Aging:

I write to you today as an American, as a mother, as a wife, as a productive and hard-working citizen who suffers from the extremely rare neurodegenerative disease Spinocerebellar Ataxia 17. I am extremely fortunate and grateful to participate in a Clinical Drug trial for Troriluzole via the Expanded Access Program administered by a partnership between Biohaven and Columbia University.

I am only 47 years old, and I have two children - ages 12 and 13. Watching me decline over the last few years, going from being hiking buddies to having to help me up the stairs, has had a dramatic impact on their lives. Yet, I still consider myself incredibly fortunate as my disease progression started later in life. As you will hear from many others, Spinocerebellar Ataxias can rob people of their mobility at any age, and many will suffer from this disease for the entirety of their life.

Troriluzole has been a miracle for me. Prior to taking this drug, I was losing my ability to walk. Within a month of taking Troriluzole, I was able to stop using my crutches and wheelchair. After three months, I was able to walk unassisted without even a cane. I am currently at five months of having my mobility back. Every single day that I am able to enjoy the use of my body again is a true miracle.

It is imperative that FDA processes have regulatory flexibility for rare and orphan diseases. The recent FDA failure to approve Troriluzole due to a lack of a gold-standard placebo study completely ignores the real-world results that folks like myself have experienced. Unfortunately, when it comes to incredibly rare diseases like mine, there simply may not be the necessary depth of participants available. It is my understanding that I am the only patient with Spinocerebellar Ataxia 17 enrolled in this study. This is hardly surprising when the literature has identified less than 100 families world-wide with this specific variation of ultra-rare neurodegenerative disease.

Esteemed Members of this Committee, I ask you today to please hold two things in balance: the need for upholding and ensuring rigorous, scientific standards; but also the pragmatism of regulatory flexibility for rare and orphan diseases in which those standards become an impossible barrier instead of a protective shield.

Thank you for your consideration of this important topic and of my story.

Sincerely,

Mariah Adin, Ph.D.

Zhanzhi Hu – February 23rd, 2026

Written Testimony

I have two sons affected by a rare genetic disease called the Hunter Syndrome (Mucopolysaccharidosis Type II, MPS II). It's a systemic disease that affects every tissue and organ, which causes physical disabilities, developmental delays, and eventually leads to organ failures and death in early adulthood. With only about 400 diagnosed patients in the entire country, virtually no one knows about the disease, including many of their doctors. The standard therapy can only partially slow down the disease progression in physical symptoms, and have no effect on developmental delays. There was a clinical trial that was actively recruiting patients shortly after their diagnosis in 2011. However, the stringent enrollment criteria delayed their eligibility for a few years due to impractical trial design, and the endpoints were destined to fail - cognitive improvements are impossible after the onset of cognitive damages. Eventually, they were enrolled but all too late. They are currently both intellectually disabled and are in palliative care. As much as we love them, they present a heavy burden to our family in terms of daily living, financially, physically and mentally.

In the past 15 years since my sons' diagnosis, science has made tremendous progress. New clinical trials include gene therapy and enzymes that can enter the brain and address brain development symptoms. Our community has engaged in multiple ways with the FDA to communicate what's important to the patient families, and the scientific community has provided undisputable evidence that the surrogate biomarker called Heparan Sulfate is clearly indicative of treatment effectiveness. Unfortunately, the FDA remained stuck in time and refused to grow with science. Their continued skepticism against surrogate biomarkers shows their arrogance and close-mindedness. The members of the current leadership team at the FDA are not fulfilling their duties to the American tax payers, and walked back their stance on accelerated approval based on surrogate biomarkers, and chose to ignore the patient community's voice and scientific evidence.

We need the FDA to be held accountable for its actions. We need the FDA to listen to the patient community and understand that clinical science is about helping patients at the end of the day, and the endpoints should be aligned with what the patients and families value with most. We need the FDA to be impartial and be science driven, rather than letting the biased view (or even political agenda) of individuals in leadership position to dominate its opinions and review results. It's too late for my sons, but new patients suffering from rare genetic diseases are born every single moment. We need actions from the FDA to give them a better start of life when the evidence of clinical trials demonstrates effectiveness.

Julie Bell – February 23rd, 2026

Written Testimony

Do you like to wake up in the morning feeling pain free ,full of energy, and ready to start your day? I wish that was my reality but it is not. I have lived with a rare disease for 31 years since the age of 28. I have Chronic Inflammatory Demyelinating Polyneuropathy.(CIPD)

I am 1 in 100,000.

Each morning I wake up sore, stiff, and in pain. I have been on IVIG - intra-venious imuglobulin gammaglobulin for 25 years. As a patient of a rare disease community the FDA is important. We need you to allow research for these rare conditions to continue. Without research we will not develop new and improved medicine to improve our quality of life. Medicine is expensive. More research allows patients and doctors options. Without medicine I would lose my quality of life. I can not go longer than 2 weeks without my medicine. I rapidly decline. Walking, daily life skills, and being a productive member of society decrease rapidly. Regulatory delays means that I will end up in a wheel chair sooner or even totally dependent on others for my care. How would you like to be living with that prognosis?

Season Harris – February 23rd, 2026

Written Testimony

Hello, I'm a young woman with a rare incurable disease called SCA3. My grandma, mom, and both of her brothers have died from this condition, after having no medications for this disease. This disease is what I like to call a "slower ALS" because it will eventually take away my ability to walk, talk, and swallow. If I follow in my mom's footsteps, I've got about 10 more years to live. My mom passed away from pneumonia. I was 13 years old.

Recently, the first drug for my disease came out, called troriluzole, and it has a 50-70% chance of slowing my progression of this disease. It is not FDA approved, which means I had to access it through a university's early access program. I'm very hopeful that this medication will help me stick around until a better treatment comes along.

Which is where you come in. I'm a daughter, aunt, sister, wife, and friend. I work with children, and even though I choose to not have my own due to the severity of this disease, I love them very much. I don't want to die in 10 years. I want to stick around to see my niece and nephew graduate college, and start their own lives. I don't want to become a burden to my family and friends, and lose my independence. I want to keep working, keep breathing, keep smiling. Which is why I need a treatment that is FDA approved. Please.

Sincerely,

SF

Julianna Shinnick – February 23rd, 2026

Written Testimony

Dear Senate Committee on Aging,

Thank you for convening the Hearing, "From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation." My name is Julianna and I am about to undergo genetic testing for Huntington's disease. When I learn whether I inherited the gene, I will learn whether—like my dad, grandfather, and uncles—I will lose my judgment, then my memory, and eventually my life to the disease. Huntington's Disease has a gene therapy, AMT-130 from UniQure, that slowed the disease by an average of 75% when compared to a natural history control trial. The trial of AMT-130 met the same scientific standards for accelerated approval that numerous gene therapies before it had. Importantly, it even met the standards that the FDA itself set out as described in their alignment with UniQure over a period of more than a year. Without an approved disease-modifying treatment, I will lose my ability to parent, to keep my job as a palliative care nurse. The Huntington's Disease community is not asking for special treatment, only asking the FDA to consider this treatment against an external control group, as it has done with numerous rare disease therapies before it and as it has advised in the past. The FDA may U-Turn and U-turn back, but at that point, it may be too late for me. My brain may have degenerated too far for AMT-130 to be helpful to me any longer. It may also be too late for other communities, as numerous rare disease clinical trials have signaled that they are moving to other countries for trials because the US regulatory space is too unpredictable. (Notably, several new Huntington's trials are starting out in Australia and New Zealand.)

Best,

Julianna Shinnick

Brittany McGraw – February 23rd, 2026

Written Testimony

My mom had HD, and her mom before that, and her grandfather before that, and her great-grandmother before that. My mom was one of 6 children and 5 of them were gene-positive. I, too, am gene-positive. When I was just 29, my mom had to move in with my husband and I (I am an only child), because she was no longer able to live independent. My father, a disabled Vietnam Veteran who had planned to be her caregiver, had died when I was 23 of complications related to Agent Orange. My mom medically retired in her mid-50s. HD symptoms hit many patients during their prime working years-removing them from the workforce far too early. I have cared for my mom for years, all while wondering what my own symptoms will be and when they will present. I live in daily questioning of whether my forgetfulness is just that - common forgetfulness - or the early signs of the disease. My husband had to help care for my mom, watching her deteriorate, while knowing that, without any changes in treatment options, the same is in store for me. My mom was spirited, stubborn, and such a fighter - she outlived all of her family members who had had HD, living to the remarkable age of 70, when all others in our family had died between their early 50s and 63. My mom was diagnosed with metastatic stomach cancer in May 2025 and died 2 months and 2 days later. My mom was advised against pursuing any cancer treatments to elongate her time with us due to her HD. HD literally prevented my mom from pursuing treatments which may have given us more than the 2 months we had with her. I am so grateful I had FMLA to be her caregiver during those 2 months. Watching your only living parent at the age of 34 die not of one terminal illness, but two simultaneously - trying to manage her cancer symptoms on top of the weakness, movement and balance challenges, and swallowing difficulty imposed upon her from the HD - is something I wouldn't wish upon anyone. And still I advocate, alongside so many others. I am not saying this to play the victim - rather I want to relay the strength and perseverance and hope of the HD community.

My mom wanted so badly to participate in clinical trials, even knowing they may not benefit herself - but to contribute to future generations. My mom never did qualify for any clinical trials. She was too sick. I haven't qualified for clinical trials, either - I am "too healthy." This is such an ironic label to carry, knowing I also carry the diagnosis of presymptomatic HD, an untreatable (as of now), neurodegenerative, terminal illness. I'll never forget the day I received my test results - acknowledging not just the impact of finding out my diagnosis in my clinic visit - but reading my note afterwards - "terminal" the note said - and I was just 28, and still "too healthy" to do anything about this diagnosis. I long, LONG to participate in a trial - even if not for me then to give to future generations of HD patients. I long for choice. I do not ask for premature approval of a drug - but for the FDA to stand by their word. When accelerated approval pathway designations are granted, they should be upheld and BLA submissions allowed. Every delay of a stage is a death sentence. More people will progress out of the window of trial or treatment eligibility; more people will progress into symptoms which are irreversible. Treatments currently in the pipeline do not demonstrate reversal of the disease, but a slowing of progression - time is absolutely of the essence. Patients deserve the opportunity to determine the level of risk they are willing to take. The HD community has contributed so much to working towards a cure. Enroll-HD, a natural history research study which started only in June 2012 ([Enroll – Clinical Research Platform](#)) has collected data from over 30,000 participants since its initiation, which allows for an incredibly robust natural history data set. In treatments for rare diseases

such as HD which can take years to progress and no options currently exist, I advocate strongly for the opportunity of natural history data to be permitted to support clinical trials.

In conclusion, I plead for the FDA to uphold it's word. The FDA needs to be transparent. The FDA needs to practice integrity and stand by what it says it will do. The FDA needs to not just say that it will streamline and ease processes for biologics approvals, but demonstrate it. For clinical trials that demonstrate efficacy with limited to no negative side effects - this should be straightforward. The FDA needs to put choice in the hands of patients - not themselves. Because if I can't make the choice of whether or not I want to incur the risks of a treatment or trial, my only choice - which isn't a choice at all - is to die from this disease, and that is the same for future generations.

Thank you for your consideration and advocacy,
Brittany McGraw

Dr. Annica Lin – February 24th, 2026

Written Testimony

Dear Senate Special Committee on Aging,

One year ago, I was diagnosed with Spinocerebellar Ataxia type 3 (SCA3), a rare, progressive, and currently incurable neurodegenerative disease. I am facing a future of steadily worsening balance, coordination, speech, and daily functioning. Without medical intervention, I am destined to end up in a wheelchair with complete reliance on caregivers.

I am a wife and a mother of two daughters, and I inherited SCA3 from my father. My father had no chance of treatment for his SCA3, as there was none available while he was alive. I witnessed how the disease stole his ability to walk, to feed himself, to speak intelligibly, and to swallow food without choking. His mind remained intact, but his body was failing. SCA3 eventually claimed his life. What echoes in my ears is one of the last understandable words that he spoke as he lay dying in the hospital. That word was "help." Distressingly, there was no help to be had.

As a doctor who witnessed how SCA3 first affected my father, I understood the implications when I unexpectedly stumbled one day. Over the following year, frequent muscle cramps became alarming occasions when I would take an extra step to catch myself from falling. I became wary of uneven ground and fearful of walking up or down stairs without railings. I was only 51. I made a bucket list of all the things I wanted to do in the next 20 years or so before I lost the ability to walk, to hold a pen, or to communicate well. The thought that my daughters had a 50% chance of inheriting this crippling disease from me kept me up at night.

However, I was given new hope 10 months ago when I started taking VYGLXIA (troriluzole), an investigational drug developed by Biohaven, through the FDA's Expanded Access (compassionate use) program. In clinical trials, Biohaven showed that troriluzole has the potential to slow disease progression by 50-70%. Astoundingly, within 3 months of starting the medication, my physical exam reflected improved balance and coordination. By 6 months, I was more confidently walking in a straight line and climbing up and down stairs without assistance. In the last 10 months, my symptoms have stabilized and I have many more good days than bad ones. I know troriluzole will not cure me, but it is my only lifeline to a better future — maybe even one without a wheelchair.

Disappointingly, in November 2025, the FDA issued a Complete Response Letter to Biohaven's New Drug Application for troriluzole. Fortunately, Biohaven remains committed to working with the FDA to find a path forward. I am fearful that I and many others will lose access to troriluzole once the Expanded Access program ends. This affects not only me, but the thousands of other spinocerebellar ataxia patients across the country who are on this medication. My biggest fear however is that my daughters will not have access to troriluzole if they should need it.

I respectfully ask that you contact the FDA and express your strong support for the expeditious review and approval of troriluzole for spinocerebellar ataxia. Your advocacy could make the critical difference in bringing the first disease-modifying therapy to those affected with spinocerebellar ataxia.

Thank you for your commitment to improving the lives of those living with rare and serious diseases. While there was no disease-modifying treatment for my father when he was dying from SCA3, you can help give me, and thousands of others who are fighting this dreaded disease, a chance to enjoy their best lives for as long as possible.

Sincerely,
Dr. Annica Lin

Sarina Smith – February 24th, 2026

Written Testimony

Dear Chairman Rick Scott,

I'm a PhD student studying genetics and rare disease at the University of Pennsylvania. I'm also from a rare disease family. When I was five years old, my mom was diagnosed with **Huntington's disease (HD)**. HD is a **rare, inherited brain disease** caused by a mutation in the huntingtin gene. Over time, it leads to the progressive loss of neurons in the brain, affecting **thinking, mood, and movement**.

The most visible symptoms of HD are often the motor symptoms — involuntary movements, balance problems, and coordination issues. But HD is much more than a movement disorder. It also causes dementia, and for many families, the most devastating symptoms are the cognitive and behavioral ones. These include memory loss, difficulty planning and decision-making, depression, anxiety, irritability, and profound personality changes.

HD typically begins between the ages of 30 and 40 and progresses over 15 to 20 years. There is no cure. My mom, pictured above, was sick for most of my life. She died last year due to complications from HD. By the time she passed, she could no longer walk, talk, or eat on her own. My aunt and grandmother also died from Huntington's disease.

HD doesn't just affect one person. It affects generations. Each child of an affected parent has a 50% chance of inheriting the mutation. That means many children grow up caring for a sick parent while knowing that this may also be their future — like my sister and me. My older sister has tested positive for the HD mutation, meaning she will develop the disease in the future. I've chosen not to undergo genetic testing at this time, which means I may or may not develop my mom's disease one day. One major reason I have decided to not undergo genetic testing is that **there are currently no approved disease-modifying therapies for Huntington's disease**. Right now, treatments only manage symptoms. They don't slow or stop the underlying neurodegeneration.

That's why recent progress in HD research has meant so much to this community. **For the first time, therapies are being developed that target the root genetic cause of the disease.** One example is a **one-time gene therapy developed by uniQure (AMT-130)**, designed to reduce the buildup of the toxic huntingtin protein. Early data suggest it may significantly slow disease progression, potentially by 75% — something that would have been unimaginable just a few years ago.

But this is where access, and timing, become critical.

Despite promising data, progress toward approval has stalled. The FDA has hesitated to allow uniQure to file a Biologics License Application (BLA) for accelerated approval of AMT-130 — not because the therapy failed, but because of uncertainty surrounding how the data are being evaluated. Specifically, the FDA has suddenly raised concerns about the use of external control data derived from large natural history studies rather than a traditional placebo group. Yet the FDA had previously expressed support for this approach, and uniQure has engaged in extensive, ongoing discussions with the agency throughout the development process. This not only jeopardizes the

viability of AMT-130 but also risks discouraging pharmaceutical companies from investing in American healthcare, especially when we desperately need innovation.

For rare, fatal neurodegenerative diseases like HD, placebo-controlled trials are often neither ethical nor practical. In these cases, natural history data — including from large, well-established efforts such as **Enroll-HD**, which has followed tens of thousands of individuals over time — have long been recognized as a scientifically valid comparator. **To ensure timely patient access to urgently needed treatments, the FDA must uphold a consistent and transparent framework for accelerating rare disease therapies, so that future innovations are not stalled by shifting regulatory expectations.**

We are not asking for shortcuts — we are asking for fairness, transparency, and consistency.

When regulatory expectations shift this late in development, the consequences are profound. **Clinical timelines are delayed, investment in rare disease therapies becomes riskier, and—most critically—patients lose time they simply do not have.** This sudden change in guidance from the FDA may force uniQure to repeat extensive clinical studies, potentially delaying patient access by many years—years that families affected by Huntington's disease cannot afford to lose.

In Huntington's disease, decline is currently irreversible. Neurons lost cannot be restored. While waiting for therapies to be approved, patients may suffer irreversible brain damage — or even become ineligible for therapies because the cells meant to be treated are lost before they gain access. **In rare disease, access delayed can mean access denied.** By the time approval comes, it may already be too late—for my sister, for many in the HD community, and possibly for me as well. Rare disease already takes enough from our families. When treatments finally exist, access should not be the next battle we have to fight. For many rare disease families like ours, barriers to access are not simply inconveniences. **Access is the difference between hope and loss — potentially the difference between life and death.**

As a researcher, I believe deeply in science. As someone at risk for this disease, I believe just as deeply in urgency. Ensuring access to rare disease therapies means honoring both. **Congress has the power to ensure that when science delivers, access is not what fails families like mine.**

Thank you for holding this meeting and for your commitment to rare disease therapeutic development.

Alpa Khushalani – February 24th, 2026**Written Testimony****Respectable Committee Members,**

My name is Alpa Khushalani. I am the parent of an 18-year-old son, Krishna Khushalani living with Duchenne Muscular Dystrophy (DMD) in Fayetteville, Georgia. Duchenne is a rare, progressive, and fatal neuromuscular disease. I am submitting this statement to share what regulatory decisions and treatment delays mean to families like mine who live every day with the consequences.

Living With Duchenne

Duchenne causes ongoing and irreversible muscle loss. It is a genetic condition often diagnosed in early childhood due to gross motor delays. Patients gradually lose the ability to walk, then lose strength in their arms and hands, followed by declining heart and lung function. Life expectancy is significantly shortened, and quality of life steadily declines despite best supportive care.

My son was diagnosed as a young child. Over the years, we have watched him lose abilities one by one; walking, standing, climbing, lifting. Today, at 18, he depends on assistance for most daily activities. Every year brings noticeable decline. Time is not neutral in Duchenne.

Treatment Experience and Access Barriers

There is no cure for Duchenne. The few available therapies are meant to slow progression, not stop or reverse it. My son participated for five years in a clinical trial. During the trial, he tolerated the drug well and remained more stable than expected for someone with his disease progression.

After the FDA approved the therapy using the Accelerated Approval Pathway, our insurance continued to deny coverage—not because the drug was unsafe, but because my son is now older than the age group studied in the trial despite already having received the therapy for years. This is a common experience in the Duchenne community: patients who survive longer and need treatment most are often the ones who are denied or lose access.

Trial Design and the Reality of Older Patients

As boys with Duchenne get older, they are frequently excluded from clinical trials like my son, who currently does not qualify for any ongoing trials. This is not because patients cannot benefit, but because it becomes riskier and harder to show large, statistically significant changes on traditional endpoints.

What gets lost in this process is what matters most to patients and families. For my son, maintaining the ability to use the toilet on his own, feed himself, adjust his arm position and use his phone makes a real difference in his independence and dignity. These changes may look “small” on a chart, but they are enormous in daily life.

When trials and regulatory decisions focus only on endpoints that favor younger patients, older individuals are left behind. Their benefits may be harder to measure, but they are no less real.

Regulatory Uncertainty and Its Impact

Recent regulatory actions including delayed reviews, complete response letters, and uncertainty around trial outcomes have created fear and instability for Duchenne families. Communications

from the FDA regarding trials not meeting primary endpoints raise serious concerns about continued access to therapies that patients are already relying on.

These are not abstract policy decisions. Every delay has consequences. Duchenne does not wait for new trials, new endpoints, or regulatory alignment.

What Time Means for My Son

My son graduates from high school soon and has been accepted at premier institutions to pursue his college education. In six months, my son could lose more function and struggle with basic self-care. In a year, further respiratory decline could permanently change his health and independence. These losses are irreversible making achieving his dreams impossible.

For families like ours, regulatory delay is not just delay—it is loss of function, loss of ability, and loss of time we cannot get back.

I urge this Committee to consider regulatory approaches that better reflect the realities of progressive rare diseases: flexibility in trial design, recognition of patients' lived experience and continuity of access for patients who age beyond trial populations. Waiting for perfect data should not come at the expense of the people living with the disease today.

For my son, time matters. Every decision made affects what he will still be able to do tomorrow.

Respectfully submitted,
Alpa Khushalani

Pamela P. Wyllly – February 24th, 2026

Written Testimony

I have a rare disease called ataxia. I am writing to urge Congress to uphold and strengthen its longstanding mandates directing federal regulators to provide flexibility in the review and approval of therapies for rare diseases. These mandates exist for a reason: patients like me with rare conditions often have few or no treatment options, and delays in access can carry irreversible consequences.

Rare disease communities face unique challenges that traditional regulatory frameworks were never designed to address. Small patient populations, limited trial enrollment, and slow disease progression can make it difficult to meet conventional endpoints, even when a therapy demonstrates strong evidence of safety and meaningful clinical benefit. Congress has repeatedly recognized this reality and has acted accordingly through legislation encouraging adaptive trial designs, accelerated pathways, and regulatory discretion where appropriate.

One such case is troriluzole, a promising therapy for patients like me with ataxia. Ataxia is a serious, progressive neurological disorder with no broadly effective FDA-approved disease modifying treatments.

Troriluzole has demonstrated a favorable safety profile and evidence of clinical benefit, and it represents a critical opportunity for patients who currently have no viable alternatives. I can attest to troriluzole's efficacy as I am currently taking the drug as part of a clinical trial at Johns Hopkins. For individuals living with ataxia, time lost and function lost is often permanent.

Congressional intent is clear: regulatory flexibility for rare diseases is not a loophole, but a lifeline. When the tools Congress has provided are not fully utilized, patients bear the cost. Ensuring that regulatory agencies faithfully apply these mandates is essential to honoring both the letter and the spirit of the law.

I respectfully ask that you support oversight, guidance, and policies that reinforce regulatory flexibility for rare disease therapies, and that you advocate for timely, science-based decision-making that reflects the realities faced by rare disease patients and their families.

Thank you for your attention to this critical issue and for your continued service to the American people. I would welcome the opportunity to discuss this matter further or to provide additional information.

Sincerely,
Pamela P. Wyllly

Frances Pimentel – February 24, 2026

Written Testimony

Dear Chairman Scott,

Thank you for the opportunity to submit this statement on behalf of our rare disease community ahead of the hearing on FDA regulatory processes, rare disease treatment delays, and opportunities to improve patient access to innovation.

Hope for PDCD represents children living with Pyruvate Dehydrogenase Complex Deficiency (PDCD), a pediatric-onset mitochondrial disorder affecting fewer than 1,000 individuals in the United States. With an estimated incidence of 1 in 40,000 live births—approximately 90 newborns annually—PDCD is life-threatening and frequently fatal in early childhood.¹ There are currently no FDA-approved treatments. In August 2025, the FDA issued a Complete Response Letter (CRL) for the first therapy developed specifically for PDCD, sodium dichloroacetate (DCA), despite encouraging survival data and caregiver-reported improvements in quality of life.

About PDCD

PDCD primarily presents with neurological manifestations and lactic acidemia. From a study of 59 consented symptomatic subjects (27 M, 32 F), who were confirmed to have PDC deficiency with defined mutations in one of the genes of PDC (PDHA1, n = 53; PDHB, n = 4; DLAT, n = 2), 39% of these subjects (23/59) died. Of these, 91% (21/23) died before age 4 years, 61% (14/23) before 1 year, and 43% (10/23) before 3 months. 56% of males died compared with 25% of females. Causes of death included severe lactic acidosis, respiratory failure, and infection. In subjects surviving past 6 months, a broad range of intellectual outcomes was observed. Of subjects for whom specific neurological data were available, the majority had hypotonia (89%), and hypertonia or mixed hyper-/hypotonia (49%) were common. Seizures (57%), microcephaly (49%), and structural brain abnormalities including ventriculomegaly (67%) and agenesis, dysgenesis, or hypoplasia of the corpus callosum (55%) were common. Outcomes of this population with genetically confirmed PDC deficiency are heterogeneous and not distinctive.²

Status of Therapy Development

No FDA-approved therapies exist for PDCD. Current management relies primarily on a strict ketogenic diet, which carries its own risks and limitations, including osteopenia, kidney stones, and growth

restriction. Other than DCA, there are two additional experimental small molecule therapies. Protein-specific target-based small molecule therapies would be beneficial for approximately 30% of

PDHA1 variants and are in early preclinical development.³ Dojolvi (triheptanoin) is already FDA-approved for long-chain fatty acid oxidation disorders, and trials for use in PDCD are ongoing, but there are limited preliminary data to support its efficacy.

Therapy development for PDCD is extremely challenging due to:

1. An extremely small patient population (less than 1,000 patients in the US), making it difficult to identify and enroll enough patients in clinical trials and achieve the statistical significance regulators expect.

2. Progressive nature of neurodegenerative pediatric disease. Time is a critical variable. Delays in research or approval are not neutral—disease progression may cause irreversible neurological or organ damage while studies are ongoing.
3. The burden of caregiving for someone with PDCD makes it hard to travel to specialty centers, loss of income and makes it difficult to participate in clinical trials
4. Limited funding, research, and lack of commercial incentives. Hope for PDCD relies heavily on academic researchers, small biotech firms, and philanthropy. Funding is fragmented and inconsistent.

Complete Response Letter for PDCD, August 2025

It's impossible to overstate the extent to which DCA would have benefited our community. Access to even one approved therapy would transform PDCD care and support newborn screening efforts. Early detection of PDCD is critical. Starting a ketogenic diet from day one can prevent metabolic crises. Combined with DCA, it offers the possibility of preventing avoidable brain injury. PDCD is the leading cause of lactic acidosis in newborns. Delay in access means preventable harm in the most vulnerable days of life.

DCA has resulted in metabolic stability and lowered lactic acid levels for patients. From our understanding, the CRL was issued due to a deemed lack of efficacy. While the novel primary observer-reported (ObsRO) outcome was not statistically significant during the double-blind trial period, benefit was seen over the longer term, including the open-label extension. Further, the trial met a key secondary endpoint (lowering lactic acid levels). The FDA also agreed to a second protocol with survival as the primary outcome and recommended comparing it to a natural history cohort. Patients treated with DCA showed greater survival compared to the natural history cohort. There were no issues with safety and manufacturing. For families with a loved one with PDCD, stability is a major factor in quality of life. Without reliable, approved access to DCA, children with PDCD face the constant risk of regression. Stability and developmental gains that families have fought for can unravel with a single illness.

Participation in Regulatory Engagement and Review Process

Hope for PDCD was founded in 2022 by PDCD parents, Jon and Frances Pimentel. Hope for PDCD, along with UMD (United Mitochondrial Disease Foundation), organized a Voice of the Patient Survey and

co-hosted a Patient Listening Session for the FDA to hear our stories in September 2023. The objective was to establish deeper relationships with the FDA reviewers to foster dialogue for future regulatory deliberations. At the time, we believed the sharing of patient and caregiver experiences and preferences would provide FDA staff with a better understanding of PDCD and demonstrate the community's urgent unmet medical need.

The clinical trial for DCA ran for 5 years and Saol had a number of meetings with the FDA throughout that time leading up to the CRL. Based on our understanding, the CRL was a complete surprise to Saol Therapeutics. The company was granted a Type A meeting in December 2025 and has been granted a Type C meeting in March 2026. Upon receiving the CRL, Hope for PDCD organized a community petition with over 17,000 signatures in just 3 weeks and submitted it to the FDA ahead of their Type A meeting with Saol. Despite asking, we have yet to be invited to meet with the FDA to discuss the CRL. Our requests for a meeting continue to be ignored.

Hope for PDCD believes that if the FDA had taken the time to understand the broad spectrum of PDCD and the sensitivity in benefits to quality of life beyond the trial's uncompromising daily ObsRO reported outcome, the CRL could have been prevented. The regulatory framework applied to DCA reflects standards built for common diseases with large patient populations. PDCD is ultra-rare. Trials are necessarily small. Traditional statistical thresholds are often unattainable.

How This Committee Can Help Us

In ultra-rare pediatric diseases, waiting for perfect data can mean missing the window in which treatment can alter a child's trajectory. The cost of delay is not abstract—it is irreversible neurological injury.

This challenge extends beyond PDCD and reflects a broader policy issue affecting multiple ultra-rare conditions. Congress has already established regulatory flexibility tools—including accelerated approval, surrogate endpoints, and adaptive pathways—to address precisely these circumstances. These tools were intended to ensure that rare children are not disadvantaged by their small numbers.

We respectfully request that Congress:

- Conduct oversight of FDA decision-making for ultra-rare pediatric therapies
- Encourage consistent application of existing regulatory flexibility pathways
- Promote meaningful patient engagement in regulatory deliberations
- Support pathways enabling timely access while maintaining safety standards

We deeply respect the FDA's mandate to ensure safety and efficacy. However, when no approved treatments exist and meaningful clinical benefit is already observed, flexibility is not a loophole—it is the mechanism Congress intended.

Our rare children do not have the luxury of time. For our daughter Violet, and for every child born with PDCD, delay risks becoming permanent damage.

Sincerely,

Frances Pimentel
Co-Founder, Hope for PDCD

Susan Haber – February 24, 2026

Written Testimony

I am writing to you as a grandmother of a spirited four-year-old boy who is navigating the realities of Mucopolysaccharidosis type II (MPS II), a rare and progressive condition that is life-limiting. My grandson is not just a patient; he is a vibrant individual filled with joy, determination, and an unwavering zest for life. Nevertheless, his diagnosis has cast a shadow over our family, revealing the painful truth of a disease that steals skills and abilities, often far too soon.

When we received the diagnosis of MPS II, we were told to embrace every moment and enjoy what he can do today, knowing that there would come a day when he might lose those abilities. It is a crushing reality to confront: the prospect of watching my grandson possibly lose his ability to walk or talk. Delayed access to effective treatment means lost abilities and time – a heartbreaking reality for families like ours.

My grandson is currently involved in a clinical trial that carries risks and uncertainties involved, but the alternative is unthinkable. Before treatment, MPS II limited nearly every aspect of his development. However, since receiving treatment, we have been blessed to see him achieve milestones that we hold dear: he now talks, runs, and forms meaningful friendships. For our family, these aren't simply developments; they are lifelines.

What quality of life looks like for my grandson with MPS II is not a pursuit of perfection but rather striding towards possibility. It means allowing his siblings to know him in his entirety before we eventually face the unthinkable. Delayed access to treatment means watching him lose abilities we fear he may not regain. It means families like ours watching time slip away, with siblings grappling with a grief that few adults ever truly understand.

I implore the FDA to acknowledge that when we discuss access to treatments, we are discussing time—an invaluable currency for families battling rare diseases. For us, time isn't just about years; it is about the quality of those moments—watching my grandson walk, talk, and grow.

Thank you for your attention to our story and the stories of countless other families like ours. We hope for your understanding and support as we advocate for expedited access to treatment for MPS II, allowing children the opportunity to thrive, live fully, and embrace the lives they deserve.

Kaylan Moitoso – February 24th, 2026

Written Testimony

Submitting on behalf of a family from Massachusetts

Patient/Family Testimony for Rare Disease Week 2026
Senate Aging Committee Rare Disease Hearing

I have a 21 year old son who lives with progressive heart failure. He barely survived three life threatening episodes in 2025. Yet, between ICU stays, he is a thriving honor roll student who just wants to live like other college kids. Duchenne Muscular Dystrophy has stolen his arm and leg muscles, and now his heart and breathing muscles are in peril. Duchenne progressively destroys skeletal, cardiac and respiratory muscles leaving teenagers' breathing abilities weakened to the point of needing ventilators, and hearts weakened to needing pacemakers, and ultimately, stopping.

While some newer genetic therapies are showing promise in a select few younger patients with Duchenne, none have specifically rescued or stopped progression in the heart. There is an extremely high unmet need for teenagers and young adults with DMD. A therapy that helps the dystrophic heart is urgently needed by the entire Duchenne & Becker Muscular Dystrophy community, not specific to ages or mutations.

Our hopes have been pinned on Deramiscoel (CAP-1002) from Capricor Therapeutics. We had hoped for an Accelerated Approval by FDA in August of 2025, based on very encouraging Phase 2 data. FDA was also reportedly impressed with the cardiac data from a Phase 2 trial, and understood the incredible breakthrough that this therapy represents to the entire Duchenne Community, and guided the company as such. However, with delays at FDA, apparently new staff did a complete U-turn on the review of the investigational therapy, cancelled an adcomm meeting and issued a CRL, despite their earlier advice given to the company. We were shocked and devastated at this delay.

While the company has time to resubmit their data to FDA, my son does not have time. He continues to lose cardiac and respiratory muscle function every day. Since the delay, this hard working college student has now been prescribed to use a daytime ventilator attached to his wheelchair. We've gone over a cliff I had hoped we would never see. Can someone still attend college on a daytime ventilator, or even leave their house? Can they still talk, speak, breathe and laugh?

We live in fear of the flu season. Even mild colds can push DMD patients to the point of no return. Deramiscoel (CAP-1002) represents the retaining of strength to stay alive. In December alone, my family lost 3 friends in their young 20's to DMD, dying suddenly due to cardiac failure - young lives that could have potentially been saved by Deramiscoel - we will never know.

Heart function in Duchenne is the matter of life and death, and therefore the review and potential approval of Deramiscoel is a matter of life and death. Delays and misdirection by FDA are costing young lives. Please help.

Sincerely, a hopeful, yet heartbroken, Mom from Massachusetts

Glenn & Eileen Hooper – February 24th, 2026

Written Testimony

Hello Senator Scott

My name is Glenn Hooper and I am a resident of Paramus, NJ.

I'd like to discuss the delay in approval by the FDA of Troriluzole for the Treatment of Spinocerebellar Ataxia. The reason why I am advocating for this is because I have been diagnosed with Spinocerebellar Ataxia 6, as has my mother and one of my sisters. My life has dramatically changed in the past 5 years since the symptoms of SCA6 appeared.

The U.S. Senate Special Committee on Aging will hold a hearing, "From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation." It will be February 26 at 9:30 AM ET. Those of us who have rare diseases are dedicated to advocating for the advancement and equitable development of and access to lifesaving treatments and cures. We are asking for the opportunity to have access to treatments that have been blocked by the FDA bureaucracy.

Spinocerebellar Ataxia (SCA) is a rare, genetic, life-threatening neurodegenerative disease with no available treatment. Troriluzole demonstrated a 50-70% slowing of SCA disease progression on the primary and secondary outcome measures at the 3-year endpoint in a real-world evidence (RWE) study. Troriluzole has a well-established safety profile and if approved, would be the first and only FDA-approved treatment for SCA.

I hope you will consider the extremely high unmet need in this rare neurodegenerative disease. Time is of the essence for patients with SCA, who are suffering relentless and irreversible functional decline including impairments in coordination and balance leading to falls, loss of ambulation, and difficulties with vision, speech, and swallowing.

Since the discovery of the first gene for SCA in 1993, patients and families affected by SCA have watched generation after generation suffer severe, progressive disability and premature death with no treatment options. The need for an intervention that can slow disease progression and help patients maintain their independence is urgent. The delay in disease decline shown in real-world evidence study is a watershed in the history of the SCAs. This is what patients have been waiting for. It is what the doctors who have been powerless, have been waiting for. Additionally, the importance of Troriluzole effect on reducing falls in this patient population cannot be overstated. I urge you to recognize this urgency because it could mean a world of difference for myself and patients like me.

I have been following the developments and the clinical trials of treatments for rare diseases and had hope until last fall when the FDA chose to delay approval for Troriluzole. Every day this disease steals more of my life and my independence. My mother is reduced to a very limited life in a nursing home for the past 16 years. This is my future. There are no treatments approved by the FDA and it continues to progress.

Glenn Hooper

Susan Lauria – February 24th, 2026

Written Testimony

Senator Scott - I implore you to request the FDA to be more fair when it comes to approving treatments for "non-curable " diseases and illnesses. Troriluzole is a new drug that has real world evidence of its positive effects on people like myself. I have SCA 6- inherited through my mother. I am fearful every day for my children and grandchildren that they may inherit this awful disease through my genes. It is my hope that further trials and clinical therapies may find a cure or at least slow the progression of this neurological nightmare. We need the FDA to work with us. Not against us. It is so painful to know that there are medicines waiting for approval but unaffected people are playing games with our fate. Days go by and it is frustrating and aggravating that such little regard is given for our lives.

I respectfully ask that you advocate for those of us who had no part in inheriting this but truly pray for drugs that can help us live our remaining lives as best we can.

Sincerely
Susan Lauria

Scott Bender – February 24th, 2026

Written Testimony

I run a multi-national company with 3,000 associates scattered over more than 25 locations. Mobility is a requirement for my job.

I developed symptoms in the early part of 2024 and was misdiagnosed twice - once with CIDP (I received IVIG infusions for 14 months) and then with ALS. A good friend thankfully suggested I go to Baylor College of Medicine where a young specialist in movement disorders suspected a genetic disorder and had me tested. In deference to the previous physicians, they had never knowingly encountered SCA 27B. I believe the testing only became available in 2023, obviously limiting recognition of the disease. I simply got lucky. BCM sent me to Columbia where I was accepted in the EAP for Troriluzole. I arrived on September 3, 2025 with a cane and returned 30 days later walking on my own. I have experienced absolutely no side effects and require no walk aids.

Since that time, I have not fallen, traveled to the Mid East twice and visited ten US facilities. Just as importantly, I have been able to reengage with my six wonderful grandkids. As you can imagine, returning to my life before Troriluzole is untenable. I urge you to approve this medication and provide life changing help to both the already diagnosed SCA patients and those understandably misdiagnosed.

Thank you.

Jeffrey Klassen – February 24th, 2026

Written Testimony

Dear Members of the Senate Committee on Aging,

Thank you for holding this hearing and for accepting statements from patients affected by FDA regulatory delays. My name is Jeff, and I am a software engineer living with Spinocerebellar Ataxia Type 3 (SCA3), a rare, progressive, and currently incurable neurodegenerative disease.

SCA3 gradually destroys a person's coordination, vision, and motor function. There is no FDA-approved treatment, and troriluzole is the only therapy that exists for this disease. It is not one option among many — it is the only option. I have been receiving it through Biohaven's Expanded Access Program (EAP) since January 2025.

Before starting troriluzole, I was experiencing progressive vision issues — a hallmark of SCA3 that typically worsens over time. Since beginning the drug, my vision issues have not progressed. For a disease defined by relentless decline, stabilization is not a small thing. It is everything.

Today, I am still able to work full-time as a software engineer and team lead. I can still rock climb and cycle — activities that are central to my identity and quality of life. I know that without intervention, SCA3 will eventually take these from me. Troriluzole is buying me time.

What concerns me deeply is the possibility that the EAP may be discontinued if the FDA does not reconsider its position. If I lose access to troriluzole, there is nothing else. No alternative treatment. No backup plan. I face the prospect of accelerated disease progression, the loss of my athletic abilities, and eventually, the loss of my ability to work and support myself.

I urge the committee to examine how the FDA's regulatory process can be improved to ensure that patients with rare, progressive diseases are not denied access to the only therapy available to them. For those of us living with SCA3, every month of delay is a month of irreversible decline with no recourse.

Thank you for your time and attention to this critical issue.

Sincerely,
Jeff Klassen

Michael Mantz – February 25th, 2026

Written Testimony

Dear Members of the Committee,

My name is Michael Mantz, and I am living with Spinocerebellar Ataxia (SCA 15), a rare progressive neurological condition that affects coordination, balance, speech, and independence over time.

I am currently receiving troriluzole through Biohaven's Expanded Access Program. As with many rare disease patients, participation in this program is one of the few opportunities to access a potential disease-modifying therapy while regulatory decisions are still pending.

Although troriluzole is not a cure, continued access may help preserve critical functional abilities that support independence, mobility, and quality of life. For individuals with progressive neurological conditions such as Ataxia, even modest stabilization can meaningfully delay disability and reduce long-term care needs. Programs such as EAPs are not theoretical pathways for patients like me. They are real-world bridges between research and survival. When access is disrupted due to regulatory delays rather than safety concerns, patients with rare diseases may lose time that cannot be recovered.

I respectfully ask the Committee to consider how regulatory processes can better balance necessary safety review with timely access for individuals living with serious and progressive rare conditions.

Thank you for your time and for your attention to this important issue.
Sincerely,

Michael Mantz

Melanie Lendnal, Esq. – February 25th, 2026

Written Testimony

On behalf of the ALS Association and the families we serve across the country, thank you for the opportunity to submit this statement in strong support of the MINI Act.

Amyotrophic lateral sclerosis (ALS) is a rapidly progressive, fatal neurodegenerative disease. There is no cure. Most people diagnosed with ALS live just two to five years from symptom onset. The disease robs individuals of their ability to walk, speak, eat, and eventually breathe all while their cognitive awareness often remains intact.

For people living with ALS, time is not an abstraction. It is everything. The MINI Act represents a meaningful and compassionate step toward reducing unnecessary administrative burdens and delays that prevent individuals with terminal illnesses from accessing critical supports and services. People living with ALS often face complex eligibility requirements, repeated documentation demands, and procedural hurdles at the very moment when their physical capacity is declining most rapidly. These bureaucratic barriers cost precious time they simply do not have.

Congress has previously recognized the urgent nature of ALS by eliminating the Medicare waiting period for individuals with ALS through the ALS Disability Insurance Access Act. The MINI Act builds on that bipartisan legacy by ensuring that individuals facing terminal diagnoses are not forced to navigate duplicative or prolonged processes to receive the benefits and assistance for which they qualify.

Every delay in access to care, home modifications, assistive technology, or income support has real and immediate consequences. Delays can mean the difference between remaining at home with family and entering institutional care. They can mean the difference between accessing life-prolonging interventions and going without.

The ALS Association strongly supports policies that:

- Streamline access to benefits for individuals with terminal illnesses;
- Reduce redundant medical certification requirements;
- Improve interagency coordination; and
- Recognize the urgent realities of rapidly progressive diseases like ALS.

The MINI Act reflects common-sense governance rooted in dignity, efficiency, and compassion. It acknowledges that when a physician has confirmed a terminal diagnosis, our systems should respond with urgency and humanity, not paperwork and delay.

We urge the Committee and the full Senate to advance the MINI Act swiftly and continue bipartisan efforts to improve quality of life for people living with ALS and other terminal conditions.

Thank you for your leadership and your continued commitment to older Americans and people living with serious and life-limiting illnesses.

Respectfully submitted,
Melanie Lendnal

Tricia Flanagan – February 25th, 2026

Written Testimony

Bioscientist and Founder and CEO, Azuza Laboratories Submitted to the United States Senate Committee on Aging February 25, 2026

Chairman Rick Scott, Ranking Member Kirsten Gillibrand, and distinguished Members of the Committee:

Thank you for the opportunity to submit written testimony and for investigating the critically important issue of the FDA's handling of emerging treatments for pediatric rare disease.

My name is Tricia Flanagan. I am a bioscientist specializing in immuno- oncology, and some of my work has been incorporated into National Institutes of Health protocols. I currently serve as Founder and CEO of Azuza Laboratories.

I am especially grateful that this Committee is bringing attention to concerns surrounding the Food and Drug Administration, and in particular its Center for Biologics Evaluation and Research (CBER), and the growing perception that regulatory roadblocks are disproportionately affecting children with rare diseases, leading many to believe there is an institutional bias in this division led by Dr. Vinay Prasad.

Throughout my career, I have focused on understanding how healthy cells behave and applying that knowledge to the development of therapeutic enzymes and advanced biologics. I have worked within rigorous protocol standards, emphasized reproducibility of results, and supported structured layers of human testing to ensure safety and efficacy. I deeply respect the role of scientific standards, evidence, and process.

But I also understand urgency.

Children with rare diseases do not live on regulatory timelines. They lose skills month by month — speech, mobility, independence, and in some cases, even the ability to breathe unassisted. Of the more than 6,800 rare diseases currently identified, approximately 70 percent begin in childhood. Among them are Duchenne Muscular Dystrophy, Gaucher Disease, Cystic Fibrosis, Hunter Syndrome, and Sanfilippo Syndrome.

The therapies being developed to treat these conditions are not simple. They require decades of research, significant capital investment, complex manufacturing processes, and carefully designed clinical trials. Companies such as Ultragenyx, Sarepta Therapeutics, and Regeneron have invested enormous resources to bring forward treatments including UX111 for Sanfilippo, Elevidys for Duchenne muscular dystrophy, and RGX-121 for Hunter Syndrome.

Yet too often, these applications stall not because of deficiencies in clinical safety or efficacy data, but because of manufacturing or procedural concerns — issues that, while important, may be addressable without halting access to treatment entirely. In

several cases, products that qualified for the FDA's accelerated approval pathway have encountered delays that appear inconsistent with the pathway's intent: to provide earlier access to promising therapies while confirmatory data are gathered.

As a scientist, I was troubled by the FDA's rejection of RGX-121 for Hunter Syndrome and the subsequent clinical hold, despite positive trial findings and use of long-accepted biomarkers such as cerebrospinal fluid measurements. Similarly, the Biologics License Application process for UX111 encountered manufacturing-related delays.

In the case of Elevidys for Duchenne muscular dystrophy, following tragic patient deaths — including one with significant underlying complications — the FDA removed access broadly, rather than narrowly tailoring its regulatory response.

These decisions raise important questions. When multiple rare pediatric therapies, across different sponsors and technologies, encounter repeated slowdowns unrelated to demonstrated clinical harm, the pattern warrants review. Is the current review framework functioning as intended? Or has it evolved into a system that unintentionally imposes a higher regulatory bar on treatments for small patient populations?

Manufacturing processes can be refined. Facilities can be updated. Documentation can be corrected. But neurons lost to neurodegenerative disease cannot be restored. Muscle fibers destroyed by Duchenne muscular dystrophy do not regenerate simply because a review cycle has extended another year.

In rare pediatric disease, time is not an abstract metric. It is developmental capacity. It is ambulation. It is a pulmonary function. It is the ability to eat without a nasogastric tube. It is life expectancy.

But mostly, it is living the longest period of time possible being loved by your family and friends.

Accelerated approval does not mean lowering standards. It means applying them intelligently and proportionally. It allows conditional access while confirmatory trials continue. It acknowledges that "wait and see" is not a neutral position — it is a decision that guarantees disease progression for children who cannot afford delay.

There are also broader implications. Orphan drug development requires substantial upfront investment with limited market return. When regulatory unpredictability increases, the incentive to pursue innovation in small, high-risk populations diminishes. If the perception takes hold that rare pediatric therapies face shifting goalposts or disproportionate scrutiny, investment will contract — and future breakthroughs may never begin.

This Committee's focus on this issue is vital. By bringing these concerns before the Executive Branch, Congress, and the American people, you

are reinforcing that oversight, transparency, and accountability are essential components of both good science and good governance.

Good science and compassion are not competing values. We can uphold rigor while acting with urgency. The FDA possesses the statutory authority to implement accelerated pathways effectively. Congress retains oversight responsibility. And the scientific community stands ready to meet high standards.

The question is not whether safety and efficacy matter. They absolutely do. The question is whether our regulatory processes are calibrated appropriately for the realities of rare pediatric disease.

The science is advancing. The tools exist. The authority is in place. The children, however, cannot wait.

Thank you again for holding this hearing, and allowing me to submit testimony based on scientific expertise.

Sandeep Saha – February 25th, 2026

Written Testimony

Dear Chairman Scott and Members of the Committee,

I have spinocerebellar ataxia type 1, a rare, inherited neurodegenerative disease with no approved treatment. SCA1 takes your balance, your speech, your ability to swallow, and eventually your life. The median age of death is 63.

I enrolled in Biohaven's Phase 3 clinical trial for troriluzole, the first-ever industry trial in SCA. I submitted to years of study visits, blood draws, and neurological exams, knowing I might receive a placebo while my disease kept progressing. The results showed troriluzole slowed disease progression by 50 to 70 percent over three years and significantly reduced falls. For a disease with zero treatments, this was historic.

After the trial, I continued on troriluzole through an expanded access program. That program is now at risk of being discontinued. Not because the drug doesn't work or isn't safe, but because the FDA issued a Complete Response Letter in November 2025 despite granting Orphan Drug, Fast Track, and Priority Review designations. The regulatory uncertainty is making continued access unsustainable.

I am also a clinical research professional. I build the statistical analyses and data systems that support FDA submissions. I believe in rigorous standards. But Congress mandated regulatory flexibility for rare diseases because ultra-rare populations cannot meet the same evidentiary bar as common conditions. That mandate is not being honored.

Every month of regulatory delay is a month of irreversible neurological decline for me and thousands of SCA patients. I volunteered my body for this clinical trial because I trusted the system. I am asking you to make sure that trust was not misplaced.

Respectfully,

A Clinical Trial Participant and SCA1 Patient

Susan McNary – February 25th, 2026

Written Testimony

To Whom It May Concern,
Re: Troriluzole Trial

My name is Susan McNary. I am a 60-year-old female diagnosed with SCA3 and have been experiencing symptoms for approximately 10 years.

I began a trial of Troriluzole in October 2026 and would like to share the significant changes I have noticed since starting the medication.

Prior to beginning the trial, I had lost my sense of smell and was experiencing difficulty with balance, slurred speech, double vision, depression, fatigue, and a lack of interest in daily activities. These symptoms had a substantial impact on my quality of life.

Since starting Troriluzole, I have experienced dramatic improvement in all of these areas. My balance has improved, my speech is clearer, my double vision has lessened, and I have regained my sense of smell. Additionally, my mood, energy level, and overall engagement in daily activities have markedly improved.

Before beginning Troriluzole, I had been taking Riluzole but did not experience any noticeable improvement in my symptoms.

I am grateful for the opportunity to participate in this trial and wanted to share my positive experience.

Sincerely,
Susan McNary

Lael Barnett – February 25th, 2026

Written Testimony

To whome it my concern,

My name is Lael Barnett. I'm am a 47 year old male with SCA type 3. I was diagnosed in 2023. Prior to that I worked on the railroad, I was an avid runner, and went to the gym. I'm also a father of two. I noticed my balance failing me prior to my diagnosis. I had to stop working shortly after.

Around sometime last year I was given the opportunity to participate in a trial medication study for the drug Troriluzole. I took it reluctantly thinking that it couldn't help my condition. Much to my surprise it did!

Troriluzole has improved my quality of life in a huge way. I'm able to walk for exercise as well as go to the gym because of Troriluzole. I walk to all my doctor and pharmacy visits which my doctor's will attest to. I walk to the grocery store. I walk everywhere.

Troriluzole has not only improved my quality of life, it has given me confidence. Troriluzole has given me some sense of normalcy.

I beg you to please continue the Troriluzole program. I pray for the day it's FDA approved. Thank you for reading my letter.

Nancy Garza-Harris – February 25th, 2026

Written Testimony

As a patient in a Huntington's Disease (HD) clinical trial for the last 5 years, I have remained objective. The purpose of this statement is to ask that the Food and Drug Administration (FDA) do the same. I am only interested in proof too. However, it does feel like the FDA is ignoring investigational data that is specific to HD patients but to what end? HD is fatal with no cure.

Thank you for the opportunity to submit a statement for the record.

Gillian Sapia – February 25th, 2026

Written Testimony

Chairman Scott and Members of the Committee,

My name is Gillian Sapia. I am a Registered Nurse and the mother of a child with an ultra-rare metabolic disease.

I am here to make one clear statement:

There should be no placebo in pediatric ultra-rare disease trials. Period.

In pediatric oncology, we do not knowingly allow children to deteriorate on placebo when a potentially disease-modifying therapy exists. Standard treatment is preserved. We use adaptive designs. We use single-arm studies. We use historical controls. We accept uncertainty because the ethical line is clear.

Ultra-rare children deserve the same ethical standard.

My daughter was randomized to placebo for eighteen months. During that time, she declined. Her neurologic symptoms progressed — more seizures, more hospitalizations. Her kidney function worsened. We came dangerously close to losing the opportunity to receive active drug. Children should not have to endure regression in order to qualify for treatment. Progression is not neutral.

That is not scientific neutrality. That is preventable harm built into trial design.

In ultra-rare disease, total populations may number only dozens of children. A trial of 40 patients may include only 10 pediatric participants. In that setting, each child represents 10 percent of the data. One outlier can shift the entire result. Two dropouts can distort the conclusion.

That is not robust statistical power. It is fragile inference.

Small sample sizes dramatically increase the risk of Type II error — concluding a drug does not work when it actually does. When only 10 children are carrying the statistical weight of a subgroup analysis, placebo exposure is not just ethically risky. It is scientifically unstable.

We are asking children to absorb irreversible progression in trials that are structurally underpowered to generate certainty.

There are no approved alternatives in most ultra-rare pediatric diseases. Placebo is not “standard of care.” It is absence of intervention.

Congress has already given FDA the authority to do this differently:

Accelerated Approval.

Single adequate study authority.

Real-World Evidence integration.

Contextual benefit-risk balancing.

The tools exist.

What is missing is a consistent operational application to protect children in ultra-rare disease. Rare pediatric disease should not be subject to placebo exposure in progressive conditions.

Scientific rigor does not require pediatric regression.

No prolonged placebo.

No built-in deterioration.

No ethical double standard between cancer and rare metabolic disease.

No placebo. Period.

Thank you.

Gillian Sapia, RN

Ron Schryer – February 25th, 2026

Written Testimony

To New Drug Applications (NDAs)

CDER Central Document Room:
FDA/Center for Drug Evaluation and Research (CDER)
Central Document Room (CDR)
5901-B Ammendale Road
Beltsville, MD 20705-1266

I am a concerned parent and have a son who has Spinocerebellar ataxia (SCA). My son is in his forties and is currently able to walk with a walker. I have watched the progression of this disease over the years and how it is slowly taking his physical abilities away.

I heard about Biohovens new drug VYGLXIA (troriluzole) and I have gotten some hope someone is finally making some progress with limiting the diseases progression. I have just learned the FDA did not approve the of this drug. My question: Does this mean Biohaven needs to start over again or is there a path for approval VYGLXIA without waiting years to do the third phase trial again?

There are many people like my son as evidenced by the National Ataxia Foundation. I hope an expediated resolution to Biohavens NDA is forthcoming. I also hope the denial of Biohavens NDA is not a phase III start over since it appears some people are currently benefiting via expanded access program.

Biohaven

- *In the CRL, the FDA recommended that Biohaven meet with the Division to discuss the evidence that will be needed to support a future NDA for the treatment of SCA with troriluzole. Following receipt of the CRL today, Biohaven is in the process of formally requesting a meeting as soon as possible given the large number of patients who are currently being treated in the expanded access program.*
- Biohaven remains committed to working with the FDA to find a path forward for its NDA for VYGLXIA and plans to meet with the FDA to discuss potential next steps.
 - *Troriluzole received Orphan and Fast Track designation as well as a Priority Review acceptance of the NDA; FDA subsequently delayed the PDUFA date by 3 months during the review period. There was no communication of the need for an Advisory Committee meeting at acceptance of the Priority Review; however, a few months later the FDA informed Biohaven that an Advisory Committee was being planned but then cancelled it weeks before the anticipated meeting, preventing qualified clinical experts the opportunity to publicly weigh in on their opinion of what is a large and robust treatment effect and after the Company spent significant resources preparing for the Advisory Committee.*
- *In the CRL, the FDA recommended that Biohaven meet with the Division to discuss the evidence that will be needed to support a future NDA for the treatment of SCA with troriluzole. Following receipt of the CRL today, Biohaven is in the process of formally requesting a meeting as soon as possible given the large number of patients who are currently being treated in the expanded access program.*

- Biohaven remains committed to working with the FDA to find a path forward for its NDA for VYGLXIA and plans to meet with the FDA to discuss potential next steps.

Jacob Mancebo – February 25th, 2026

Written Testimony

Good day, I was diagnosed with Ataxia last year. As you know this is a quickly degenerative inherited disease that impacts the quality of life(I have no balance, prone to falls, shrinking brain, no control of extremities, slur speech and more) I have left as a man of only 50 years old, a full time employee for the municipality I work for and a proud father of 3 school age children. My father and my son suffer from this disease severely and it hurts to know that there is no cure at the moment. However, a company by the name of Biogen just concluded some successful studies with a pill that the FDA did not approve even though their clinical trials showed success within the subjects they recruited. Unfortunately, I cannot get the pill Biogen designed because of all the regulatory decisions. I am imploring to please approve Biogens treatment for Ataxia so that I may live longer and live a better quality life. FDA—please approve Biogens pharmaceutical treatment for Ataxia so that my father, who is now dying at 72 because of this disease, my son is now completely disabled, myself and others an opportunity at a slightly better life with treatments targeting Ataxia. Thank you and I hope you can bring some hope to those of us who are suffering in the dark.

Vicky Chang – February 25th, 2026

Written Testimony

I was diagnosed with spinocerebellar ataxia 6 (SCA) 6 in 2021. My slurred speech and dizziness forced me to retire as a cardiology nurse practitioner from a VA hospital where I provided important care to veterans. I loved my job and feel that I still have a lot to give had not been the SCA 6. The worry for falls due to dizziness and poor gait is a constant fear. Having treatment will give me hope to slow down the disease progression and continue to live independently with dignity. Please expedite the FDA process for any treatment for SCA's.

Thank you for your attention.

Vicky

Angelina Olivera – February 25th, 2026**Written Testimony**

Mother to a teenager with Duchenne Muscular Dystrophy and sister to two brothers who died from DMD.

Submitted to the United States Senate Committee on Aging
February TK, 2026

Submitted TK:

Thank you, Chairman Scott, Ranking Member Gillibrand, and distinguished members of the Senate Special Committee on Aging.

My name is Angelina Olivera. I am a mother of three from El Paso, Texas. I am here as the sister of two brothers, Angelo and Antonio, who died from Duchenne muscular dystrophy in 2000 and 2015, respectively; and as the mother of my 14-year-old son, Ryu, who is living with the same terminal disease.

For my family, living with the fatal countdown of Duchenne is all we've ever known. We have experienced the heartbreak of watching our loved ones become sicker by the day and eventually dying. We live each day racing against a clock we cannot stop. Time is muscle in Duchenne. Time is mobility. Time is childhood.

I come before you with significant concerns about the roadblocks facing emerging therapies at the Food and Drug Administration — particularly within the Center for Biologics Evaluation and Research (CBER). While scientific rigor and patient safety must remain paramount, the current regulatory environment is too often marked by delay, uncertainty, and shifting standards that don't put patient and family needs first.

I appreciate the opportunity to submit testimony today to emphasize the critical importance of incorporating patient voices into FDA decision-making for rare disease treatments.

Families living with Duchenne understand risk differently from those in Washington. We weigh it against inevitable progression and premature loss. We ask this Committee to support lives like my son Ryu and other members of the rare disease communities by urging meaningful reforms to the accelerated approval pathway and by ensuring that families have a formal, respected seat at the table when life-altering decisions are made.

Eight years ago, President Donald Trump signed the Right to Try Act to give patients facing life-threatening illnesses a chance at access to investigational treatments. That law represented a promise—one rooted in agency, urgency, and respect for families confronting terminal diagnoses. Although Duchenne does not meet the six-month requirement under the Right to Try statute, families like ours have been living under a terminal prognosis from day one. For us, the "right to try" is not just a legal framework. It is our only source of hope.

Today, I am asking whether that promise still applies.

Duchenne is progressive and irreversible. Muscle loss cannot be recovered. Delay is not neutral—it accelerates decline. My son is 14. His projected life expectancy is 20 to 22 years old, the same ages at which my brothers passed away. We can do the math.

This disease loomed over my childhood and made good on its threats in early adulthood. My oldest brother Angelo died at 20, when I was 16. My youngest brother, Antonio, died at 22 when I was 31. I held my baby brother in my arms as he passed, while my infant son, newly diagnosed with Duchenne, sat at my feet.

When I was seven months pregnant, I learned I was a carrier. When Ryu was born, we waited for the blood test results. I still remember the call confirming he was positive. My soul broke that day. I knew what was in front of me and my baby because I had lived it twice before. I couldn't do it again.

By the grace of God and by assistance from groups like the Muscular Dystrophy Association, my son is still with us and I am here with you in-person today.

Financially, rare disease is devastating.

My husband and I are fortunate to have insurance, but even so, the costs are staggering as not every needed resource is covered by that insurance.. My son has required a \$30,000 power wheelchair since age 12. His steroid medications *alone* cost approximately \$30,000 per month, and even with insurance, our out-of-pocket costs have reached thousands of dollars monthly.

These medications also come with serious side effects—weight gain, brittle bones, intense mood changes, and physical changes that are difficult for a teenage boy to accept. One steroid made Ryu feel skin-crawling pain 24/7. All I could do was join him in tears on the floor—begging to take some of the discomfort.

For decades, the Muscular Dystrophy Association helped my family with co-pays and costs for these medicines and other essential equipment. Then, without warning, that assistance ended. We were told funds were being redirected toward research to find a cure. The news was devastating, but my entire family—including my son—supported that decision. We believed that sacrifice would lead to meaningful research and treatments.

Now, when that research *has* produced a gene therapy designed to address the underlying cause of Duchenne like the Elevidys gene treatment, developed by Sarepta Therapeutics, families are being told to wait. Last summer, FDA regulators halted shipments and rejected broader accelerated approval, citing safety concerns. But waiting is a luxury my son cannot afford.

From where we stand, it feels like another wave crashing down on top of us as we tread water just to keep our heads above the surface. We sacrificed financial support in the name of research. Now access to the results of that research is stalled. Duchenne families feel they are being asked to sacrifice in the name of progress while being denied the opportunity to benefit from it. That is not right—morally or practically.

We understand risk. Every night we put our son to bed, we understand that he may not wake up because a simple cold could become life-threatening as Duchenne weakens the muscles

needed to cough. His heart could stop at anytime. Our children with this disease live with risk every single day. When families say they accept risk, it is because we understand the certainty of doing nothing.

The Trump administration once championed patient agency and choice. That clarity should not be lost now. We are not asking for shortcuts or the abandonment of science. We are asking regulators to put patients first because their lives matter more than any political concern or regulatory hurdle.

When assistance funds were redirected toward research, we were told it would bring hope. If that hope is now blocked at the point of access, families are left asking: what are we sacrificing for?

My brothers never had this opportunity. My son does.

Every day with him is precious. Every month matters. Through this hearing, we hope that you will ensure that the Right To Try principles of urgency, agency, and compassion guide regulatory decisions affecting rare disease families. Do not let bureaucratic delay take away the chance at life that research has worked so hard to create.

Thank you for the opportunity to submit this testimony.

Samir Noori – February 26th, 2026

Written Testimony

Ataxia, including conditions such as Spinocerebellar Ataxia, is a progressive neurodegenerative disorder that gradually impairs coordination, balance, speech, swallowing, and overall independence. As the disease advances, patients often lose the ability to walk, work, and perform basic daily activities. Currently, there are very limited treatment options available, and no broadly approved therapies that effectively slow disease progression.

Troriluzole represents meaningful hope for patients and families affected by this devastating condition. Designed to modulate glutamate pathways in the nervous system, it has the potential to slow progression and preserve neurological function. For patients facing steady decline, even modest slowing of disease progression can translate into additional years of mobility, communication, and independence.

For rare disease communities, timely regulatory review and expanded access pathways are not abstract policy issues—they are matters of quality of life and, in many cases, survival. Delays in approval or limited access can mean irreversible loss of function for patients whose conditions continue to progress.

I respectfully urge continued support for the evaluation, regulatory flexibility, and appropriate access pathways for Troiriluzole so that individuals living with ataxia may have the opportunity to benefit from this promising therapy.

Thank you for your consideration and for your commitment to patients living with rare and neurodegenerative diseases.

Regards

Mystique Bontems – February 26th, 2026**Written Testimony**

To the Senate Aging Committee;

I am representing the community of those affected by the rare disease Mucopolysaccharidosis Type II (MPS II), otherwise known as Hunter's Syndrome, in support of the proposed gene therapy, RGX-121 (clemidsogene lanparovec). In the following excerpts, I will discuss my family's experiences with losing my brother to Hunter's, along with the newfound journey of my sister who now has a son with Hunter's. Additionally, I will go further into detail about how this life-altering gene therapy will have positive outcomes not only for our family, but to all families that have a child with Hunter's Syndrome.

I have been both a sibling and now an aunt to an individual with Hunter's Syndrome. Growing up with my brother, Dylan, and presently my 1.5 year old nephew, Maximus, whom was diagnosed with the disease just this last summer in 2025. In a family of 5 children, I am the middle child with two older brothers, a younger sister and what was once our youngest brother, Dylan. Dylan was born with Hunter's Syndrome in 1996, and would have turned 30 this February. Unfortunately, his predestined disease only allowed him to make it to 13 years old, back in 2009.

My parents were unaware of my mother being a carrier of this genetic anomaly, seeing as Hunter's Syndrome is an X-linked genetic disorder. Dylan's diagnosis was made known when he was 2-3 months old, with doctors making it significantly clear that this was a very rare disease & his lifespan would be cut notably short due to it. Without a treatment or cure that could cross the blood brain barrier, the missing link to his DNA would ultimately be his demise. At the time, only being 5 years old myself, I remember my parents telling us four kids that Dylan was special & we didn't know how much time we would get with him on Earth. But that we would treat him just the same as any other child, and give him the same life experiences possible. And that we did.

Everyone knew Dylan, mainly because in his younger more able days he loved to rip off his diaper and hightail it down the street with my mom chasing after him—as he laughed in a guttural, pure sort of way. He was a gentle bliss of a human, despite the downfalls of his condition. He knew no different, as did we. He had a twinkle in his eye that let you know he understood feelings and emotions, even if he couldn't speak it outwardly. Especially in his younger years, he could run with all of us kids along with surrounding neighbors, he could throw and kick a ball like a pro, and ride his big wheel tricycle into the sunset. My mom definitely had her hands full, but Dylan had a way of making your heart even more overfilled with joy without even trying. Unfortunately this made his decline as he aged that much more apparent and heart wrenching to watch before our very eyes, as his spark of life slowly fizzled out as the disease progressed throughout his innocent body.

Some of the downfalls of Dylan's disorder lasted the entirety of his life, not just during the swift decline in later years. He spent his life in diapers with messy bowel movements that were never solid. Even though I never heard my parents complain, he slept in my

parent's bed for all 13 years of his life. This was primarily so my mom could keep watch over him 24/7, as he also did not sleep through the night in younger years. This even evolved to long nights of watching Barney in the living room, where my mom would lay half awake on the carpet with her arm around him as he sat up watching into the wee hours of the night. If I woke up in the middle of the night, I remember the soft glow of the television down the hallway & would come out to join them. I remember my mom giving him nightly breathing treatments, the sound of the machine humming is a heavy reminder of one of the many ways my mom did all she could to bring comfort to her child. I remember occupational therapists and speech therapists coming to our home to work one-on-one with Dylan, some more patient with his diagnosis than others.

One thing was for sure, my mom and Dylan were inseparable. She never let him out of her sight, aside from the few times she allowed him to be apart of some special needs school programs in his younger years when he was active. Unfortunately, even many of the special education teachers were not proficient in dealing with such a specialized child, and it ended in Dylan communicating with us that he was being abused by them. Dylan could say few words, but did learn some basic sign language to help communicate. My mom never entrusted anyone with him after that.

As time went on, the more nonverbal he became as he aged. He went from being a lively wild child full of spunk and joy riding his big wheel, to a quiet sedentary teen as he lost all his mobility. He began losing his balance before the age of 10 and eventually had to have a specially made walker, and eventually a custom wheelchair where he resided most of his days. He suffered from debilitating seizures, heavy mucous production (some families opt for tube feeding), as well as breathing treatments to help reduce the potential for pneumonia (this would eventually be the means by which took Dylan's life). Given the limited knowledge on MPS II back then, my mom did all that she could for Dylan. In his last week of life, we knew it was his time. It seemed like hundreds of people who had been impacted by Dylan walked through our front door to pay their respects as he laid there calmly and quietly analyzing each one. He held on for his final visitor, his home helper. My mom told him teary eyed, "It's okay, you can go now" as he took his last breathe. Then, as if the heavens lit up, the darkly lit bedroom was glowing with golden rays of sunshine and Dylan's sparkling blue eyes lit back up as he smiled his final goodbye.

Losing a family member leaves a heartache no one can heal, and outliving your own child is something most parents will never have to be concerned with. There is a feeling of hopelessness and deep sadness when you are told your child may only live a certain number of years. It is clear that my mom was Dylan's around-the-clock caregiver, so his absence struck her the hardest & she has never fully healed from his passing. Our entire family has a special place in their heart for Dylan, and can easily get choked up talking about memories of him. There are numerous emotions that accompany this sort of loss, the "what if's", along with each family member feeling their own sense of guilt and regret, longing to see their loved one yet being thankful they are no longer suffering from such disease. It has been 17 years since his passing, and simply writing this while reflecting on his life has taken me weeks to finish due to the heavy hearted nature of this topic. With how gut-wrenching and painful the healing process has been after almost two decades, any sort of lasting solution to save children with MPS II is essential. Prevention by means of treatment of those diagnosed with Hunter's is a must, as well as saving their families from having to go through this in the same way that

Dylan and we did. I believe we should stop at no obstacle, by all means necessary, to make this dream a reality.

Our family's life with Dylan was not always negative or sad—he played a significantly important role in not only our lives, but with everyone he met. He touched the souls of everyone he laid eyes on, and in his younger years, when he still had facial expressions, he had a smile that could melt a stone cold soldier down to their boots. His special happiness brought a peace to the challenges that his life presented. Adjustments usually had to be made to make life work better for our situation, but it never seemed like that much of an issue in the moment.

However, recalling past memories, it is apparent there were quite a few sacrifices we made to have Dylan present in anything we did together as a family unit. Average households got to take flights on vacation, whereas we were advised not to take Dylan on a plane. Our friends got to go out to dinner regularly, whereas it was a common occurrence that Dylan had a build-up of mucus & choked violently anytime he ate—disrupting surrounding tables, and many people acting openly disgusted that we would bring him out in public. Some people even voiced their opinions to us, as if we didn't have the same rights and freedoms to be there. We never even were able to fulfill most childhood dreams to go on a family trip to Disneyland, because it was deemed as unsafe for Dylan to go on any of the rides. All of this to say, even though our "normal" may have been different than the average family, we were able to conduct our lives in our own version of normal.

What had become our normal sometimes puzzled passerby's who didn't always understand Dylan's condition and ailments. As a child, I remember asking my mom why other children and more distinctly, why grown adults, would stare blatantly at Dylan when we were out in public. To me, he was just my baby brother. But to the average person, Dylan was... different. With Hunter's Syndrome there are features that go along with having the missing enzyme in their DNA. Some key physical attributes such as "coarse" facial features along with large heads and abdomens with a short stature to name a few.

Nevertheless, we didn't let any of this get in the way of having time with family and we knew no different than having Dylan along for every memory while he was here. He will forever be a blessing in our life, and I wish the options available and, hopefully soon to be available, were around when he still had a chance. He may have lived the course of his life, but my baby nephew, Max has just begun his. With the studied and successful treatments of RGX-121, this new therapy is able to cross large necessary enzymes across the blood brain barrier—something we waited for all of Dylan's life. I believe there is a significantly higher possibility of Max being able to live a long, prosperous & cognitively capable life—given that a treatment such as RGX-121 has achieved the unthinkable.

Understanding the specifics on how Hunter's Syndrome inhibits those affected may also help emphasize the importance of treatments available and the timeliness that this medicine can be made available. Hunter's Disease is a deficiency in the enzyme iduronate-2-sulfatase (I2S), meaning that this missing enzyme has the primary job to breakdown complex sugars (glycosaminoglycans). Without this important enzyme, the sugars build up & consequently wreak havoc in the affected individual's organs, bones,

& joints. This build up leads to progressive physical and cognitive decline, including aforementioned coarse facial features, enlargement of organs (organomegaly), joint stiffness, and developmental delays, usually appearing between ages 2 and 4.

This is why the gene therapy RGX-121 is so important. It is a one-time AAV9-based treatment developed by RegenxBio to specifically treat Hunter's Syndrome. It aims to deliver a functional iduronate-2-sulfatase (IDS) gene to the central nervous system to treat neurological manifestations. This single dose treatment targets the cognitive and behavioral impacts of Hunter's, which the current available standardized enzyme replacement therapy cannot address. The IDS gene is delivered using the NAV AAV9 vector, enabling cells in the central nervous system to produce the missing enzyme that causes Hunter's Syndrome. NAV AAV9 (Adeno-associated virus 9) is a leading gene therapy vector from RegenxBio's proprietary platform, which is well-known for its capability of crossing the blood-brain barrier (BBB). By crossing the BBB efficiently, genetic enzymatic material can be delivered to the central nervous system and peripheral tissues. NAV AAV9 is famously used in treating spinal muscular atrophy (SMA) and is widely adopted for treating various genetic diseases due to its high transduction efficiency and tissue-targeting capabilities.

Ultimately, the CAMPSIITE trial (NCT03566043) has been investigating safety and efficacy of RGX-121 therapy in patients with MPS II. Despite positive data, in February 2026, the FDA issued a Complete Response Letter (CRL) for the Biologics License Application (BLA), requiring further analysis, thus to our dismay has postponed the approval of the gene therapy. The primary target for the treatment are males aged 4 months to 5 years old.

Given that majority of children with MPS II have the life expectancy of 10-20 years, every minute counts. The sooner these children can receive treatment, the less damage they will undergo by improving the quality of their life while increasing the number of years they can live a healthier life. The cognitive and physical damage eventually costs these children their lives, just like it did to my baby brother Dylan. Most do not make it into their twenties even with precautions such as special diets, which may lessen the build up of sugars. With the missing enzyme in their DNA, their bodies eventually lose the battle.

Until now. For the first time, there are new treatment options being discovered. Enzyme Replacement Therapy (ERT) is currently available in the United States, that of which my 1.5 year old nephew, Maximus, has been undergoing weekly. The reality of ERT is that an implanted medical port had to be put in place in Max's chest, we call this his "Iron Man". Meaning that he had to be put under anesthesia as an infant, which already came with its own risks. Not to mention the detrimental risks that a port itself has, with infection being the most common concern especially with a toddler. The first signs of infection in or around the port would be a fever, meaning that any time Max spikes a fever he must be rushed to the children's hospital—which is an hour away. Sometimes toddlers get sick & have a fever for more than 24 hours. But if Max's fever persists, he must return to the hospital to check for infection of the port by means of culture sample—that of which takes 72 hours for the sample results to grow a bacteria culture if present. All of these precautions and tests, then add another hour long commuting time to receive his weekly enzyme infusion into his port. This includes keeping an active toddler busy in a hospital room, while his chest is connected to an IV. The visit all

together usually is about 5-6 hours, along with the 2 hour round trip from home to the hospital.

It should be made known that children with Hunter's do not have normal sleep patterns. Just to simply take a nap, my sister has to bounce on a yoga ball with 33-pound Max as a means of calming him down enough to fall asleep in her arms for an hour or so. Night time sleeping is just as erratic and typically ends with both my sister and Max exhausted with less than a few combined hours of rest each night.

Between the lack of sleep, potential port infection complications, and weekly treatments— the need for an alternative upgraded treatment option for Max is more evident than ever, as is likewise for all the other families affected by a loved one with Hunter's. Though the enzyme replacement therapy has been a decent option to begin with, unfortunately, it does not cross the blood brain barrier to halt the cognitive decline of Hunter's Syndrome. However, this is what sets apart the treatment we are requesting be approved at the earliest convenience. The RGX-121 treatment does cross the blood brain barrier & with a single treatment can give children like Max, the best chance at the most normal life possible. Max's life is in the hands of your discretion to pass and approve this treatment. Please don't let him down. Thank you for your time and consideration on this matter.

Best Regards,

Mystique Bontems

Guetty Constant – February 26th, 2026

Written Testimony

To may it concern

Triluzole made me worse.

Julianne Tino – February 26th, 2026

Written Testimony

Subject Line: Statement for the Record – Rare Disease Hearing – Huntington's Disease
Dear Chairman, Ranking Member, and Members of the Committee,
I am gene positive for Huntington's disease (HD). Thank you for the opportunity to submit this statement for the record.

Huntington's disease is a fatal, inherited neurodegenerative disorder caused by a mutation in a single gene. Each child of an affected parent has a 50% chance of inheriting the condition.

Symptoms most often begin in adulthood. HD progressively affects movement, cognition, and behavior, ultimately leading to complete dependence and death. In Juvenile Huntington's disease (JHD), children develop symptoms that include seizures, loss of speech, loss of mobility, difficulty swallowing, and often require feeding tubes and full-time care.

HD's impact on families is devastating. HD imposes severe, progressive social and economic burdens on families, including lost income, high caregiving costs, and intense psychological distress, while driving significant, rising public healthcare expenses as the disease advances. There are currently no approved therapies that slow or stop disease progression.

For my family, HD means shock and anxiety. HD was not in our family. My sibling noticed some minor movement abnormalities a few years ago, but did not get a full workup until a few years later. They were diagnosed with HD after a neurologist ran a panel. When I received the news of their diagnosis, I was not immediately concerned because I never heard of HD. One hour later, after Googling HD, I was completely stunned and devastated. Fear for them, but also their kids at 50/50 risk, then wondering if I had the same fate ahead as well as my own children. This disease is what I call shrapnel. I was then diagnosed with reduced penetrance HD. My oldest child is recently married and just tested for the gene as they want children. Unfortunately, they are also carrying the HD gene in the reduced penetrance range. Their potential children have a 50/50 chance of inheriting in the reduced penetrance range or full penetrance range. The last week has been spent talking to fertility clinics about IVF-PGT for having a gene negative child.

This means destroying the HD positive embryos, and mentally this is a heavy burden. They have spent tens of hours on the phone regarding insurance. Testing alone for the gene involved seeing multiple providers who could not help, until we connected with a vital resource, HDGenetics testing. This is a journey no one wants, least of all for our children. There is enormous guilt. My other children have not tested, and they carry the burden of wondering their fate like a chain.

I drive out-of-state to participate in EnrollHD at an HD Center of Excellence. The hours spent traveling and hours of testing at the clinic are my way of moving forward with cures, in the hope that the data from this vast database of our blood and personal data can be used as a placebo arm in trials.

2 studies have shown 1/325-1/400 people have an elevated CAG number and are at risk of developing HD themselves or passing to children at 50/50 rate. Anyone on this panel could have an elevated CAG without knowing. I did.

In recent years, research into disease-modifying therapies has brought hope to our community. We deeply respect the FDA's responsibility to ensure that treatments are safe and effective.

Patient safety must remain central to every decision.

At the same time, rare disease research presents unique structural challenges. Huntington's disease affects a relatively small population living with a relentlessly progressive condition. Clinical trial design in this context is complex.

In a small, progressive rare disease population, extended placebo exposure presents both ethical and practical challenges. As objective biological indicators become more refined, they may help verify treatment impact with greater precision. We encourage thoughtful consideration of how these advances can inform trial design while preserving scientific integrity.

For families affected by Huntington's disease, time is not neutral. Decline continues, and lost function cannot be restored. Each year without meaningful progress represents irreversible neurological loss for people living with this disease.

We respectfully ask for:

- Clear and consistent regulatory guidance for rare neurodegenerative diseases
- Transparent communication regarding evidentiary expectations
- Continued incorporation of patient perspectives into benefit–risk assessments
- Regulatory pathways that reflect both scientific rigor and the urgency of progressive, fatal conditions

The Huntington's disease community has demonstrated its commitment to participating in research, advancing science, and working collaboratively with regulators, researchers, and policymakers. We seek a system that maintains high standards while recognizing the realities of rare, inherited, life-limiting diseases.

Thank you for your attention to rare diseases and to the families who live with them every day.

Carol Strickland – February 26th, 2026

Written Testimony

I have spino-cerebellar ataxia, a genetic condition causing balance and coordination problems as my cerebellum progressively degenerates.

I urge Congress to make research and treatment a priority, especially if new pharmaceutical options appear.

I used to be very active, skiing, ice-skating, climbing mountains, hiking. Now if I only could walk without a walker I'd be content.

The condition severely affects my quality of life. It's more and more difficult to go outside, interact with my grandchildren, and do domestic chores like cooking and gardening—anything that involves standing or walking really.

I remember an elderly aunt saying to me in my vigorous days, "Why run when you can walk, walk when you can sit, or sit when you can lie down?" This was incomprehensible to me then, but—as I sink into a sedentary or recumbent life—I understand and lament the closing-off of an active life.

Thank you for anything you can do to help.

Kathy Flynn – February 26th, 2026

Written Testimony

Dear Chairman Scott, Ranking Member Gillibrand, and Members of the Senate Special Committee on Aging,

On behalf of the National Tay-Sachs & Allied Diseases Association (NTSAD) community, I respectfully submit this statement for the record for the Senate Special Committee on Aging hearing examining the FDA's role in the rare disease community.

NTSAD, one of the nation's oldest and highly respected patient advocacy organizations for rare diseases, represents individuals and families affected by four ultra-rare, life-limiting neurodegenerative diseases: Tay-Sachs, Sandhoff, GM1 gangliosidosis, and Canavan disease.

These genetic disorders affect infants, children, and adults, leading to relentless neurological decline, loss of abilities and mobility, seizures, and death. For young children with the infantile form, life expectancy is measured in only a few short years. Affected juveniles usually succumb to the disease in their teens, and adults living with the late-onset form face progressive and irreversible neurological deterioration.

There are currently no FDA-approved therapies for any of the four ultra-rare diseases NTSAD represents.

For our community, time is not theoretical. Time is the enemy that steals children's ability to crawl, walk, speak, swallow, see, or feed themselves. Most children experience seizures and respiratory distress, resulting in frequent hospitalizations. Affected adults face progressively debilitating physical impacts, and functioning independently becomes impossible; some also experience psychiatric illness.

These disorders are devastating not only because they are fatal, but because they are relentlessly progressive. Children often appear healthy at birth, only to lose developmental milestones over months. Parents become full-time caregivers—managing feeding tubes, respiratory support, seizure protocols, and complex medical equipment in the home. Siblings witness their brother's or sister's decline in real time. Families experience profound emotional, physical, and financial strain.

In recent years, NTSAD has hosted three Patient-led Listening Sessions and an Externally-led Patient-Focused Drug Development Meeting. Listening Session summaries and the Voice of the

Patient Report are available on the FDA's website and at [FDA Engagement - NTSAD](#). Common themes shared by patient families and affected adults included:

- An urgent need for approved therapies that slow disease progression and preserve rapidly declining abilities;
- The profound physical, emotional, and financial burdens imposed by these diseases; and
- Strong opposition to placebo-controlled trials in the context of these progressive, life-limiting conditions.

Testimonies shared during these meetings are not isolated or unique. They reflect the reality of daily life for most members of the NTSAD community. Developing treatments for ultra-rare neurodegenerative diseases like Tay-Sachs, Sandhoff, GM1, and Canavan disease presents extraordinary scientific and logistical challenges, including but not limited to delays in diagnosis and early intervention, extremely small patient populations, rapid disease progression, and ethical and practical challenges in conducting placebo-controlled trials.

In diseases that are uniformly progressive, fatal, and lacking approved therapies, requiring placebo-controlled trials raises profound ethical concerns. Families are asked to accept the possibility that their child, whose neurological function is measurably declining month by month, may receive no active treatment while irreversible degeneration continues. For these families, requiring a placebo-control group carries real and irreversible consequences. It represents lost time and developmental capacity that can never be restored. When a disease is relentlessly progressive and fatal, and when patient populations are exceedingly small, alternative regulatory approaches such as the use of robust natural history data, external controls, adaptive trial designs, and biomarker-supported endpoints should be exercised.

Despite these barriers, the scientific field has advanced significantly. Gene therapy, enzyme replacement strategies, and small molecule substrate reduction approaches have shown promise in preclinical and early clinical research. NTSAD has actively supported this progress by partnering with academic investigators, biotech sponsors, and regulatory stakeholders to advance trial readiness, natural history studies, endpoint development, and patient recruitment. Since 2002, NTSAD has invested more than \$5.1 million in 76 research grants.

Most recently, NTSAD was one of two patient advocacy organizations selected to receive a grant from the NORD IAmRARE program to establish a patient registry for GM2 (Tay-Sachs and Sandhoff diseases).

Currently, there is one 2:1 randomized, placebo-controlled clinical trial underway for GM2 and GM1, two active gene therapy trials for GM1, and two active gene therapy programs for Canavan disease. Development of a drug that demonstrated benefit in the GM2 patient population, and is approved for a similar lysosomal storage disorder, Niemann-Pick disease type C, was halted by the sponsor following multiple regulatory meetings that resulted in a Complete Response Letter requiring an additional placebo-controlled trial. Additional preclinical programs evaluating enzyme replacement and gene therapy approaches for GM2 remain in development. However, despite the urgent need, there are still no FDA-approved therapies for any of these diseases.

In the past several years, multiple biotech companies have advanced programs for GM2, GM1, and Canavan disease, only to shelve them for financial reasons rather than scientific failure. The high cost of development and limited commercial viability in very small patient populations have hindered promising efforts—underscoring how consistent and predictable regulatory flexibility from FDA could help de-risk development and sustain progress for these ultra-rare conditions.

In the ultra-rare disease context, regulatory flexibility is not a convenience: it is a necessity. Hence, we hope that the new Plausible Mechanism Framework will be applied to the conditions NTSAD represents.

Families understand uncertainty. They live with it every day. What they cannot survive is indefinite delay or requirements that are ethically misaligned with the realities of rapidly progressive, fatal disease.

In a matter of months, a child with infantile GM2 may lose the ability to sit independently; within a year, that same child may lose the ability to swallow. A previously verbal child with juvenile GM1 or GM2 may become nonverbal and confined to a wheelchair. For Canavan disease, spasticity and seizures may intensify while cognitive and communication skills rapidly decline.

Time lost to regulatory delay is not recoverable. Neurons lost do not regenerate. Developmental milestones, once gone, do not return. The moral imperative before this Committee is clear: regulatory systems must reflect the urgency of diseases where time is a critical factor and there is no second chance.

In conclusion, we respectfully urge the Committee to examine how FDA policies and practices can:

- Ensure predictable and consistent application of regulatory flexibility, including the Plausible Mechanism Framework;
- Facilitate earlier and more structured engagement with patient communities;
- Recognize validated natural history data and patient-prioritized endpoints;
- Provide clear, feasible pathways forward when issues arise; and
- Avoid unnecessary delays and ethically untenable trial requirements in the review of therapies for life-limiting ultra-rare diseases.

For NTSAD families, this is not a policy debate. It is about whether children will live long enough to have a chance and whether adults will have access to therapies that halt the progression of their disease. Every day without progress is a day of irreversible loss.

We appreciate the Committee's attention to the rare disease community and stand ready to work collaboratively to ensure that regulatory processes meet both scientific rigor and the urgent needs of patients facing fatal conditions without treatment options.

Respectfully submitted,

Kathleen M. Flynn Chief Executive Officer

Rebecca Conrow – February 26th, 2026

Written Testimony

Dear Mr. Chairman and Members of Congress:

I submit this statement for the Congressional Record in conjunction with the February 26, 2026, hearing convened by Rick Scott, Chairman of the U.S. Senate Special Committee on Aging, entitled “From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation.” This important hearing examined how regulatory processes and evolving standards at the U.S. Food and Drug Administration (FDA) *delay* patient access to safe and effective therapies—particularly for individuals living with rare diseases such as Huntington’s disease.

[Huntington’s disease](#) (HD) is a rare, fatal, inherited, progressive neurodegenerative disorder that slowly robs individuals of their movement, cognitive abilities, and ultimately their independence; the medical community best describes HD as having ALS, Alzheimer’s, and Parkinson’s combined. Each child of a parent with Huntington’s disease faces a 50 percent chance of inheriting the condition. Families do not merely confront a diagnosis—they live with the certainty of progression, decline, and inevitable loss of their loved ones. Currently, there is no cure nor FDA-approved treatment to **slow down** HD progression.

Unfortunately, my family and I are affected by this horrific disease. My husband is a firefighter who has recently been diagnosed, and he can no longer carry our seven-year-old son into his arms. For families affected by Huntington’s disease, time is not an abstract concept. Time is cognitive decline. Time is motor functions lost. Time is speech diminished, and the inability to eat peacefully without choking. Time is memory fading – years muddled by the gradual death of neurons. *When promising therapies are slowed by regulatory uncertainty, evolving evidentiary standards, or procedural inefficiencies, the consequences are deeply personal and irreversible to families such as mine.* Interruptions in review are not simply administrative—they are life- altering for families!

Recent Regulatory Hurdles: [uniQure](#) AMT-130

One of the most significant recent developments in Huntington’s disease research has been [AMT- 130](#), an investigational gene therapy developed by uniQure. AMT-130 is designed to reduce the production of the toxic mutant huntingtin protein believed to drive disease progression.

Shockingly, AMT-130 is the first gene therapy (in more than 30+ years) to show a statistically significant 75 percent slowing of disease progression.

The FDA previously granted AMT-130 several expedited designations, including Breakthrough Therapy, RMAT (Regenerative Medicine Advanced Therapy), Fast Track, and Orphan Drug designations, to help accelerate its development and review based on early clinical data suggesting it could meaningfully slow disease progression. Regrettably, in late **2025**, uniQure and the FDA **diverged on the regulatory pathway for AMT-130**. Specifically, the FDA **informed the company that the clinical data available from the Phase I/II studies are currently *insufficient* to support a Biologics License Application (BLA) submission** — even under accelerated approval pathways that rely on early efficacy signals and external control comparisons. Clinical holds and additional data requests contribute to holdups and uncertainty. While patient safety must remain paramount—particularly in first-in-human gene therapy trials—the evolving requirements and pauses in development have underscored broader concerns about regulatory predictability for rare disease innovators.

The FDA regulatory shift for AMT-130 has several important implications for the Huntington's community:

- **Uncertain Approval Timeline:** Because the FDA now requires additional evidence beyond the Phase I/II data, uniQure cannot currently file a BLA as planned, making the timing of any U.S. approval unclear.
- **Shift in Regulatory Alignment:** The change represents a substantial **reversal in alignment** between the company and the FDA compared with earlier guidance, causing uncertainty about the path forward.
- **Increased Development Burden:** The FDA's position suggests that more robust data — possibly from additional or longer-term controlled trials — may be needed to satisfy regulatory standards, which could extend development time and costs.

My question is, why? Why this shift when evidence suggests a drastic reduction in HD progression? Time for my family is of the essence. With all my heart, I long to see my husband walk our daughter down the aisle.

The FDA plays an essential role in protecting patients by ensuring therapies are safe and effective. I understand that this mission must never be compromised. However, for rare disease communities, including Huntington's disease, the balance between rigor and responsiveness is particularly **urgent**. Rare disease trials often involve small patient populations, complex endpoints, and rapidly advancing science. **Clear guidance, predictable standards, and efficient review pathways are critical to ensuring that innovation is not unintentionally stalled.**

Chairman Rick Scott's hearing appropriately explores whether regulatory processes have, in some cases, shifted from safeguard to barrier. For HD families, innovation is not

theoretical.

Advances in gene-silencing therapies, biomarker development, and precision medicine represent tangible hope for altering the course of this devastating disease. *Yet innovation can only translate into impact if regulatory pathways are transparent, consistent, and timely. Uncertainty in trial endpoints, shifting expectations mid-development, or prolonged review cycles can deter investment and delay progress in areas where urgency is greatest.*

Chairman Scott's continued oversight underscores an important principle: **the FDA must fulfill its dual mission—to protect patients and to foster innovation**. These goals are not mutually exclusive. Indeed, they are mutually reinforcing when guided by transparency, accountability, and patient-centered decision-making.

As this Committee examines opportunities to improve regulatory clarity and predictability, I respectfully urge continued attention to the rare disease community, including those living with Huntington's disease. My husband's life, and my two at-risk children, should be a reminder that behind every regulatory file number is a family waiting for time they cannot afford to lose.

For my family, progress delayed is progress denied.

Thank you for the opportunity to submit this statement for the record.

Sincerely,
A Wife and Mother

Brenda Hernandez – February 26th, 2026

Written Testimony

Rare Disease Story – PDCD

What disease community are you representing?

I am representing the Pyruvate Dehydrogenase Complex Deficiency (PDCD) community — a small, medically fragile, and often overlooked group of children and families living with a rare mitochondrial disease that affects the body's ability to convert food into energy. Although the community is small, our challenges are immense, and time moves very differently for our children.

How the disease affects our life

PDCD impacts nearly every part of my daughter's life. Because her body cannot properly produce energy, her brain and muscles are constantly struggling. This leads to developmental delays, low muscle tone, feeding difficulties, neurological complications, and episodes of metabolic crisis that can become life-threatening.

Her quality of life is shaped by doctor visits, therapies, medical equipment, and careful monitoring to prevent regression. Things that other families take for granted — eating, sitting, walking, speaking, or even having the energy to stay awake and interact — can be incredibly hard for her.

PDCD is progressive and unpredictable. Milestones are uncertain, and skills can be lost. Life expectancy varies, but for many children it is shortened, and parents live with the constant fear of metabolic decompensation, illness, or a sudden setback that could change everything.

Our life is measured in moments of stability — and in how quickly those moments can disappear.

Treatments and unmet needs

There is currently no universally effective, FDA-approved cure for PDCD. Some patients may benefit from supportive therapies such as:

- ketogenic diet
- thiamine supplementation
- dichloroacetate (in research or limited use)
- physical, occupational, and speech therapies

These treatments can help manage symptoms for some individuals, but they are not a cure and they do not work for everyone. Many children with PDCD either do not qualify for certain therapies or receive only partial benefit. Even when treatments help, they do not stop the progression of the disease or fully protect the brain from damage.

This leaves huge unmet medical needs for our community.

The Potential of DCA for Children with PDCD

For families in the Pyruvate Dehydrogenase Complex Deficiency (PDCD) community, dichloroacetate (DCA) represents more than a possible treatment — it represents time, stability, and hope.

PDCD prevents the body from properly converting carbohydrates into energy, leading to a dangerous buildup of lactic acid and a constant energy crisis in the brain. This energy failure is what causes the progressive neurological damage that takes skills away from our children and, too often, takes their lives.

DCA targets the core biochemical problem in PDCD. By activating the pyruvate dehydrogenase complex, it helps the body use glucose more effectively and reduces lactic acidosis. In simple terms, it helps restore a pathway that our children's cells desperately need in order to produce energy.

For some children, this could mean:

- improved metabolic stability
- fewer life-threatening lactic acidosis episodes
- better brain energy metabolism
- preservation of developmental skills
- longer survival

This is not just about numbers in a lab result — it is about protecting the brain from ongoing injury.

Every metabolic crisis causes damage that cannot be undone. If DCA can reduce those crises or slow that damage, it has the potential to change the course of the disease. It could mean the difference between a child gaining skills instead of losing them, between repeated hospitalizations and time at home, between decline and the chance to grow.

However, access to DCA has been limited, and families are often left in a position where a scientifically rational and potentially life-saving therapy exists but is not readily available to the children who need it most.

For a progressive disease like PDCD, timing is everything. A therapy that comes years later may come too late for the children who are already losing brain function today.

DCA is not just a treatment possibility — it is a chance to intervene before irreversible damage occurs.

For our children, that chance could mean:

more first words
more first steps
more birthdays

It could mean life.

Challenges and delays in developing treatments

Because PDCD is so rare, research moves slowly. Small patient populations make clinical trials difficult. There are ongoing challenges in determining what type of data is considered sufficient for approval, and families often watch promising therapies remain stuck in the research phase for years.

Every delay — whether from funding, trial design, regulatory requirements, or the need for additional evidence — has real consequences for children like my daughter. While systems move cautiously, our children's disease continues to progress.

We do not have the luxury of waiting.

What time means to us

For our family, time is not measured in years — it is measured in abilities.

In six months, a child with PDCD can lose skills they fought so hard to gain.
In a year, a medical setback can permanently change their future.

Time means:

- the chance to hold on to a skill a little longer
- the possibility of gaining a new word, a new movement, a new smile
- fewer hospitalizations
- more birthdays

Regulatory delays are not abstract to us. They can mean the difference between a child receiving a therapy while it can still help — or receiving it too late.

We are racing a disease that does not slow down.
Our children cannot pause their progression while the world decides what evidence is enough.

For us, time is brain cells.
Time is function.
Time is life.

And that is why urgency matters for the PDCD community.

Laura Ford – February 26th, 2026

**Written Testimony
Huntington's Disease Community Perspective**

Dear Chairman, Ranking Member, and Members of the Committee,

I am the wife and long-term care partner of a man who has been living with Huntington's disease (HD) for nearly fifteen years. I am also a mother and an advocate within the Huntington's disease community. Thank you for the opportunity to submit this statement for the record.

Huntington's disease is a fatal, inherited neurodegenerative disorder caused by a well-characterized mutation in a single gene. Each child of an affected parent has a 50% chance of inheriting the condition. Symptoms most often begin in adulthood and progressively affect movement, cognition, and behavior, ultimately leading to complete dependence and death.

In Juvenile Huntington's disease (JHD), children develop symptoms that can include seizures, loss of speech, loss of mobility, difficulty swallowing, and the need for feeding tubes and full-time care. The burden on families begins early and intensifies quickly.

Our family's HD journey began with my mother-in-law's diagnosis. We supported her through the progression of the disease and cared for her until she passed away, all while my husband was undergoing genetic testing and learning that he also carries the mutation that causes the disease.

Over the years, he has lost a sibling, aunts, uncles, and cousins to this disease, knowing all the while that the disease was coming for him, and possibly for our children as well. Huntington's disease does not impact one individual – it reshapes entire families.

I have watched my capable, vibrant husband gradually lose cognitive clarity, physical coordination, and independence. Our family has suffered employment loss, caregiving strain, medical complexity, and the profound emotional weight of a disease that affects generations. Despite my husband's decline, I have seen him fight to participate in research studies and clinical trials, determined to contribute in any way he could to the search for treatments or a cure. Across nearly two decades we, like so many other families, have steadfastly held onto hope for effective treatments before the next generation gets sick.

But today there still are no approved therapies that slow or stop Huntington's disease progression.

In recent years, research into disease-modifying therapies has brought meaningful hope to our community. Families like mine follow clinical trials closely because science represents the only path forward. We deeply respect the FDA's responsibility to ensure that treatments are safe and effective. Patient safety must remain central to every decision.

At the same time, rare disease research presents unique structural challenges. Huntington's disease affects a relatively small population living with a relentlessly progressive condition. Clinical trial design in this context is complex.

In a small, progressive rare disease population, extended placebo exposure presents both ethical and practical challenges. As objective biological indicators become more refined, they may help verify treatment impact with greater precision. We encourage thoughtful consideration of how these advances can inform trial design while preserving scientific integrity.

For families affected by Huntington's disease, time is not neutral. Decline continues, and lost function cannot be restored. Each year without meaningful progress represents irreversible neurological loss for people living with this disease.

We respectfully ask for:

- Clear and consistent regulatory guidance for rare neurodegenerative diseases
- Transparent communication regarding evidentiary expectations
- Continued incorporation of patient perspectives into benefit–risk assessments
- Regulatory pathways that reflect both scientific rigor and the urgency of progressive, fatal conditions

Huntington's may be one of the most scientifically-understandable neurodegenerative diseases, and the Huntington's disease community has demonstrated its commitment to research participation, scientific advancement, and collaboration that will likely lead to advances across neurodegenerative diseases.

What we're asking for is the support of a regulatory system that maintains high standards while recognizing the realities of rare, inherited, life-limiting diseases that affect children and entire family systems.

Thank you for your attention to rare diseases and to the families who live with them every day.

Laura Ford

Mandi Arlaud – February 27th, 2026

Written Testimony

I was a small child when I first met Jacob. He is an older brother of my childhood best friend, a few years older than us. She and I would spend summers at each other's houses and while at her house Jacob often spent time with us. In those early years, we'd run and play. Tag, hide and seek, swimming, typical kid stuff. As pre teens, Jacob's disease progressed. She and I would swim and Jacob would sit on the deck, chatting with us. We also loved to play computer games, something that didn't require much movement. As teenager girls, we hung out mainly by ourselves but Jacob would still make sure to say hi by driving his scooter to us. Years past and we fell out of touch. We got back together this summer, she and I now 31 and Jacob in his mid 30s. He is confined to his chair, however, that does not define him. He is kind, he is funny, and he is beloved by all who know him. He is also one of the smartest people I have ever met. He has lived beyond what anyone ever thought possible thanks to Ataluren. He has thrived against the odds. And now he faces this challenge, something he shouldn't have to do. This drug has been proved to be safe and effective. You must approve it. You are sending a death sentence to him and so many others if you do not. APPROVE ATALUREN. Approve it now.

Mandi Arlaud

Amy Messigian – February 27th, 2026

Written Testimony

Dear Senator Johnson and Senator Scott,

Thank you both for your leadership and for taking part in the recent Senate Special Committee on Aging hearing, "From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation." I was honored to be a guest of Dr. Schmahmann at the hearing and sincerely appreciate your attention to the ways FDA regulatory processes affect patients with rare diseases and their families.

I live with spinocerebellar ataxia type 1 (SCA1), a rare, progressive, and fatal neurodegenerative disease. There are no FDA-approved treatments. I was diagnosed in my 30s, and I watched this disease take my mother's life at just 60 years old. SCA1 slowly robs individuals of balance, speech, motor control, and independence. Every year that passes with preserved function is precious — not abstract — time with family, ability to work, mobility, and dignity.

Since 2017, I have participated in a clinical trial and expanded access program for an investigational medication called troriluzole. It does not cure SCA1, but it has meaningfully slowed my decline. In a condition where patients typically accumulate one to two points of functional loss per year and experience steep deterioration within five years, I did not reach that inflection point for nearly a decade. This is time I otherwise would not have had. I have no side effects and continue to live independently.

During the hearing, expert testimony — including from Dr. Jeremy Schmahmann — underscored a critical truth: in relentlessly progressive neurodegenerative diseases, slowing functional loss is itself a clinically meaningful outcome. Measures like balance, coordination, and speech aren't abstract endpoints; they define real independence and quality of life.

Unfortunately, the [Food and Drug Administration](#) declined approval of troriluzole last year, citing a need for additional data, which in rare diseases is extremely hard to generate due to small patient populations and the nature of progressive decline. Patients like me are left in limbo, and expanded access programs that provide treatment while regulatory pathways are clarified can be jeopardized.

One idea reportedly discussed — taking patients off a medication like troriluzole to observe how rapidly they deteriorate — would have real human consequences. With a progressive neurodegenerative condition, lost function is not typically regained. If I were withdrawn from treatment that has safely preserved my abilities for years, I could lose abilities permanently. Neurons that degenerate do not regenerate. Asking patients to discontinue a treatment that has demonstrated safety and slowed decline in order to generate additional regression data would not be scientifically neutral — it would risk irreversible loss of independence, mobility, and quality of life.

Senator Johnson, your long-standing advocacy for patients' access to experimental treatments — including championing the federal Right-to-Try law — emphasizes that people facing terminal or degenerative illnesses deserve the ability to try promising therapies rather than wait years for approval. Your work helping pass the federal Right-to-Try Act reflects a commitment to giving patients hope and access to treatments when traditional pathways are too slow.

Senator Scott, as Chair of the Senate Special Committee on Aging, your focus on how regulatory processes impact patient access and innovation has helped bring this issue into a forum where patient voices and expert testimony are heard. The Committee's examination of how regulatory clarity and predictability can help ensure that safe, effective therapies reach patients faster is deeply important to individuals with rare diseases and their families.

I respectfully ask that the Committee translate the concerns raised during the hearing into concrete oversight actions. Specifically:

- Request a written explanation from the FDA within 30 days clarifying how it applies rare disease flexibility standards in progressive, fatal neurodegenerative diseases.
- Seek formal clarification on whether requiring stable patients to discontinue long-term treatment in order to demonstrate deterioration is considered ethically appropriate in irreversible conditions.
- Convene a follow-up briefing with FDA leadership focused specifically on small-population neurodegenerative diseases and the use of real-world evidence.
- Ensure that patients currently benefiting from expanded access programs are not forced into treatment interruption while regulatory pathways are being debated.

The hearing made clear that rare disease patients face unique structural barriers. Oversight is essential — but its value will be measured by whether it produces meaningful regulatory accountability. I respectfully ask that your offices inform patients and stakeholders what specific steps will follow this hearing.

Thank you again for your time, leadership, and willingness to examine how regulatory decisions affect patients and families living with rare diseases. Your involvement brings attention to an issue where delay has real human costs — and patients like me are grateful to have our voices heard.

Shannon Schlachter – February 27th, 2026

Written Testimony

To whom it may concern,

I am writing this statement because I am a 47 year old female who was diagnosed with SCA a little over a year ago. My mother had the disease and my brother was diagnosed three years ago.

Living a long, productive life is important to me. I have been married for over 20 years and I have two teenage sons. I currently work as a high school social studies teacher and have held that position for over 20 years. I walk and talk in front of over 100 teenagers on a daily basis and I already feel my body deteriorating. I would like to continue to teach for many years, but I am worried my body won't let me.

Treatment is a priority. I currently take Troriluzole and I have noticed a tremendous difference with my walking and speech. My doctor has also noted my improvement. It breaks my heart that the FDA has not approved a drug that has proven beneficial. Approval of Troriluzole would provide hope to a very scary future.

I cannot even begin to think about the possibility of my children receiving a diagnosis. Unfortunately this could be a reality. I can only hope that if that day comes there will be treatments. Please approve any new treatments, especially drugs that could help. Thank you.

S. Schlachter

Ken & Cathy Jo Gunvalson – March 1st, 2026

Written Testimony

Our nephew Jacob was diagnosed with DMD as a preschooler and accepted into a trial for the drug Ataluren. It has been a life changing drug that enabled him to graduate from college with a Master's degree in social work and share his skills while working with high school students. Without Ataluren, Jacob would not have survived or succeeded for the past 34 years. This is the only drug currently available that treats the decline associated with a premature stop codon.

We ask that you please reconsider the FDA denial of Ataluren for use by patients with DMD. Real-world data—Jacob's life story—supports this drug's effectiveness over the past 20 years.

Ken and Cathy Jo Gunvalson

Jennifer Handt – March 2nd, 2026

Written Testimony

Dear Chairman Scott, Ranking Member Gillibrand, and Members of the Committee,

The Little Hercules Foundation (LHF) appreciates the Senate Committee on Aging's focus on FDA regulatory processes and the critical barriers that prevent patients from accessing life-saving innovations. We submit this testimony on behalf of families fighting Duchenne muscular dystrophy (DMD) and other rare genetic diseases to highlight a paradox at the heart of our healthcare system, one that is central to LHF's mission: the FDA and HHS have made historic progress in expediting the approval of rare disease therapies, yet patients still cannot access these approved treatments.

The missing link we wish to highlight is not FDA approval; it is payer access. Without private insurance and Medicaid coverage, FDA approval becomes a cruel promise—a therapy that has made it through the scientific goalposts but remains out of reach for patients and families. We would like to take this opportunity to underscore the payer barriers that prevent the FDA's innovation efforts from fully benefitting patients, and highlight how state policy choices leave patients behind, even as science moves forward.

Along with other rare disease advocates, we applaud FDA efforts to more urgently bring desperately needed therapies to waiting patients, including the Framework for Accelerating Development of Individualized Therapies announced just this week. At the same time, we urge this committee to recognize that expedited FDA approval is only the first step. Congress and HHS must work in partnership to ensure that payer policies—particularly at the state Medicaid level—do not become the new regulatory bottleneck that defeats the purpose of innovation.

FDA Progress Only Matters if Patients Can Access Treatments

The FDA deserves credit for advancing rare disease policy and for utilizing pathways such as Breakthrough Designation, Fast Track Review, and Accelerated Approval to bring life-saving therapies to patients faster. In recent years the Accelerated Approval pathway has helped to increase the number of approved DMD therapies to eight. One of those therapies is Elevidys, the first gene therapy for DMD, which was approved under the Accelerated Approval in 2023.

For Duchenne families, this was a watershed moment, as evidence has shown that Elevidys can meaningfully slow disease progression. DMD is a uniformly devastating, 100 percent fatal disease that robs patients (mostly male) of their ability to walk in their teens; ultimately, it robs them of their lives in young adulthood. After decades of watching their children lose muscle and independence, with Elevidys' approval families finally had hope that science could rewrite a devastating disease trajectory.

This hope rapidly collided with reality. Immediately following FDA approval, both state Medicaid programs and private insurers began denying coverage. The barrier was not efficacy, not safety, not the rigor of the clinical trial, but payer policy, which continues to put families—who vary widely in their health literacy and access to resources—in endless cycles of denials and appeals. These policies and determinations put these

families in lopsided David-and-Goliath battles with commercial insurance behemoths and state-run agencies in order to access therapies determined by FDA to be safe and effective.

New York's Elevidys Denial: When FDA Approval Meets Medicaid Roadblocks

In October 2025, the New York Department of Health made a decision that exemplifies this payer-access

crisis: it recommended against coverage for Elevidys under Medicaid, despite the FDA's expanded approval of the therapy for all patients ages 4 and older who are able to walk. This life-altering determination was not made by the FDA or by treating physicians. It was made by a state payer, proxied by a Drug Utilization Review Board (DURB), a state payer body with no clinical expertise in rare genetic disease. It threatens to deny access to the only FDA-approved gene therapy for DMD patients in New York State receiving Medicaid.

The FDA's expansion of Elevidys approval to patients 4 and older was based on rigorous review of clinical data demonstrating the therapy's ability to stabilize or improve motor function and slow irreversible disease progression. The FDA determined that the benefits—including prevention of mobility loss in boys at critical developmental ages—outweigh the risks based on the well-characterized safety and efficacy profile. This represented the FDA's expert judgment that the clinical evidence was sufficiently robust to expand access.

Yet the New York DURB recommended against coverage, disregarding the FDA's expert judgment and the clinical evidence the agency weighed. This position directly contradicts New York's stated commitment to healthcare innovation and patient-centered policy. The DURB's recommendation fails to acknowledge that Elevidys is not experimental—it is an FDA-approved therapy, the first and only approved treatment of its kind for Duchenne. By allowing a state advisory board to second-guess the FDA's clinical determination, New York has effectively converted FDA approval into a payer recommendation, not a guarantee of access.

The result is a crisis of access. New York families testified before the DURB with candor about their lived experience—the relentless progression of Duchenne, the daily challenges their children face, and their profound need for access to FDA-approved treatments. Yet the DURB's recommendation disregards those patient voices and the clinical evidence alike. A boy born with DMD in New York today cannot access Elevidys through Medicaid. A boy born blocks away in New Jersey can. For Duchenne families, timely access to approved therapies is not a matter of convenience—it is essential. Every month of delay, while disease irreversibly progresses, is a month lost. The window for intervention closes and the opportunity for this child is gone forever.

The DURB's recommendation also represents an inappropriate exercise of state authority under federal law. The Social Security Act Section 1927 (SSA 1927) requires states to cover FDA-approved drugs with rebate agreements for their medically accepted uses. Elevidys has an FDA-approved label for ambulatory children 4 and older with Duchenne. A state Medicaid program's pause or denial of coverage directly violates this federal requirement. New York's DURB recommendation, if it is upheld, would place the state in violation of federal law—not merely a policy disagreement with the FDA, but a violation of the Medicaid statute itself.

Accelerated Approval Is Weaponized Against Access

New York's Elevidys denial is not an isolated incident. Across the country, payers are using Accelerated Approval status as a blanket rationale to deny coverage, label therapies as experimental, and refuse reimbursement until confirmatory trials are complete. This represents a fundamental misunderstanding—in some cases, deliberate misuse—of FDA policy.

The FDA's Accelerated Approval program exists precisely because some patients cannot wait for traditional approval timelines. For fatal genetic diseases like DMD, waiting 5-10 years for confirmatory trial data while the disease progresses means losing the biological window for intervention. Early-stage boys who could benefit from gene therapy will be too advanced in disease when confirmatory data arrives. Accelerated Approval was created to solve this problem.

When payers use Accelerated Approval as grounds to deny access, they nullify the FDA's clinical judgment and impose their own additional gatekeeping layer. For DMD specifically, this is unconscionable. Once a boy reaches his mid-teens, the window for therapeutic efficacy begins to close. Disease progression becomes irreversible. Every month of delay—not due to science, but due to payer denials—costs families irreplaceable time. In recent years, FDA has moved with appropriate urgency. Payers are moving in the opposite direction.

The Structural Problem: Payer Coverage Gaps in Rare Disease

The Elevidys denial in New York illustrates a broader structural problem: there is no coordinated mechanism to ensure that payer policies align with FDA's innovation objectives for rare diseases. State Medicaid programs make independent coverage decisions with no requirement to consider the clinical urgency of a condition, the rarity of alternatives, or the time-sensitive nature of early intervention.

In rare diseases, the stakes are high: Patients have no alternatives. They cannot switch to a competitor product or try a different treatment. For DMD, if a boy misses the window for gene therapy because his state Medicaid program denied coverage, that opportunity is lost forever. Unlike common diseases where delayed access to one drug still leaves other options, rare disease patients often have access to one therapy alone.

Additionally, payers cite cost as a rationale to deny rare disease therapies—therapies with one-time or limited treatment populations. Yet the cost of a gene therapy that may halt disease progression is economically justified when compared to decades of supportive care, wheelchair use, ventilator dependency, and cardiac monitoring. Payers are making these determinations without transparent health economic analysis or patient input.

The committee should understand: FDA approval means nothing to a patient if their payer denies coverage. The FDA cannot compel coverage, but HHS can.

Recommendations to Congress and HHS

To address the payer-access crisis in rare disease, we urge the Congress and HHS to

take the following steps:

1. Establish clear federal guidance that Accelerated Approval does not justify coverage denial.

CMS should issue guidance explicitly prohibiting state Medicaid programs and private insurers from using FDA Accelerated Approval status as grounds to deny or delay coverage. Accelerated Approval reflects FDA's clinical judgment that benefits outweigh risks based on available evidence. Payers should defer to that judgment, especially in life-threatening rare diseases where delays are irreversible.

2. Require state Medicaid programs to align payer policy with FDA orphan drug and rare disease designations.

When a drug receives FDA Breakthrough Designation or Orphan Drug designation for a rare disease, state Medicaid programs should have a presumption of coverage unless there is compelling clinical evidence of harm or inefficacy. Payer coverage policies should not impose a higher standard of evidence than the FDA itself requires. This would ensure that FDA and HHS policy objectives are not undermined by state-level gatekeeping.

3. Establish a federal review mechanism for state Medicaid denials of rare disease therapies.

A CMS pathway for patients and providers to appeal state Medicaid coverage denials of FDA-approved rare disease therapies could prevent a patchwork of coverage across states and ensure that a child's access to treatment does not depend on their geography. New York's Elevidys denial should trigger federal review; such a consequential decision about patient access to a rare disease therapy should not rest with a single state payer without federal oversight.

4. Include patient representatives in state Medicaid coverage decisions for rare diseases.

5. Coverage decisions that affect whether children with life-threatening rare diseases can access the only available therapy should not be made by actuaries and administrators alone. State Medicaid programs should be required to convene patient and clinician input in coverage deliberations for orphan drugs and rare disease therapies. These voices understand the clinical urgency and stakes in ways that generic payer reviews cannot. Include patient representatives in state Medicaid coverage decisions for rare diseases.

Coverage decisions that affect whether children with life-threatening rare diseases can access the only available therapy should not be made by actuaries and administrators alone. State Medicaid programs should be required to convene patient and clinician input in coverage deliberations for orphan drugs and rare disease therapies. These voices understand the clinical urgency and stakes in ways that generic payer reviews cannot.

The FDA and HHS have earned credit for advancing rare disease policy and expediting

access to promising new therapies. But that progress is being undermined by payer coverage denials that occur after FDA approval and with no federal oversight. When a state Medicaid program can deny access to an FDA-approved gene therapy for a fatal disease of childhood, the payer system has become the new regulatory bottleneck.

New York's denial of Elevidys coverage demonstrates the urgency of this problem. But it is not unique. Across the country, families face similar barriers. A child's access to a life-saving therapy should not depend on whether their state's Medicaid program agrees with the FDA's clinical judgment.

Congress has the authority and responsibility to act. We urge this committee to pursue the recommendations outlined above to align payer policy with FDA innovation efforts and ensure that expedited approval translates into expedited patient access. For children with rare genetic diseases, time is not an abstract policy concern—time is life itself.

Thank you for this opportunity to contribute to the

record. Sincerely,

Kelly Maynard,
President Little
Hercules Foundation

Paige Gustavo – March 2nd, 2026

Written Testimony

To the people who are deciding on my cousins life:

My amazing, intelligent, and funny, cousin, Jacob, was diagnosed with DMD as a preschooler and accepted into a trial for the drug Ataluren. It has been a life changing drug that enabled him to graduate from college with a Master's degree in social work and share his skills while working with high school students. Without Ataluren, Jacob would not have survived or succeeded for the past 34 years. This is the only drug currently available that treats the decline associated with a premature stop codon.

I ask that you PLEASE reconsider the FDA denial of Ataluren for use by patients with DMD. Real-world data—Jacob's life story—supports this drug's effectiveness over the past 20 years.

This drug matters. His life matters.

Paige Gunvalson

Jason Rodriguez – March 2nd, 2026

Written Testimony

Dear Special Senate Committee on Aging,

Every year matters when a child is living with Duchenne muscular dystrophy, because once abilities are lost to this disease, they can never be regained.

My nephew Benjamin lives with Duchenne, a fatal rare disease that progressively destroys muscle and significantly shortens life expectancy. Boys with Duchenne gradually lose the ability to walk, develop serious breathing complications, and eventually require full-time care. Benjamin is now 13 years old and has been taking the investigational therapy Ataluren (Translarna) for more than nine years through a clinical study. Today, he continues to outperform many untreated boys his age on physical assessments and remains partially ambulatory, relying on a scooter only during periods of fatigue. His physicians consistently report that his muscle strength, mobility, bone health, and pulmonary function remain stronger than typically expected for someone with Duchenne, and they believe Ataluren is helping slow the progression of his disease.

Clinical trials involving hundreds of patients worldwide—including large randomized, double-blind Phase 3 studies—have shown that Ataluren can delay loss of ambulation by approximately four years and slow pulmonary decline by about two years compared to untreated patients. For families facing Duchenne, those additional years are profoundly meaningful. More time with the ability to walk, breathe more easily, and remain independent significantly improves quality of life. The therapy has also demonstrated a favorable safety profile and is already approved for use in more than 50 countries.

Despite this evidence and the urgent unmet medical need, the U.S. Food and Drug Administration has not approved Ataluren for patients in the United States. Decisions and delays in the regulatory process for rare disease therapies have real and irreversible consequences for families like ours. Duchenne is relentlessly progressive. Within six months to a year, a boy can permanently lose the ability to walk, climb stairs, or maintain lung function. Once these abilities are lost, they cannot be regained.

For Benjamin and thousands of other families facing Duchenne, time is measured in preserved abilities, independence, and precious years of mobility. For Benjamin, treatments that slow this disease are not theoretical—they determine how long he can walk, breathe independently, and live life as a child rather than a patient. As the Senate examines the role of the FDA in rare disease drug development, we respectfully ask that the real-world impact of regulatory delays on patients with limited treatment options be fully considered. For children like Benjamin, every year—and every function preserved—matters.

Thank you,

Jason Rodriguez

Nicholas Stuber – March 2nd, 2026

Written Testimony

To the people who are deciding on my cousins life:

My amazing, intelligent, and funny, cousin, Jacob, was diagnosed with DMD as a preschooler and accepted into a trial for the drug Ataluren. It has been a life changing drug that enabled him to graduate from college with a Master's degree in social work and share his skills while working with high school students. Without Ataluren, Jacob would not have survived or succeeded for the past 34 years. This is the only drug currently available that treats the decline associated with a premature stop codon.

I ask that you PLEASE reconsider the FDA denial of Ataluren for use by patients with DMD. Real-world data—Jacob's life story—supports this drug's effectiveness over the past 20 years.

This drug matters. His life matters.

Nick Stuber

Joseph 高杰 Gunvalson – March 2nd, 2026

Written Testimony

To the people who are deciding on my cousins life:

My cousin, Jacob, was diagnosed with Duchenne's Muscular Dystrophy when we were both young. I still remember seeing the heartbreak my aunt and uncle went through upon learning about his future as an individual diagnosed with the disease. Throughout nearly his entire life, he has persevered through trial after trial so that he could live as normal a life as possible. In spite of it all, he has been able to graduate from college with a Master's degree in social work; giving him the opportunity to share his unique life experience with high school students. None of this would have been possible without Ataluren. Jacob would not have survived or succeeded for the past 34 years; this is the only drug currently available that treats the decline associated with a premature stop codon.

Real-world data supports this drug's effectiveness over the past 20 years. By choosing to deny Ataluren for use by patients with Duchenne's Muscular Dystrophy you are condemning my cousin and many others. I am pleading with you to reconsider this decision.

Joseph 高杰 Gunvalson

Corby Legault – March 3rd, 2026

Written Testimony

Chairman, Ranking Member, and Members of the Committee:

Thank you for the opportunity to submit this statement for the record.

I am the husband of Amy Messigian, who lives with spinocerebellar ataxia type 1 (SCA1), a rare, hereditary, progressive, and fatal neurodegenerative disease. I offer this statement not as a scientist or policymaker, but as a spouse who witnesses firsthand the human consequences of regulatory decisions.

SCA1 slowly robs individuals of balance, coordination, speech, swallowing, and ultimately independence. There are currently no FDA-approved treatments for this disease.

Amy was diagnosed in her 30s. Before that diagnosis, we watched this same disease take her mother's life at just 60 years old. We know what untreated progression looks like. We know where this disease leads.

In 2017, Amy enrolled in a clinical trial for an investigational medication, tririluzole. It is not a cure. It does not reverse the genetic mutation that causes SCA1. But it has meaningfully slowed her decline.

In a disease where patients typically worsen year after year and experience steep deterioration within several years, Amy's expected trajectory was delayed for nearly a decade. She remains ambulatory. She continues to work. She lives independently. She has experienced no side effects.

As her husband, I see what preserved function actually means. It means she can climb the stairs in our home. It means she can walk beside me without constant fear of falling. It means she can speak clearly enough to be understood in conversation. These are not abstract clinical endpoints. They are daily realities.

Last year, the Food and Drug Administration declined to approve tririluzole, citing the need for additional data. I understand the importance of rigorous standards and patient safety. However, rare diseases like SCA1 present structural challenges: small patient populations, irreversible progression, and limited trial enrollment capacity.

One proposal reportedly discussed — withdrawing stable patients from treatment in order to observe deterioration — would carry profound personal consequences for families like mine.

SCA1 is not episodic. It is progressive and irreversible. Neurons that degenerate do not regenerate. If Amy is removed from a medication that has safely preserved her function for years and she deteriorates, there is no guarantee that lost abilities will return. The independence she has fought to maintain could be permanently lost.

From a clinical standpoint, deterioration may be data. From a family's standpoint, it is loss.

In progressive neurodegenerative disease, treatment withdrawal is not a neutral scientific exercise. It is an ethical decision with potentially irreversible consequences.

I respectfully urge the Committee to consider the following:

1. Ensure that rare disease flexibility tools are applied consistently in progressive, fatal conditions with no approved alternatives.
2. Seek clarity from the FDA regarding ethical standards governing treatment withdrawal in irreversible diseases.
3. Support regulatory pathways that allow meaningful functional outcomes and real-world evidence to inform approval decisions in small patient populations.
4. Protect patients currently receiving therapy through expanded access programs from forced treatment interruption while regulatory deliberations continue.

For families like ours, time is not theoretical. Every year of preserved function is another year of independence, dignity, and shared life. Regulatory processes should reflect the reality that in progressive diseases, delay has consequences that cannot be undone.

Thank you for your attention to this issue and for considering the lived experience of patients and families when evaluating regulatory policy.

Corby Legault

Lourdes Campos – March 3rd, 2026

Written Testimony

Dear Senator Scott,

I have been a Florida resident for most of my life and lived here when you were Governor. I appreciate you fighting for us especially when it comes to rare diseases and as you may know most treatments are very expensive and they just sustain us. I have CVID, Common Variable Immunodeficiency and require weekly infusions to help keep my IGG levels but there is no cure. I do not go out in public very much and only am able to visit my grandkids if they are healthy.

Please keep fighting for us!

Lourdes Campos

Nadia Amokrane – March 3rd, 2026

Written Testimony

Chairman, Ranking Member, and Members of the Committee:

Thank you for holding the February 26 Senate hearing on regulatory roadblocks at the FDA for rare disease applications. I left that hearing moved by the bipartisan recognition that rare disease communities cannot afford regulatory unpredictability and unnecessary delay.

I am a clinical research coordinator at an academic medical institution that enrolled patients in both a natural history study and the pivotal clinical trial that generated the clinical data for a therapy intended to treat a rare ataxia. Over more than six years, I worked closely with patients, with the National Ataxia Foundation, and with Biohaven Pharmaceuticals. My work on these studies was audited by the FDA, and the agency's letter reported no findings regarding my conduct or the data collection processes. I enrolled 28 patients in the interventional clinical trial and have enrolled more than 100 patients in an observational "real-world" study.

Because of this role, I have been entrusted with an unusual and deeply personal body of qualitative information—what it looks like, in real life, when the system works and when it doesn't. I have watched families try to navigate eligibility rules, travel burdens, and study requirements while a progressive disease continues to take loved ones. I have enrolled siblings where one qualified and one did not. I have watched patients who did not make it into the trial deteriorate and die, while those in the trial often declined more slowly—and then carried profound survivor's guilt because they received access while a sibling, parent, or child did not. I have sat with grandparents and parents begging to understand why a 17-month-old child could not access a potentially meaningful therapy. Every time a patient dies, the only thing that steadies me is believing their sacrifice—the monthly visits, the blood draws, the questionnaires, the unknown risks, and sometimes placebo—was not in vain.

I respect the FDA's responsibility to be careful, consistent, and scientifically rigorous. I also recognize that pharmaceutical companies are businesses. But my experience has shown that scientific rigor and humanity are not mutually exclusive—and that responsible sponsors can respond to patient needs in ways that support both safety and study integrity. One example stays with me: an 18-year-old participant entered the trial with limited resources while her grandmother, father, older brother, and younger sister all lived with the same diagnosis. Within a year, she lost her grandmother, father, brother, and sister to the disease. Understandably, she began to struggle with depression. In response, Biohaven provided additional support funding so our institution could offer mental health counseling—helping protect her wellbeing, maintain consistent follow-up and safety monitoring, and allow her to remain in the study. That is what ethical, patient-centered development can look like. At the same time, I have learned that critical information does not flow equally to the people who need it most. Academic institutions work hard to honor IRB requirements and patient trust. But strict communication constraints can unintentionally limit how well patients can advocate for themselves, understand timelines, and meaningfully participate in the regulatory process—especially when FDA actions shift abruptly.

This brings me to my request.

I urge the FDA to reconsider and/or provide an immediate, transparent, fair, and consistent re-review of the rare ataxia application(s) that, beginning in July 2025, resulted in the cancellation of an advisory committee that had been scheduled, followed by issuance of Complete Response Letters that appeared to contradict prior FDA discussions and expectations communicated by agency leadership. If an advisory committee was warranted enough to schedule, the public deserves a clear

explanation for why it was canceled—and the patient community deserves the opportunity for that expert, transparent forum to occur.

My specific asks are:

1. Reinstate (or promptly convene) the advisory committee that was canceled, with a public explanation of the scientific questions the FDA believes remain unresolved and how patient experience and unmet need are being weighed.
2. Ensure a consistent, documented, cross-division FDA position on the evidentiary standards being applied—so sponsors, investigators, and families are not harmed by shifting expectations late in the process.
3. Provide greater transparency to the rare disease community about what data would be sufficient for approval or accelerated approval pathways, including how real-world evidence and natural history data are being considered in diseases where traditional trials are exceptionally difficult.

The consequences of inconsistent and unpredictable FDA actions in this space are not abstract. They are irreversible. They affect whether families believe the system is trustworthy enough to volunteer for research at all. They influence whether companies will invest in rare disease programs where patient populations are small and trials are burdensome. If sponsors cannot rely on a transparent and stable regulatory process, the incentive to pursue these therapies will shrink. The ripple effects could include reduced investment in the ataxia community, reduced funding and capacity for patient foundations, and a devastating erosion of trust among patients who gave years of their lives to research with the belief that their data would receive a fair and equitable review.

I care deeply about every patient who comes to our institution—especially those who volunteer for clinical research with known and unknown risks. They agree to strict protocols, travel demands, medication restrictions, lifestyle changes, additional procedures, and constant reporting. They do it because they believe the regulatory system will listen, evaluate the evidence fairly, and act consistently. If they come to believe that participation is futile—or that decisions are opaque and unpredictable—patients will stop enrolling. And without patients, there is no research and no progress.

Please do not allow these patients' sacrifices to be for nothing. The ataxia community deserves transparency, consistency, and the fair process that was promised—including the advisory committee that was scheduled and then canceled without explanation. I respectfully ask this Committee to continue its oversight and urge the FDA to provide an equitable re-review and a clear public accounting of its decision-making.

Thank you for the opportunity to submit this statement for the official record.

Kindly,

Nadia Amokrane, B.A.
 Senior Clinical Research Manager
 Movement Disorders Division, Department of Neurology
 Vagelos College of Physicians and Surgeons, Columbia University

Parna Mukherjee – March 3rd, 2026

Written Testimony

I was born with SCA (Spino Cerebellar Ataxia) type 2 from my father's side of the family. I started showing symptoms around 40 and was formally diagnosed at Columbia university at 2020, when I was 50 years old. Also at that point I was very excited to enter the first ever disease modifying Biohaven's drug trial of BHV 4157 200 mg. The first year was double blind and I received the medication from October 2021 onwards. I had no side effects to the medication. SCA (Spino Cerebellar Ataxia) is a dreadful progressive neurodegenerative disease which slowly robs you of all abilities- gait (drunken gait), choking, slurring, writing, eating, cognition and basically everything you can think of. Currently there is no medicine to cure the condition or to slow the progression of the disease; in fact BHV 4157 is the very first disease modifying medicine which slows down the progression of the disease. For patients like me, it is deeply discouraging to see this therapy not approved despite the urgent unmet need and the profound consequences of untreated progression. I respectfully urge you to approve BHV-4157 as soon as possible so that patients may access a therapy that could meaningfully slow decline and preserve function for as long as possible.

Melanie Santos – March 3rd, 2026

Written Testimony

I am a born and raised New Yorker and a constituent of Brooklyn, New York City. I teach movement, yoga, meditation, and somatic practice to communities virtually and around the world. My work lives entirely in my ability to stand, move, speak, demonstrate, and be physically present for the people I serve. My work is not just what I do, but how I serve and who I am.

My grandmother was a gifted seamstress whose hands were her livelihood and her art, until Spinocerebellar Ataxia Type 3 (SCA3), a neurodegenerative genetic disease, took them from her. My mother was an early childhood educator who changed lives in inner city classrooms every day for decades, until she physically couldn't. She was diagnosed with SCA3 in 2020 and is now clinically disabled.

In March of 2024, my life changed forever when I received the same diagnosis they did a few months shy of my 35th birthday.

The diagnosis did not land as a medical fact, but as a future I could already see for myself because I had spent my entire life watching this disease take everything from the people I love most. Taking their work, their lives, their independence, and their ability to simply exist in their bodies without limitation.

SCA3 is progressive, but less than two years after my diagnosis, I am already living that truth. My balance and coordination are no longer things I can assume, so I modify what I teach and how I demonstrate it. On camera, I manage my body carefully so that the communities I serve cannot see the effort it takes to simply be still. I am adapting constantly in ways invisible to most people but present to me every single day.

This is what early progression looks like from the inside in a disease that does not plateau or reverse. And that careful calculation lives in everything.

I am a young woman who cannot consider moving into a new home without factoring in ADA accessibility, because I do not know how quickly this disease will progress in my body compared to how it moved through my mother's, or my grandmother's. It lives in how I structure my life, in what I commit to, in how I think about my daughter's future and my own. Losing my ability to live a full life is not a distant fear because its happening more and more every single day.

My daughter is eight years old. She does not know about my diagnosis. She does not know there is a 50 percent chance that she carries this gene mutation and could also have SCA3. Right now she knows me as someone who moves through the world with care, intention, and strength, and I am doing everything in my power to stay that way for her and my family. But I cannot do it on will alone. I need access to treatment that can slow what is coming, because I have watched what comes.

There is a medication that can help. Troriluzole, developed by Biohaven, demonstrated a 50 to 70 percent slowing of disease progression in clinical trials, representing a year and a half to two additional years of life before the disease advances to its next stage.

I have seen this with my own eyes as my mother was a participant in the Biohaven clinical trial. She was told she could be in a wheelchair by now, and she is not. The medication has slowed her progression in ways our family did not dare to hope for. It gives me hope I couldn't have dared to

hope for. For me, being able to take that medication means time with my daughter during the years she needs me most. It is time to remain present, capable, and myself.

In November 2025, the FDA declined to approve Troriluzole, citing concerns about the use of real-world evidence and external controls in the trial design. A decision that was simply procedural for them is completely life-altering for us.

I understand that the approval process exists to protect people. But the researchers and physicians dedicated to helping those with this disease built the strongest evidence they could with what they had. It showed real, meaningful results, and was rejected on procedural grounds while patients continue to progress. The leading ataxia experts in the country wrote to the FDA six times between 2023 and 2025. They never received a response.

The denial of this medication is not an abstraction for me. It is the difference between a life that stays somewhat my own and a life this disease reshapes entirely. Every month without treatment is a month of irreversible neurological damage because ataxia does not pause while a regulatory process works through its concerns.

This committee held this hearing because you believe patients deserve better. I am here because I am one of them.

There is an urgency to this that cannot wait. Right now, nearly 300 patients who have been stable on Troriluzole through a compassionate use program — my mother being one of them — are being forced off the only medication that has helped them because of this denial.

What the estimated 20,000 people in this country living with spinocerebellar ataxia and I are asking for is not extraordinary. We are asking for access to something that is already working, already changing lives, and already giving people and families like mine a sense of hope we did not think we were allowed to have. This committee has the authority to make that happen. We are asking you to use it.

Respectfully,

A Constituent Living with SCA3

Julie Thrift – March 4th, 2026

Written Testimony

Dear Chairman, Ranking Member, and Members of the Committee,

I am submitting this statement as a caregiver, family member, and longtime advocate in the Huntington's disease (HD) community. My brother-in-law has been living with devastating symptoms of HD for nearly fifteen years. I am also an aunt to his children, including a niece who is at risk for this disease. Thank you for the opportunity to submit this statement for the record.

Huntington's disease is a fatal, inherited neurodegenerative disorder caused by a well-characterized mutation in a single gene. Each child of an affected parent has a 50% chance of inheriting the condition. Symptoms most often begin in adulthood and progressively affect movement, cognition, and behavior, ultimately leading to complete dependence and death. In Juvenile Huntington's disease (JHD), children develop symptoms that can include seizures, loss of speech, loss of mobility, difficulty swallowing, and the need for feeding tubes and full-time care. The burden on families begins early and intensifies quickly.

I have been involved in supporting and advocating for the HD community for fifteen years. In that time, I have accompanied my sister and brother-in-law to HD clinic appointments when his symptoms made it impossible for her to go alone. I have watched a capable, vibrant man gradually lose cognitive clarity, physical coordination, and independence. I have watched my sister carry burdens that no family should face without the hope of effective treatment. And I look at my niece, a young woman who does not yet know what her future holds, and I feel the urgency of this moment deeply. Huntington's disease does not impact one individual. It reshapes entire families, across generations. There are currently no approved therapies that slow or stop HD progression.

I believe strongly in American innovation, in science-driven solutions, and in the capacity of our regulatory institutions to serve patients well. The FDA has publicly committed to using the full regulatory flexibility available to it to accelerate the development of therapies for rare diseases. The HD community welcomes that commitment and asks this Committee to help ensure it is honored consistently, transparently, and with urgency.

At the same time, rare disease research presents unique structural challenges that require thoughtful regulatory engagement. Huntington's disease affects a relatively small population living with a relentlessly progressive condition. Clinical trial design in this context is genuinely complex.

In a small, progressive rare disease population, extended placebo exposure presents both ethical and practical challenges. Asking patients to forgo potential treatment while neurological decline continues for months or years is not a neutral scientific choice. It is a decision with real and irreversible consequences. As objective biological indicators become more refined, they can help verify treatment impact with greater precision, potentially reducing the burden on patients in control groups while maintaining scientific rigor. We encourage thoughtful consideration of how these advances can inform trial design.

For families affected by Huntington's disease, time is not neutral. Decline continues, and lost function cannot be restored. Each year without meaningful progress represents irreversible neurological loss. We respectfully ask for:

- Clear and consistent regulatory guidance for rare neurodegenerative diseases
- Transparent communication regarding evidentiary expectations
- Continued incorporation of patient perspectives into benefit-risk assessments

- Regulatory pathways that reflect both scientific rigor and the urgency of progressive, fatal conditions

Huntington's disease may be one of the most scientifically well-characterized neurodegenerative diseases. The genetic cause is known. Biological markers of progression are advancing. The HD community has demonstrated sustained commitment to research participation, scientific collaboration, and partnership with regulators and policymakers. Progress in HD has the potential to illuminate pathways for other neurodegenerative diseases as well.

What we are asking for is a regulatory system that maintains the highest standards of safety and scientific integrity while recognizing the realities of rare, inherited, life-limiting diseases, including those that affect children and reshape entire family systems across generations.

I am writing this because I love my family. I am writing this because I have spent fifteen years watching what this disease takes. And I am writing this because I believe our institutions can and should do better for families like mine.

Thank you for your attention to rare diseases and to the families who live with them every day.

Respectfully,

Julie Thrift
Mechanicsville MD
Sister-in-law, caregiver, and HD advocate

Emily Messigian – March 4th, 2026

Written Testimony

I am writing this message as a daughter and a sister of someone impacted by a rare genetic disease. I'm also a mother of a young child with another rare genetic disease.

My mother died from spinocerebellar ataxia type 1 (SCA1) in 2011, at 60 years old. I watched a strong, independent woman gradually lose her balance, her speech, her independence, her ability to swallow, and ultimately her life to a disease that offered no cure and no FDA approved treatment. Today, my sister, is fighting that same debilitating, hereditary disease.

SCA1 is a rare, progressive neurodegenerative disorder. It impacts a persons coordination, speech, mobility, and the ability to perform the most basic daily tasks. Things like taking a shower or eating a meal can be a challenge.

In 2017, my sister, enrolled in a clinical drug trial. The purpose of the drug was to slow the progression of SCA1. And it has done that for my sister. What's even more amazing, it's done this with no negative side effects for her.

Last year, the FDA, declined the drug, citing additional data was needed. Safety measures for approving medicines is important. It is also important that we find speedier ways to approve medications for people with rare diseases. A few years may seem like not long, but for someone with a debilitating disease it is everything. Time means significantly worsening symptoms and the ability to live independently. It has been shown that when patients stop using the medication my sister takes, the patients symptoms worsen. These worsening symptoms are abilities that cannot be regained. My mother did not have the ability to use this medication. But there is still time and hope that my sister can continue to use a medication that has been working for her for 9 years.

Thank you for your consideration.

Respectfully,

Emily Messigian

Sam Visser – March 4th, 2026

Written Testimony

I am submitting this statement for the Senate record as someone living with Spinocerebellar Ataxia Type 7, a rare genetic disease that progressively destroys vision and neurological function.

I am a 26 year old man who began noticing problems with my eyesight about five years ago. Since then my vision has continued to deteriorate, and I now live with the reality that I am slowly going blind.

At a relatively young age, I have built a career in the fashion industry working with some of the largest brands and public figures in the world. My work has placed me at the forefront of a global industry that shapes culture and creative expression. It is a field where vision and creativity are essential, which makes living with a disease that is slowly taking my eyesight and mobility especially frightening.

This is not simply a job for me. My work carries significant responsibility, supports many people, and represents years of dedication and achievement. I am fortunate that I am still able to work today, but the future feels uncertain.

For people living with SCA7, the absence of treatments makes the path ahead feel very dark. Potential therapies like Troriluzole represent hope that the progression of this disease could be slowed and that people like me could continue contributing, working, and living independently.

I also think about the people who will be diagnosed after me. Without continued research and access to promising therapies, many of them will face the same devastating progression without options to change its course. For those of us living with rare degenerative diseases like SCA7, time is something we are steadily losing. Every delay in advancing potential treatments means more vision lost, more independence taken away, and fewer years to continue building the lives and work that define us.

Sam Visser

Marie Phillips – March 4th, 2026

Written Testimony

Dear Senator Scott and Committee Members:

I am writing as a family member of someone with Spinocerebellar Ataxia, the rare disease which Dr. Schmahmann testified about at the hearing on February 26.

My husband has been taking part in the Right To Try for Troriluzole, which Dr. Schmahmann discussed at the hearing, since July 2025. The news of FDA's Complete Response Letter came as a shock, and a devastating one, to us.

My husband submitted a statement himself prior to the hearing and I am following up with my own perspective. As a family member and with children who could be affected and the thought of a future without this life changing (and it truly has been) therapy is frightening, especially since we have seen it's positive effects. Watching my loved ones deteriorate and become less and less capable of living a full life is heartbreaking.

While Troriluzole is not a complete cure, it has helped my husband tremendously with symptoms; people, myself and other family members included, can understand his speech now, instead of either continually asking him to repeat or simply giving up and ignoring what he has to say. The progression of mobility impairment has all but stopped and he has not even been on the medication a year yet, often when people start to notice the most benefit as we have heard from other patients.

This has given us hope and I beg you to intervene, to encourage FDA to implement their flexible approval authorities and get this drug approved so that it can continue or start making a difference in patient's lives and give them the hope to live a life that most of us take for granted.

Thank you for your time and consideration.

Eric Feigen – March 5th, 2026

Written Testimony

March 5, 2026
Senate Special Committee on Aging
United States Senate
G16 Dirksen Senate Office Building
Washington, DC 20510-6050

RE: Statement for hearing entitled “From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation.”

Dear Committee Members,

The Immune Deficiency Foundation appreciates the opportunity to provide input on the U.S. Senate Special Committee on Aging’s hearing entitled “From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation.” Our foundation is the leading national organization representing Americans with primary immunodeficiency (PI), a group of more than 550 rare, chronic conditions in which part of the body’s immune system is missing or does not function correctly. For individuals in our community, delays in accessing effective treatments can have serious and lasting consequences. When the regulatory processes of the Food and Drug Administration (FDA) slow patients’ ability to obtain novel, potentially life-saving therapies, the impact can be devastating—reducing quality of life and, in some cases, putting lives at risk.

The process for developing new treatments to address the unmet needs of patients with PI is long and complex. Since PI encompasses a wide range of rare and ultra-rare conditions, developers face significant challenges, including small patient populations, limited natural-history data, manufacturing hurdles for individualized therapies, and the absence of established clinical endpoints. These barriers slow progress, stall promising therapies, delay clinical trials, and ultimately leave families waiting while their conditions continue to worsen. To ensure people with PI have a chance at timely, potentially life-saving treatment, we continue to urge the FDA to apply regulatory flexibility, predictability, and consistency to encourage innovation.

Example: Delays in promising gene therapy treatment for LAD-1, a PI with unmet need

One example of a PI where the development of a life-saving treatment has stalled in FDA’s review process is leukocyte adhesion deficiency type 1 (LAD-1). Infants with LAD-1 have a high mortality and morbidity rate due to serious recurring infections. While there is a treatment, hematopoietic stem cell transplantation (HSCT), it is not accessible to all patients. Some may not be able to find a suitable donor. For others with significant comorbidities, HSCT is too risky. Twenty-five percent of children with LAD-1 who undergo HSCT don’t survive.

KRESLADI, a lentiviral vector–based gene therapy, offers a promising alternative. All nine LAD-1 patients treated with KRESLADI in clinical trials are alive and have not experienced any complications or treatment-related serious adverse events in the 12 months following their treatment. Despite meeting all primary and secondary endpoints of its Phase III clinical trial, in June 2024, FDA issued a complete response letter (CRL), declining to approve KRESLADI. The CRL cited a need for more data on chemistry, manufacturing, and controls, but no efficacy or safety concerns. Over a year after the initial CRL, FDA accepted the resubmitted biologics license application for KRESLADI in October 2025. During this long process, we have encouraged FDA to act with urgency and contextualize its evaluation against the unmet needs of children with LAD-1 who cannot undergo HSCT. Despite the treatment’s clinically proven efficacy, lack of safety concerns, and FDA-granted Fast Track and Orphan Drug designations, our patients continue to wait for access to this potentially life-saving treatment.

Hope for the future

We applaud the FDA's rigor in evaluating medicines and share the agency's concern for patients' safety. Our foundation seeks only to emphasize the moral imperative behind establishing regulatory policies that are consistent, predictable, and flexible, so that members of the PI community can access life-saving treatment without unnecessary delays.

We are also hopeful that FDA's recent release of its draft guidance, "Considerations for the Use of the Plausible Mechanism Pathway to Develop Individualized Therapies that Target Specific Genetic Conditions with Known Biological Cause," marks an important step toward a renewed commitment to accelerating innovation in individualized treatments. The recent rise in gene therapy rejections suggested a shift away from the flexible regulatory approaches previously promised. However, if the Plausible Mechanism Pathway is paired with meaningful, consistent action, FDA could reopen the door to scientific breakthroughs across the rare disease landscape. By grounding reviews in predictable regulatory flexibility and rigorous, data-driven scientific evaluation, we hope the pipeline for novel PI therapies will strengthen—bringing new possibilities to the many members of our community who continue to face unmet medical needs.

We appreciate the Senate Special Committee on Aging's continued prioritization of rare disease innovation through holding this hearing. Please contact Lynn Albizo at lalbizo@primaryimmune.org for questions and additional information.

Sincerely,

Lynn H. Albizo
Chief Public Policy Officer

Wanda Landres – March 5th, 2026

Written Testimony

Hi my name is Wanda

I was diagnosed with SCA in 2019

I'm currently living in a retirement home. It has not been easy for me. I currently walk with a walker because I keep losing my balance. I try not to be a burden on my family. So I order a lot, I send my clothes out to be washed, use assistance of an aide when I have appointments. Luckily I am blessed financially to do those things because it is not easy.

Thank you

WL

Thomas Logie – March 5th, 2026

Written Testimony

PUBLIC STATEMENT CONCERNING GOVERNMENT IMPEDIMENTS TO INNOVATIVE TREATMENT FOR AORTIC VALVE STENOSIS WHICH POSE LESS RISK FOR AGED PATIENTS THAN WOULD A "TAVR"

I write as a 74-year-old male married to and living with my wife, aged 87, who has been diagnosed with aortic valve stenosis, osteoporosis already contributing to 2 broken femurs, high blood pressure under good control, shingles and neuropathy. We are native-born American citizens and reside full-time in the same State as the Chairman of the Senate Committee. We have consulted 3 cardiologists so far, all of whom indicate that focused, pulsating ultrasound or histotripsy directed at the aortic valve is not presently approved as a treatment for the aortic valve stenosis. There have already been good results in European trials. This procedure would be less expensive and less dangerous to many patients of advanced age than would a TAVR; the barrier is a fear of government sanctions for using a novel treatment rather than any major risk of harm from the pulsating ultrasound or similar treatment.

Insurance companies also need to be freed to cover newer treatments within reason under Medicare Advantage and competitive policies.

There is already a published article stating that pulsating ultrasound has been used to clear the aorta of calcified lesions. This is not a case where the novel treatment involves the use of an unusually risky device or drug. At worst this is an off-label use of a device already approved for use in the human body.

The required risk disclosures made by companies that manufacture TAVR equipment such as Medtronic or Edwards and by eminent providers such as Mayo Clinic and Cleveland Clinic make clear that the TAVR risks are substantial. Blood thinners are mandatory as part of a TAVR and appear to be associated with additional risk for patients with osteoporosis. It is a known risk that a TAVR may cause sufficient electrical disturbance so as to require the installation and maintenance of a pacemaker for the rest of a patient's life. A stroke is also known as a TAVR risk. The pulsating ultrasound would likewise eliminate risk from an imperfect fit or other fault of the replacement valve. Kidney failure is also a risk from a TAVR. Medtronic's list of potential adverse events during or after a TAVR as a result of an attempted or completed TAVR runs almost a full page, starting with physical death.

Both my wife and I believe that a TAVR poses unreasonable risks to her of mortality or further morbidity which would be mostly avoided by the alternative of the pulsating ultrasound that would shrink or remove the calcium which narrows her aortic valve. These decisions should be within the province of the patient assisted by her (or his) family and a licensed specialist, such as the cardiologist in this real-life example. Aortic stenosis is not an example of a rare disease, but it is an example of how less-invasive, less expensive and safer treatments are stifled by government regulation.

Tyler D. Maxwell – March 5th, 2026

Written Testimony

To whom it may concern,

My name is Tyler Maxwell and I am an Assistant Professor at a College of Pharmacy in New York City. I have been living with spinocerebellar ataxia type 3 (SCA3) since my diagnosis around 13yo. Fortunately for me, my symptoms are not very severe, allowing me to hold a job, give speeches, and advocate for myself. Though as time goes on, I am beginning to notice the progressive effects of ataxia, including balance coordination, affect on my speech (slurring words), and find muscle movements.

As a full-time professor, the affect on my speech is particularly concerning - as I know that I will not be able to stay in academia forever. At some point in my disease course, my students may not be able to understand me, so I need to keep my career options open. As a licensed pharmacist, I could always retain a position in hospital pharmacy (where I may not need to speak as often), though to be a hospital pharmacist, I need to use fine motor skills to correctly compound intravenous medications for the hospital. Already, my lack of fine motor skills has resulted in a number of needle sticks to myself and delays in care/profit losses because I have spilled medications in the compounding hood.

The reason I mention the above accounts surrounding my career are to encourage action, approval or compassionate use approval, and further research regarding treatments of this disease (genetic ataxias in general). Currently there is 1 medication that has shown to somewhat halt the progression of the disease (riluzole) though unfortunately the study did not show any benefit specifically in the SCA3 population. Recently trilizole was given compassionate use status while the FDA reviewed its approval - though in spite of a fair amount of data, FDA approval was denied. This action essentially took away any treatment for this disease from those of us living with it. In an effort to preserve my way of life (including the 3 family members I have with the same disease), I urge you to reconsider the medication for approval and/or consider compassionate use options to expand treatment possibilities.

Thank you and have a great day!

Sincerely,

Tyler D. Maxwell Pharm.D., BCIDP, AAHVP
Pronouns: He, Him, His
Assistant Professor of Pharmacy Practice
Touro College of Pharmacy

Vicky Hsu - March 5th, 2026

Written Testimony

Dear committee,

My sister and I both are the SCA3 patients , we have been house bound for years , we can not see doctors or friends without from others! It is a lonely world ahead !

I have been counting on the trial drug from Bioheaven which has helped my balance issue ! But without FDA approval made me worries of my only hope to slow down the deterioration will be gone soon !

Unfortunately I saw my mother stayed in bed for 7 years before passing !

Please kindly approve the drug from Bioheaven !

Sincerely,
SCA patients

Pam Steebler – March 5th, 2026

Written Testimony

Hi, my name is Pam Steebler, and I live with Spinocerebellar Ataxia Type 3.

My father had the same disease. He passed away at 56 because of it. I grew up watching how relentlessly this condition progresses when there is no treatment, and that experience shapes how I view my own future.

Today, I am taking a medication called Troriluzole. Since starting it, I have not progressed in over a year and a half. My balance is steadier and my walking is stronger. When I compare my trajectory to what I saw happen to my father, the difference is profound.

Living with SCA3 is still filled with uncertainty. I live with a constant fear of falling and injuring myself. Balance is not something I can take for granted. I have three young children, and there are moments when I hesitate to pick them up because I do not feel completely steady.

The emotional burden can be just as difficult as the physical symptoms. Watching my father decline and eventually lose his life to this disease makes the possibility of progression very real for me. Knowing that a medication helping me remain stable has not been approved creates anxiety about access and the future. That stress itself affects my symptoms, because anxiety can worsen coordination and increase the fear of falling.

For diseases like SCA3, where decline is expected, stabilization is not a small outcome. It allows people like me to continue parenting, working, and participating in daily life with dignity.

Troriluzole has not shown harmful effects, yet it has not been approved. I am asking for your support in encouraging regulatory flexibility for rare, progressive diseases and for consideration of real world patient data when evaluating therapies like this one.

Families like mine do not have time to wait.

Thank you for your time and consideration.
Pam

Megan Maxwell – March 5th, 2026

Written Testimony

Hello,

I am writing to inform you of my Spinal Cellebram Type 2 , the troriluzole is the only drug that could fix my side effects. I experience loss of balance, comprehension issues, and slurred speech. Please rethink your decision.

Chris Louie – March 5th, 2026

Written Testimony

To the Committee:

I am writing to you as a constituent from Flushing, NY. My Father has been diagnosed with spinocerebellar ataxia (SCA) 3, a rare, progressive, and currently incurable neurodegenerative disease that severely impacts coordination, balance, speech, and daily functioning. As someone diagnosed with SCA type 3, he unfortunately has a future of steadily worsening disability and life-altering symptoms with no FDA-approved disease-modifying treatments available today.

My Father is currently receiving troriluzole, an investigational therapy being developed by Biohaven, through the FDA's Expanded Access (compassionate use) program. Since starting troriluzole, he has shown marked improvement in his symptoms and was able to regain his ability to speak. While he has begun to regress, that he was able to show marked improvement demonstrates that this drug can and has provided real-world benefits for patients. This, along with the promising data from Biohaven's clinical trials, has given me and my family genuine hope for the future. Unfortunately, because troriluzole has not yet received full FDA approval, his continued access—and the access of thousands of other SCA patients across the country—remains uncertain once the expanded access program ends. Without approval, patients like my father will lose the only treatment that has shown the potential to slow or halt the relentless progression of this devastating disease. Slowing the progression will also buy us the time to find further treatment options before it is too late. Slowing the progression will allow my Father, a Coast Guard Veteran, to enjoy the best quality of life he has left, as well as help my Mother and ease her burden. SCA3 is a genetic disorder, and I also carry the gene. As a relatively young person (40s) I have many expected years of life. Unfortunately, because of SCA3, many of those years is not expected to be great as I will deteriorate due to having this disease; I have already begun to show symptoms. I was fortunate to be able to take troriluzole under the EAP, and my symptoms went away. This has given me hope that I can have a good quality of life and not be a burden on our healthcare system and continue to contribute meaningfully.

I am currently two months in on a temporary 90-day hiatus from taking troriluzole for personal reasons. I have noticed that my symptoms have returned and look forward to when I will be back on troriluzole. This is anecdotal, but I know that it has helped me.

We were recently informed that troriluzole was not approved by the FDA for continued use, for reasons that were not fully clear. I work in the research and scientific space, and while I understand that one of the roles of the FDA is set regulations to safeguard the American population, the reality is that in these limited and specific circumstances, the FDA is actually acting as a bureaucratic roadblock using metrics that do not reflect the data, science, or reality for patients.

My Father and I will soon lose access to this drug which has been deemed safe and has been effective in helping us minimize the progression of our diseases, with evidence convincingly presented by the many witnesses during the hearing. This news is devastating to us, especially since there does not seem to be a medical or scientific reason behind it.

I respectfully urge this committee to work with the Food and Drug Administration in updating and amending the rules and guidelines for the review and approval of treatment options for rare diseases. These are unnecessary roadblocks, and we must use our knowledge and resources to update and streamline the process given the current information.

Thank you for your attention to this matter.

Chris L

Branden Cordeiro – March 5th, 2026

Written Testimony

Comments for the Record

Submitted by Praxis Precision Medicines

Hearing: "From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation"

U.S. Senate Special Committee on Aging

Praxis Precision Medicines appreciates the opportunity to submit comments for the record on the regulatory environment for innovative therapies, particularly those intended to treat rare and complex neurological diseases.

Praxis is a precision neuroscience biopharmaceutical company, based in Boston, focused on developing therapies for central nervous system (CNS) disorders, including developmental and epileptic encephalopathies (DEEs), focal and generalized epilepsies, and Essential Tremor. The patients we serve include children with devastating rare genetic epilepsies and older Americans whose independence and daily functioning are significantly impaired by movement disorders. We have deep respect for the FDA's public health mission. At the same time, we believe that regulatory predictability, institutional stability, and adequate resourcing are critical to maintaining U.S. leadership in biomedical innovation and ensuring patients receive timely access to safe and effective therapies.

I. A Pivotal Moment for Praxis

Praxis is at a transformational stage as a company, following a year of meaningful clinical and regulatory progress. Our pipeline reflects both the promise of precision medicine and the importance of a regulatory system that can evolve alongside scientific advances.

Ulixacaltamide (Ulix) for Essential Tremor

Ulixacaltamide recently delivered positive results in two pivotal Phase 3 trials in Essential Tremor, representing the first successful late-stage pharmacologic development program specifically designed for this condition. The therapy demonstrated rapid, sustained, and clinically meaningful improvements in activities of daily living, along with a safety profile that addresses many of the limitations associated with existing treatments.

Essential Tremor disproportionately affects older Americans and remains inadequately treated. Our recent NDA submission for Ulix is an important step toward expanding therapeutic options for this large and underserved population.

PRAX-562 (Relutrigine) for SCN2A and SCN8A DEEs

Relutrigine is a first-in-class precision sodium channel modulator developed to address the underlying electrophysiologic drivers of severe developmental and epileptic encephalopathies.

In 2025, relutrigine received Breakthrough Therapy Designation and demonstrated such compelling efficacy at interim analysis that a pivotal study was stopped early. Praxis has now submitted an NDA to the FDA. For families confronting these catastrophic pediatric epilepsies, this progress represents real hope.

Elsunersen – Early-Seizure-Onset SCN2A DEE

Elsunersen is an antisense oligonucleotide designed to selectively reduce expression of pathogenic SCN2A gain-of-function mutations. It reflects the maturation of mutation-specific, mechanism-driven therapies.

Last year, the FDA agreed to allow Praxis to proceed with a single-arm, baseline-controlled registrational study, recognizing both the high unmet need and the strong mechanistic rationale in this

ultra-rare indication. That flexibility is essential where traditional randomized designs are neither feasible nor ethically appropriate.

II. Support for FDA's Rare Disease Modernization Efforts

Praxis commends the FDA, under Commissioner Makary's leadership, for advancing initiatives that bring greater clarity and predictability to rare disease development. Rare Disease Evidence Principles (RDEP)

The Rare Disease Evidence Principles framework provides sponsors with a clearer pathway for ultra-rare genetic diseases. It appropriately recognizes that approval may, in certain circumstances, be supported by a single adequate and well-controlled trial combined with robust confirmatory evidence, such as mechanistic data, biomarkers, pharmacodynamic findings, nonclinical models, or well-characterized natural history.

Importantly, this approach does not lower statutory standards. It clarifies how substantial evidence can be established when traditional large randomized trials are infeasible due to extremely small patient populations.

Plausible Mechanism Framework

The Plausible Mechanism guidance further strengthens regulatory clarity for highly targeted therapies. It outlines how evidence may be sufficient when:

- The disease has a clearly defined molecular cause;
- The therapy demonstrates target engagement;
- The natural history of the disease is well understood; and
- Clinical findings are robust and inconsistent with known disease progression.

For mutation-specific therapies, including antisense oligonucleotides, this framework appropriately incorporates mechanistic science into regulatory decision-making. We applaud the

Agency for operationalizing these principles and hope they will continue to evolve in a way that benefits additional rare disease communities.

III. The Rare Disease Innovation Hub

Praxis strongly supports the Rare Disease Innovation Hub and its mission to improve cross-Center coordination, reduce fragmentation in review processes, and strengthen engagement with rare disease stakeholders.

If fully supported, the Hub can:

- Improve consistency across review divisions;
 - Reduce duplicative or conflicting regulatory feedback;
 - Facilitate early alignment on innovative trial designs;
 - Increase transparency around expert consultation; and
 - Accelerate communication for high-unmet-need therapies.
- However, these objectives require adequate and stable funding.

We respectfully urge Congress to provide dedicated, sustained appropriations for the Rare Disease Innovation Hub to ensure:

- Retention of specialized scientific reviewers;
- Timely development of guidance for emerging modalities;
- Durable cross-Center coordination infrastructure; and
- Capacity to manage increased engagement under RDEP and the Plausible Mechanism framework.
- Without sufficient resources, even well-conceived reforms risk being constrained by capacity limitations.

Ensuring Innovation and Stability Move Forward Together

Praxis' recent progress demonstrates what is possible when scientific innovation aligns with constructive and predictable regulatory engagement.

We commend the FDA for advancing rare disease modernization through RDEP, the Plausible Mechanism framework, and the Rare Disease Innovation Hub.

At the same time, modernization must be paired with institutional stability. Dedicated funding, retention of experienced reviewers, and consistent application of policy are essential to maintaining investor confidence and sustaining rare disease innovation.

For children living with rare pediatric epilepsies and older Americans struggling with Essential Tremor, regulatory stability is not an abstract policy concern, it can determine whether a therapy reaches patients in time to alter the course of disease, preserve independence, and meaningfully improve their quality of life.

Praxis Precision Medicines stands ready to work with the FDA, Congress, and stakeholders to ensure that the United States remains the global leader in rare disease innovation, grounded in scientific rigor, supported by institutional continuity, and focused on patients.

Sincerely, Marcio Souza

Chief Executive Officer
Praxis Precision Medicines, Inc.

Mrudula Patil – March 5th, 2026

Written Testimony

Our family is affected by SCA. My mother and her 2 siblings are affected with severe mobility issues. Myself and my brother have mobility issues that are starting. My children have a 50 percent chance of inheriting it and also their children. Therefore, we need treatments as soon as possible to stop the progression or reverse the disease. We cannot live a normal life. Please help us with availing new treatments as soon as possible to stop this terrible disabling disease. Thank you.

Missy Zolecki – March 5th, 2026

Written Testimony

Chairman Scott and Members of the Committee,

On behalf of the National Fragile X Foundation (NFXF) and the individuals and families we represent, we thank you for convening this important hearing and for recognizing that, for people living with rare diseases, time directly affects function, independence, and quality of life.

Fragile X syndrome is the most common inherited cause of intellectual disability. Despite decades of scientific progress and a growing understanding of its underlying biology, Fragile X syndrome remains one of the many rare diseases for which there is no FDA-approved, disease-targeted medication and no cure. Families affected by Fragile X live daily with the consequences of this gap while knowing that promising therapies have existed, have demonstrated benefit, but ultimately never reach patients.

Our community's experience reflects the core concern raised in Chairman Scott's opening remarks. Despite clear Congressional intent, the regulatory system has not consistently or effectively moved with urgency, flexibility, and in keeping with scientific developments that should translate into timely access to actual therapies for patients with rare diseases. The Fragile X community has experienced these challenges directly, in the near-past and within the past year.

For neurological rare diseases like Fragile X syndrome, validated clinical outcome assessments are limited and may not accurately reflect how individuals are impacted across their lifespan. While the FDA appropriately prioritizes scientific rigor, the requirement to re-validate outcome measures for each new use, rather than allowing for the application of established tools across related drug discovery efforts, creates needless delays. These delays are not something that rare disease communities can absorb, including our academic research and industry partners. Companies working to develop treatments for Fragile X and other conditions also too often face evolving expectations from the FDA late in development and limited flexibility in weighing open-label and real-world evidence. These barriers can halt otherwise promising programs that are impossible to restart.

As Chairman Scott emphasized, Congress has provided the FDA with tools intended to support flexibility and urgency in rare disease drug development, including through the 21st Century Cures Act. For Fragile X and similar conditions, where developmental timing and treatment matter, regulatory delay has lasting consequences for our loved ones. Skills and functional gains are time-sensitive, and interruptions in access can permanently alter outcomes.

We strongly agree that safety must always remain a priority for our nation's drug approval process, but safety and speed are not and must not be mutually exclusive. Regulatory frameworks need to recognize clinically meaningful benefit, allow endpoints to evolve alongside scientific understanding, and meaningfully incorporate patient and caregiver experience to protect patients while addressing profound unmet need. Especially for life-altering and life-ending conditions with no approved treatments, the absence of therapeutic options is itself a significant burden.

We respectfully urge the Committee to continue its oversight and to advance policies that promote:

Greater consistency and transparency in rare disease review standards

Early and sustained engagement with patient communities on endpoint selection

Broader consideration of real-world and open-label evidence when traditional endpoints are limited

Clear pathways for continued access, including compassionate use, when benefit has been demonstrated and no alternatives exist

We thank the Committee for its leadership and for ensuring that the voices of rare disease patients and families remain central to this discussion.

Take care,

Missy Zolecki
Senior Director, Community Empowerment
National Fragile X Foundation

Karen Suchomel – March 5th, 2026

Written Testimony

I would like to submit a statement.

Living with a rare degenerative disease is a frustrating experience. Not only am I preoccupied each day dealing with the pain and difficulty of my condition, I'm constantly anxious about detecting new symptoms. I'm in constant pain from neuropathy, I'm losing my balance and can no longer walk with a normal gait, I've already had surgery to repair double vision in the hopes that I can stop see for a while longer. I am destined for a wheelchair, slurred speech, double vision and tremors that will make it impossible for me to do anything. Knowing that there is no cure and not even symptomatic relief just adds to the frustration.

As a society, we must come up with ways to incentivize pharmaceutical companies to develop medications for rare conditions. We are a small population and without incentive, it's not economically viable to develop a cure for us. But the FDA is by far the greatest hindrance to drug development. The unnecessary rules and regulations, the refusal to relax any scrutiny is just ridiculous. This disease is going to kill me - I am not worried about safety in a trial, I am worried about roadblocks to research. I have a genetic condition - I will do anything or risk anything to help my son. But the FDA thinks they know better than I do, they think they are the only ones qualified to make decisions about my safety. They may think they're helping, but they are hindering research in rare disease.

The first drug to delay progress of my disease has been tied up with FDA bureaucracy for years. We're all agree it's not a perfect drug, but it's soul wrenching to see the FDA withhold approval on a technicality. They should approve Troriluzole immediately, if only to incentive other companies to do research in our disease.

My first grandson will be born soon and I have to celebrate knowing that the only time I can hold him is when I am sitting down, so that I don't drop him due to my balance or my tremor. I sometimes think that nothing will change in the FDA until decision makers are stricken with their own rare disease.

I'm begging Congress to do something for the millions of folks who suffer physically and emotionally because the FDA only cares about power and not about people. Support research for rare diseases.

Maryellen Tseng – March 5th, 2026

Written Testimony

Dear Members of the U.S. Senate Special Committee on Aging:

My name is Maryellen Tseng. I have lived in New York City and Brooklyn since 1988, moving here to work as a graphic designer after graduating from Syracuse University.

I live with Spinocerebellar Ataxia Type 3 (or Machado-Joseph Disease), a rare inherited neurodegenerative disorder affecting coordination and mobility. My family watched as my mother suffered with Ataxia at a time with no therapeutics and no hope of cure. In SCA3, the impairment of nerve cells and nerve fibers causes degeneration of the cerebellum (the coordination center of the brain) and related brain regions. My grandmother, uncles, and aunt had Ataxia as well. They all suffered from difficulty walking, eventually using a wheelchair, and then being bedridden; trouble eating and swallowing; slurred speech; and deterioration of fine motor skills, leaving them unable to feed, bath, and dress themselves. Eventually the disease led to their early deaths. My older sister and two of my cousins have also been affected by SCA3.

Six or seven years ago, when I was in my early 50s, I stopped being able to do things like run for the bus or walk quickly to cross the street in case a car had suddenly veered into my path. My vestibular system—which send signals to the brain, and uses the information to coordinate eye movements for clear vision and to make rapid, compensatory movements that keep you from falling—was challenged by common daily situations a New York City resident faces leaving their midtown office and making their way to the subway to return home. Things like the darkening evening sky, the rushing commuters, the traffic, and the streetlights became overwhelming to my cerebellum. It became harder for my brain to make sense of these everyday factors of urban life and eventually made it impossible for me to continue commuting to work.

I am now 60 years old. I am unable to do many everyday tasks that other adults my age typically can, such as walking unaided, carrying groceries, driving a car, using the oven, taking out trash, or sweeping. My father stressed the importance of excellent handwriting when I was growing up and it was important to me to meet his expectations so I worked hard to perfect my penmanship, but now it is very difficult for me to write legibly at all. Everyday tasks that most adults take for granted became very difficult or impossible for me.

Although there is no cure for SCA3, I am fortunate to have received Biohaven's experimental drug Troriluzole (in March 2024) through the expanded access program (and my excellent and compassionate neurological team at Columbia University). Troriluzole helps to reduce glutamate dysfunction in the brain, which is a common symptom for many forms of Ataxia. Controlling the amount of glutamate in the brain improves Ataxia symptoms. Troriluzole has slowed down my disease's progression and given me hope for myself, my children, and others who may be affected. I have volunteered for a number of ataxia studies with the hope that more research will one day lead to a cure for those who suffer from the disease.

Thanks to the Troriluzole, my progression has slowed and I am able to continue working as a graphic designer from home, walk with the assistance of a rollator around my neighborhood in Brooklyn, methodically climb the stairs, go swimming, socialize with friends, and experience activities like visiting a museum. Without the drug my disease progression would have been much quicker, as I've seen in the case of my sister for instance, who is not on the drug and is wheelchair bound and no longer able to work. Troriluzole has given me a life that I would not have otherwise and it has given me and my loved ones hope.

Despite the incredible benefits I have experienced taking the drug, Troriluzole has not been approved by the FDA. In November 2025, the FDA issued a Complete Response Letter (CRL) to Biohaven declining the New Drug Application (NDA) for Troriluzole or Spinocerebellar Ataxia (SCA). The CRL cited concerns about issues inherent in real-world evidence (RWE) studies. This is devastating news to me and my family who have seen the clear benefits of my taking the drug. How can the FDA not approve something that has been proven safe and effective and is the only therapeutic available to those of us who suffer from this devastating disease? What is the point of such cruelty to ataxia sufferers and their families?

I am urging you to meet with the FDA to discuss a path forward for Troriluzole's approval, as I have cited real-world, firsthand experiences of this insidious disease and the tremendous benefits the drug has offered me and the hope it has afforded me and my loved ones.

Thank you.

Sincerely,
Maryellen Tseng

Rachel Chen – March 5th, 2026

Written Testimony

Dear Sir/Madam ,

I am 73 years old. Took a medical retirement at the age of 57 due to the debilitating disease of SCA3. It has been a long and difficult journey of almost 16 years.

In the beginning when I first took the generic testing and was confirmed I had the gene passed onto me from my mother, I sought quite a few medical helps but was told by numerous doctors that there was nothing they could do because there was no treatment, no medication

I am pretty much home bound now. Falling due to the immobility and imbalance is the major issue. I had a surgery in 2023 for the broken femur because of the fall.

Please expedite the approval process of the new medicine for the rare disease. As a patient I should be able to improve the quality of life. I am also fully aware of the risk and side effects of all the drugs. But it definitely worth the try.

Thank you so much for your time.

Very truthful Yours,
Rachel Chen

Shriya Kakde – March 5th, 2026

Written Testimony

To the Members of the U.S. Senate Special Committee on Aging,

I work as a clinical research coordinator in an academic movement disorders program, primarily supporting members of the spinocerebellar ataxia (SCA) community. My role with this population involves conducting longitudinal assessments for a natural history study and visits for patients receiving troriluzole through an expanded access program (EAP).

Every day, I see the raw face of this genetic neurodegenerative disease and what it does to our patients and their families. It's impossible not to put myself in the position of what I have seen here: a wife desperately watching her husband shake as he fails to stand up by himself, a child accompanying a parent seeing their sober future play out in front of them, a patient battling against their own body to prove that they can still walk a few more steps.

These are the people spending hours in our research rooms completing assessments, giving blood samples, and coming back year after year, just so they can make any contribution possible to bring treatments to the SCA community. With hope in their eyes, many ask me the same question: when will troriluzole or another disease-modifying therapy become available?

Day in and day out, people with SCA adapt their lives around a body they are gradually losing grasp of, and each year without treatment they grow closer to permanent loss of mobility and independence. For many of my patients, troriluzole promises a chance for control over their illness, control over their lives. Since the FDA's Complete Response Letter for troriluzole in November, patients in the EAP have asked whether they should begin rationing their medication or if there is a way to obtain a large supply. Questions of this nature reflect the uncertainty and fear experienced by patients grappling with the possibility of losing access to a potentially meaningful and safe therapy.

Patients with rare diseases do not have the luxury of waiting for regulatory frameworks designed for large populations. Congress and regulators must modernize FDA review processes by incorporating natural history data, allowing greater flexibility in evaluating functional endpoints, and expanding accelerated approval pathways so patients with rapidly progressing conditions can access necessary therapies sooner.

Thank you.

Ashira Vantrees – March 5th, 2026

Written Testimony

Dear Chairman Scott:

KIF1A.ORG is a global community dedicated to improving the lives of those affected by KIF1A Associated Neurological Disorder (KAND). KAND is a rare neurodegenerative genetic disorder caused by mutations in the KIF1A gene, impacting neurological function. KIF1A.ORG is a resilient network of families, researchers, and advocates united by a common goal: finding a treatment for KAND.

KIF1A.ORG appreciates the Food and Drug Administration's (FDA) efforts to advance research and development into rare disease treatment options. We particularly applaud the FDA's recent launch of the Framework for Accelerating Development of Individualized Therapies for Ultra-Rare Diseases. To support the FDA's efforts, KIF1A.ORG urges Congress to pass the MINI Act and provide additional clarity on how ultra-rare disease treatments can reach their small global populations.

I. Maintaining Investment in New Innovation (MINI) Act

There are an estimated 7,000 rare disorders within the United States, and only 500 of these disorders have disorder-specific treatments available. As such, for the thousands of rare disorders without treatment options, like KAND, our families are eager to find treatment options that treat and improve the health of those living with these conditions. Genetically targeted technologies (GTT) offer a new frontier of hope.

GTTs are particularly promising therapies for rare disorders, as this technology allows the body to correct an improper output produced by a genetic mutation, essentially addressing these mutations at their core. Without disorder-specific treatments, individuals living with rare disorders are required to manage the symptoms of their disorder, which can include multiple prescription drugs, therapies, and other clinical and non-clinical interventions. GTTs allow health care providers to treat the root causes of these conditions rather than their symptoms. GTTs are also being used in research for new cardiovascular disease treatments, pediatric conditions, and neurological conditions like Parkinson's, multiple sclerosis, and Alzheimer's disease.

The Inflation Reduction Act (IRA) has many important protections for consumers, including the \$2,000 out-of-pocket cap for Medicare Part D beneficiaries and \$35 insulin. The IRA also allows the Department of Health and Human Services to negotiate the cost of certain prescription drugs. Under the IRA, prescription drugs that are defined as "small molecules" are eligible for negotiation after 9 years; meanwhile, "large molecule" prescription drugs are eligible for negotiation after 11 years. The IRA does not address GTTs. As a result, these therapies are considered "small molecule" treatments. To address this ambiguity, the Maintaining Investment in New Innovation Act (MINI Act) recognizes the complexity of GTTs and clarifies that these treatments are "large molecule" drugs under the IRA.

The MINI Act will ensure these technologies are properly recognized as large molecule drugs, helping ensure continued research and investment in these novel treatment options for individuals living with rare disorders and their families.

II. Clarify How Treatments Can Reach Ultra-Rare Populations

Ultra-rare communities like those living with KAND are global communities that benefit from their treatments being available internationally, as this ensures a more comprehensive understanding of treatment efficacy and impact on disease progression. However, due to complex regulatory barriers, sharing treatments for ultra-rare disorders is not currently easy or often feasible. For example, within the KAND community, some individuals living with a specific KIF1A mutation have a GTT therapy available. This treatment is currently expanding from an n of 1 trial to be more widely available for those with the same mutation. However, members of the KAND community who are eligible to receive this treatment; and who would benefit from the treatment, are currently unable to access it due to being located outside of the United States. Therefore, KIF1A.ORG is urging the FDA to provide greater clarity on how ultra-rare disease treatments can be shared internationally and improve access and outcomes for those living with these complex conditions.

Sincerely,
Dr. Dominique Lessard KIF1A.ORG Executive Director

Jackie Ward – March 5th, 2026

Written Testimony

Dear Chairman Scott, Ranking Member Gillibrand, and Members of the Committee,

Veeva Systems appreciates the opportunity to submit this statement for the record following the February 26, 2026, hearing regarding the regulatory hurdles impacting rare disease innovation. We commend the Committee's focus on ensuring that 30 million Americans living with rare diseases are not deprived of life-saving treatments by bureaucratic delays or outdated infrastructure.

As a technology partner to the life sciences industry, we believe that modernizing the nation's clinical research infrastructure is essential to achieving the Committee's goals of ensuring that the FDA fulfills its mission to protect patients while fostering innovation and, importantly, maintaining America's leadership in biomedical research.

The Digital Disconnect in Clinical Research

While the U.S. healthcare system has largely transitioned to electronic health records (EHRs), clinical trials remain anchored in the past. Research is still overwhelmingly conducted using paper binders, manual spreadsheets, and isolated systems that do not communicate with one another. This "digital disconnect" is a primary driver of the high costs and unnecessary delays that Chairman Scott identified as a "roadblock" to innovation.

As just one example: currently, research staff often act as manual data scribes, spending significant time reconciling information across disconnected systems rather than supporting trial participants. This fragmentation delays data availability and increases research costs as sponsors of potential rare disease therapies manually verify source data that have been collected through paper case report forms or in fragmented, in-house record systems. This source data verification accounts for up to [40% of the cost](#) of clinical trials and significant contributions of staff time - delaying innovation. Auditable, certified technology systems that supported source data input that could significantly reduce these time and cost barriers for rare disease therapies.

Modernizing Rare Disease Research Through Certified Technology

As the Special Committee on Aging is considering ways that FDA, and HHS overall, could encourage innovation and ensure expedient patient access to safe and effective therapies, we urge you, along with your colleagues across the Senate and House, to consider a voluntary federal certification for clinical research technology. This could be modeled after voluntary certification for electronic health records (EHRs) that was established by the HITECH Act and the 21st Century Cures Act. This program could be promulgated by the HHS Assistant Secretary for Technology Policy (ASTP/ONC), in collaboration with FDA, to specifically address the unique challenges of rare disease research. ASTP/ONC would need to establish the standards and voluntary certification process for clinical research technology, something they already do for EHRs. Sponsors who submit regulatory applications (e.g., New Drug Applications) could receive expedited review consideration if they demonstrate that their clinical trials were conducted using certified, auditable research technology that improves data integrity and transparency. This would be particularly impactful for the small biotech companies that develop the majority of rare disease therapies. This would result in:

- **Real-Time Oversight:** By meeting high standards for remote access and auditability, sponsors can reduce the need for routine, expensive onsite inspections.
- **Eliminating Redundancy:** Interoperability allows data to be captured once for clinical care and reused securely for research, eliminating the duplicative data entry that increases error risk.

- **Reaching Every Patient:** Rare disease patients are often geographically dispersed. Certified technology would support remote consent, electronic data capture, and virtual monitoring, allowing rare disease patients in rural communities and working families to participate more easily with less travel.
- **Improving National Security and Leadership:** American leadership in clinical research is a national security priority. Establishing a neutral federal framework for interoperable research technology will ensure the U.S. remains the preferred global location for clinical innovation.

About Veeva Systems

Veeva Systems is a global leader in cloud-based software for the life sciences industry, supporting more than 1,000 pharmaceutical, biotechnology, and medical device organizations. Our solutions span clinical operations, regulatory data exchange, quality, safety, and real-world evidence generation. In 2021, Veeva became the first publicly traded company in the U.S. to convert to a Public Benefit Corporation (PBC), legally aligning our business purpose with the public good. One of our core PBC objectives is to enable faster and less expensive clinical trials that are less burdensome and more accessible to patients.

Conclusion

Better infrastructure is a prerequisite for better, faster research. By establishing a certification program for clinical trial technology, the federal government can provide the foundation needed for AI and other modern tools to work safely and at scale. We would be thrilled to work more with the Committee to turn these technological opportunities into meaningful outcomes for patients who cannot afford to wait.

Sincerely,

Jackie Ward (Director of Public Policy) & Anthony Corso (VP of Public Policy)

Veeva Systems

Jackie Ward, PhD
Director of Public Policy, Clinical Trials
Veeva Systems

Pamela Gavin – March 5th, 2026

Written Testimony

National Organization for Rare Disorders

Testimony by Pamela Gavin, Chief Executive Officer

Submitted on March 5, 2026

Senate Aging Committee Hearing on February 26, 2026

From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation

Chairman Scott and Ranking Member Gillibrand,

The National Organization for Rare Disorders (NORD), on behalf of the more than 30 million Americans living with one of the over 10,000 known rare diseases, thanks you for holding a hearing on February 26, 2026, titled From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation and for the opportunity to submit comments for the record.

With a more than 40-year history, NORD is the leading and longest-standing patient advocacy organization for the estimated 1-in-10 Americans living with a rare disease. NORD is an independent 501(c)(3) nonprofit dedicated to caring for individuals with rare diseases and the organizations that serve them. Along with over 355 patient organization members, NORD is committed to improving the health and well-being of people with rare diseases by driving advances in care, research, and policy. We believe that all individuals with a rare disease should have access to high quality, affordable health care that is best suited to meet their medical needs.

NORD's three overarching policy priorities for 2026 fall within three categories:

1. Encourage Innovation to Bring New and Better Therapies to Patients
 2. Promote Access to Therapies for Patients with Rare Diseases by Eliminating Barriers to Care
 3. Support Timely Diagnosis in Patients with Rare Disease to Enable Care and Treatment
- NORD advocates for the development of safe and effective therapies, supporting policies that strengthen rare disease research, improving regulatory approval processes, protecting incentives for the development of rare disease treatments, and increasing access to innovative therapies by removing hurdles and expanding coverage.

Two bills that can greatly benefit the rare disease community are the Medical Foods and Formulas Access Act of 2025 (H.R. 5684 / S. 3304) and the Access to Genetic Counselor Services Act of 2025 (H.R. 6280 / S. 3607). Medical Foods and Formulas Access Act would provide coverage under Medicare, Medicaid, the Children's Health Insurance Program (CHIP), and the Federal Employees Health Benefits Program for medically necessary food and associated equipment and supplies. The Access to Genetic Counselor Services Act would provide Medicare coverage for genetic counseling services conducted by a genetic counselor, both of which would have a significant impact on the health of people living with rare disorders.

While all three priorities above are equally important, the first most directly relates to the work of the Food and Drug Administration (FDA) and therefore is the focus of my comments below.

To encourage innovation to bring new and better therapies to patients, policy makers need to do the following.

Maintain vital incentives for rare disease drug development including protecting the intent and integrity of the Orphan Drug Act in awarding orphan drug exclusivity.

For decades since the passage of the Orphan Drug Act (P.L. 97-414) in 1983, industry and FDA have been making huge strides in research and development and the approval of rare orphan therapies, saving and improving quality of life for rare disease patients. Incentives such as the rare pediatric priority review voucher and orphan designation and exclusivity, as well as regulatory tools such as fast track, breakthrough therapy designation, priority review, regenerative medicine advanced therapy designation, and the accelerated approval pathway, have encouraged companies to research and develop rare disease therapies that once were cost prohibitive or too complicated to pursue. NORD thanks Congress for reauthorizing the rare pediatric priority review voucher (PRV) program through 2029, for preserving the intent of the orphan exclusivity program, and for continuing support for these other programs. With support and action from Congress, FDA has evolved to utilize greater flexibilities without compromising safety and efficacy standards when reviewing rare disease treatments. As a result, more than 500 treatments for rare diseases have been approved by the FDA, and rare disease therapies account for more than half of the approvals over the past several years.

Ensure that the patient voice is a critical part of the reauthorization of the Prescription Drug User Fee Reauthorization Act, including by promoting patient-centric rare disease therapy development through expanded patient engagement opportunities and supporting cross-cutting rare disease efforts such as the Rare Disease Innovation Hub.

At the urging and direction of Congress, FDA has made great strides to include a patient-centric approach when considering rare disease therapies and established the Rare Disease Innovation Hub in 2024 to further strengthen the agency's cross-agency interactions and engagements with the rare disease patient community. Patients are not an afterthought. Patient groups are often the catalysts to securing seed funding necessary to initiate research into rare disease treatments. Patient organizations have been responsible for generating natural history data to support a drug application. Nowadays it is common for most rare disease development programs to engage with patients to understand what is important to them in terms of treatments and incorporate that into development programs. In some instances, patient groups have even participated in FDA meetings with sponsors helping convey to regulators their unique understanding of disease burden and why a particular treatment is important to them.

NORD urges Congress to strengthen the Rare Disease Innovation Hub through dedicated resources. If adequately resourced and supported, the Hub has the potential to significantly improve the development and review of orphan drugs and diagnostics by enhancing internal cross-collaboration

and streamlining regulatory processes across FDA. Further, it can serve as a platform for engaging and partnering with external stakeholders to accelerate therapeutic innovation.

NORD also recommends Congress continue to encourage FDA to expand its efforts to incorporate the patient voice earlier and more consistently throughout the drug development lifecycle to help ensure more patient centric product development programs. This includes directing resources toward the development of additional guidance documents that enhance and build upon the existing patient-focused drug development (PFDD) framework. Providing education and training to patient groups and further enhancing patient listening sessions to allow for more proactive and structured dialogue (rather than simply listening) between patient communities and the Agency would better prepare patients to participate in regulatory engagement opportunities. Patients also must have a meaningful seat at the table early in development discussions, and advisory committee meetings must remain a transparent forum for expert and patient input.

Advance policies that support predictable and flexible regulatory pathways to encourage development and facilitate more timely development of rare disease therapies.

The advances in science since the mapping of the human genome and even more within the last decade have made it possible to correct certain genetic defects and, in some instances, cure a disease. This has been an incredible time for scientific advancement, giving hope and opportunity where once there was none. Both companies and FDA were emphasizing patient focused drug development and investment was increasing in several promising areas of treatments. Over the last several years the rare disease community has risen to meet the moment by amplifying their engagement with excitement over the potential and promise that comes from such advancements.

Historical changes at FDA were in large part a result of the commitments to focus on patients in the Prescription Drug User Fee Act (PDUFA) VII agreement, which included increased agency staffing and opportunities for reviewer training and sharing knowledge. These efforts were supported, encouraged, and modeled by leadership across the FDA. The patient centric approach was having a measurable impact with approximately half of all new drug approvals being for orphan products, and more than 20 new cell and gene therapies approved since 2017. Although promising, with over 95 % of rare diseases lacking an FDA-approved therapy, this momentum needs to continue exponentially to meet the unmet medical need in the rare disease community. .

Several changes at FDA this past year, including severe staff attrition, significant reduction in resources for training and engagement, and seeming shifts in regulatory decisions, however, appear to be putting the momentum at risk. Uncertainty that stems from such changes threatens to halt or reverse many of the scientific advancements made over the last few decades at the detriment of rare disease patients and their families.

NORD is pleased to hear FDA leadership voice commitment to flexibility and maintaining momentum. However, the juxtaposition between the agency's statements and actions is cause for concern. Lending to the trend of uncertainty, since July 2025 alone, there have been at least eight instances of

FDA reversing feedback in pre-filing meetings or FDA issuing complete response letters (CRLs) sending many of these rare disease development programs into disarray.

- Concept Therapeutics (New Drug Application (NDA)) for Relacorilant for hypercortisolism (Cushing's Syndrome).
 - Uniqure (Biologics License Application (BLA)) for AMT-130 for Huntington's disease.
 - Capricor Therapeutics (BLA) for Deramiscoel for cardiomyopathy associated with Duchenne Muscular Dystrophy.
 - Ultragenyx (BLA) for UX111 (ABO-102) for Sanfilippo syndrome type A.
 - Atara Biotherapeutics / Pierre Fabre Pharmaceuticals (Biologics License Application (BLA) resubmission) for EBVALLO (tabelecleucel) for Epstein-Barr virus post-transplant lymphoproliferative disorders.
 - Pharming Group N.V. (sNDA) for Joenja (leniolisib) for Activated PI3K delta syndrome.
 - Regnxbio (BLA) for RGX-121 (AAV9-IDS) for Mucopolysaccharidosis Type II (Hunter syndrome).
 - Disc Medicine (NDA) for Bitopertin for erythropoietic protoporphyria / X-linked protoporphyria.
- NORD believes deeply in strong science and patient safety. Rare disease patients deserve safe and effective treatments - not ones that do not work or worse, could cause harm. However, this is an unprecedented trend of many sponsors reporting that the FDA changed or reversed its agreement from what was a previously acceptable clinical trial design. Families and innovators need clarity and consistency. It is unethical to ask patients to participate in clinical trials that are later determined to be futile. Further, when expectations shift late in the review process or decisions become unpredictable, it creates uncertainty that ripples far beyond a single product.

For small biotech companies, many of whom are developing therapies for rare diseases, a CRL can significantly impact financial stability, future research programs, and investor confidence. That uncertainty can slow or even halt additional rare disease programs, making it harder to attract the sustained investment on which this field depends.

Rare disease drug development is already complex, expensive, and high-risk. When the regulatory pathway seems unpredictable, it sends a chilling signal to the broader investment community and that ultimately affects the entire innovation ecosystem. Investors will not direct millions of dollars into orphan product development programs when the goalposts keep changing. While some development programs are turning to Europe or Asia, others are terminating their programs altogether.

Regulatory uncertainty is setting back possible treatments for rare disease patients by years and decades. For many rare disease families, these decisions do not just represent back-and-forth regulatory engagement — they can mean delays to what may be their first or only treatment option in their loved one's lifetime. When you are living with a progressive or life-threatening rare disease, time is not an abstract concept.

Innovation only works when it is supported by scientific rigor, regulatory consistency, and a stable environment that encourages continued investment. Patients are waiting and the system must work in a way that gives them real confidence that promising science can become real treatments.

Congress can continue to exercise oversight to hold FDA accountable for consistent application of FDA's newly announced policies and long-time regulatory and statutory requirements to improve consistency, reliability, and transparency.

Protect crucial resources for Food and Drug Administration (FDA) to advance discovery and development of rare disease therapies.

Importantly, policies alone are not enough. Frameworks only work if there are experienced reviewers, scientific leadership, and infrastructure in place to implement them. It is critical that FDA is adequately resourced to advance rare disease discovery and therapy development. Continued investment in the Rare Disease Innovation Hub, retention and recruitment of expert staff, and timely reauthorization of PDUFA VIII, with expanded patient engagement provisions, are essential to ensuring these policies do not sit on a shelf.

Therefore, NORD urges Congress to continue to adequately resource the FDA to sustain and expand its work in rare disease drug development. The United States remains a global leader in orphan drug innovation, but continued progress depends on FDA's capacity to keep pace with scientific advances, evaluate novel therapies efficiently, and support new areas of need. Without sufficient investment, regulatory innovation may stagnate, potentially leaving patients without timely access to life-altering treatments.

We currently face a challenging environment, but we remain hopeful. It has been heartening to hear support from agencies and Congressional leaders during these many rare disease events. We need FDA leadership to provide reliable and consistent advice to drug developers, resume engaging with patients and refocus to a patient-centric approach, bring back transparency through Advisory Committees, recommit to hiring and training staff in innovative platforms and techniques, and provide the resources needed for cross-cutting initiatives such as the Rare Disease Innovation Hub. We encourage Congress to continue to exercise its oversight authority to ensure that the FDA makes these changes so that the drug development pipeline in the United States is preserved and rare disease patients have the treatments they need to live and thrive. With the right resources, consistency, and partnership, we can see to it that robust, promising science becomes real-world treatments for the rare disease community.

NORD stands ready to assist in making these actions a reality. Thank you again for the opportunity to provide comments.

Sincerely,

Pamela Gavin
Chief Executive Officer
National Organization for Rare Disorders

Anonymous – March 5th, 2026

Written Testimony

Living with this disease is very difficult. All your coordination an balance are effected.The FDA should approve this medication that will help so many with this disease.

David Davenport – March 5th, 2026

Written Testimony

March 5, 2026

The Honorable Rick Scott Chairman

Special Committee on Aging United States Senate Washington, DC 20510

The Honorable Kirsten Gillibrand Ranking Member

Special Committee on Aging United States Senate Washington, DC 20510

Dear Chairman Scott and Ranking Member Gillibrand:

On behalf of the Alliance for Regenerative Medicine (ARM), which represents more than 400 members across 25 countries, including emerging and established biotechnology companies, academic and medical research institutions, and patient organizations, I commend the Special Committee on Aging for holding a hearing on how regulatory processes and evolving standards at the Food and Drug Administration (FDA) can unintentionally delay patient access to safe and effective therapies, particularly for individuals living with rare diseases. ARM is the leading international advocacy organization championing the benefits of engineered cell therapies and genetic medicines for patients, healthcare systems, and society. Because approximately 80 percent of rare disorders have genetic causes,¹ cell and gene therapies (CGTs) are critical in targeting the root causes of these diseases rather than treating symptoms and have the potential to transform the lives of afflicted patients.

The FDA's recent reversal of previous agency guidance and rejection of several CGTs for rare diseases has raised concerns over regulatory clarity and predictability at the agency. An efficient and predictable review process at FDA is essential to maintain the U.S.'s biomedical leadership in the face of growing competition from countries like China and to ensure that patients with rare diseases have access to life-saving CGTs. We urge the Committee to work with the White House, HHS, and the FDA to ensure that practical and actionable steps are taken to address growing concerns over regulatory inconsistencies and late-stage shifts in guidance for CGT rare disease programs at the FDA.

CGTs can offer life-saving treatment options for patients with rare diseases

The U.S. has introduced more CGT products into the market than any other country and is a world leader in promoting access to CGTs. To date, the FDA has approved 48 CGTs.² Research has projected approvals of between 75 and 96 new CGT product-indications by 2033,³ with estimates of the number of patients receiving CGT treatments increasing approximately tenfold in a similar period.⁴

¹ Marwaha S, Knowles JW, Ashley EA. A guide for the diagnosis of rare and undiagnosed disease: beyond the exome. *Genome Med.* 2022;14(1):23. doi: 10.1186/s13073-022-01026-w

2 U.S. Food and Drug Administration. Approved Cellular and Gene Therapy Products. December 9, 2025. <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products>. 3 Cell and Gene therapy (CGT) pipeline deep dive. Center for Biomedical System Design. Tufts Medical Center. 2023. <https://newdigs.tuftsmedicalcenter.org/payingforcures/defining-disruption/cell-and-gene-therapy-products-and-%20pipeline/cgt-pipeline-deep-dive/#gsc.tab=0>. 4 Phares S et al. The next decade in cell and gene therapy. Drug Discovery Today. January 2026; 31(1). <https://www.sciencedirect.com/science/article/pii/S1359644625002648>.

It is becoming increasingly clear that the promise of CGTs is bearing fruit for rare disease patients. CGTs are remarkable in that they treat the root cause of disease and have proven to be life-saving for rare disease patients who have few or no other options. Gene therapies seek to modify or introduce genes into a patient's body with the goal of durably treating, preventing, or potentially curing a disease. There are currently 15 gene therapies available for rare genetic diseases and conditions, such as Duchenne muscular dystrophy, sickle cell disease, and two forms of hemophilia. Cell therapies involve the administration of viable, often purified cells into a patient's body to grow, replace, or repair damaged tissue. In 2024, the FDA approved the first- ever adoptive cell therapy – for metastatic melanoma. FDA also approved new cell therapies such as those for advanced synovial sarcoma, a rare type of cancer that often attacks joints, and for dystrophic epidermolysis bullosa, a rare skin condition that causes widespread blistering that can lead to vision loss or permanent scarring.

Congress has long-supported progress in rare disease therapy and CGT development

It takes years and considerable capital to bring new rare disease therapies to market, and companies need predictability to make business decisions, plan future research and development, and attract investors. On average, the development timeline for rare disease treatments is 10-15 years.⁵ The cost of bringing CGTs to market is nearly \$2 billion,⁶ and only 13.8 percent of CGT therapeutic development programs that enter phase 1 of the approval process complete phases 2 and 3 and reach FDA approval.⁷ We thank Congress for recent passage of the Mikaela Naylor Give Kids a Chance Act, which reauthorizes the Rare Pediatric Disease Priority Review Voucher (RPD PRV) Program and provides crucial incentives for companies to invest in developing treatments like CGTs for children with rare diseases.

Congress has long recognized the importance of policies to address the inherent complexities in developing CGTs and treatments for rare disease populations. Through the 21st Century Cures Act, for example, Congress authorized the FDA to establish the Regenerative Medicine Advanced Therapy (RMAT) designation program that provides sponsors of CGT products with enhanced FDA interactions. In FY 2024 alone, the FDA approved 73% of RMAT requests, a significant jump from the previous high of 51%. Many RMAT-designated products also hold orphan designation, reflecting the program's impact in accelerating therapies for rare diseases. Moreover, one-third of all RMAT designations granted since the program's inception were awarded in the past two years, underscoring the program's growing role in expediting innovative therapies.

By making RMAT-designated products eligible for accelerated approval, a pathway established by Congress in 1992, the RMAT program also encourages flexible clinical trial designs, novel

5Lumsden JM, Urv TK. The Rare Diseases Clinical Research Network: a model for clinical trial readiness. *Ther Adv Rare Dis.* 2023;4:26330040231219272. Published 2023 Dec 26. <https://pmc.ncbi.nlm.nih.gov/articles/PMC10752072/>

6 See Sabatini MT, Chalmers M. The Cost of Biotech Innovation: Exploring Research and Development Costs of Cell and Gene Therapies. *Pharmaceut Med.* 2023;37(5):365-375. doi:10.1007/s40290-023-00480-0; De Luca M, Cossu G. Cost and availability of novel cell and gene therapies: Can we avoid a catastrophic second valley of death?. *EMBO Rep.* 2023;24(2):e56661. doi:10.15252/embr.202256661.

7 Wong, C.H., Li, D., Wang, N. et al. The estimated annual financial impact of gene therapy in the United States. *Gene Ther* 30, 761–773 (2023). <https://doi.org/10.1038/s41434-023-00419-9>.

endpoints, and real-world evidence while maintaining FDA standards for safety and efficacy. These flexibilities include the use of surrogate endpoints, which are substitute measures used in clinical trials to predict clinical benefits, allowing for faster drug approvals by the FDA. Gene therapies are especially amenable to the use of surrogate endpoints because the protein product of many gene therapies lies directly in the causal pathway of disease (e.g., a gene mutation causes a lack of protein production that is restored with a functional gene).

Recent actions by the FDA undermine the Trump Administration's bold vision for CGTs

Over the past year, the Trump Administration, including HHS and FDA leadership, have publicly stated unprecedented support for CGTs to ensure America remains a global biotech leader. In 2025, the FDA convened a CGT roundtable and listening sessions with biotech CEOs, providing forums on how accelerate CGT development. The FDA has also proactively outlined multiple new policies to advance the CGT sector, such as the Rare Disease Evidence Principles program (RDEP) to clarify efficacy requirements; a new Plausible Mechanism of Action Pathway for individualized treatments, like N-of-1 gene therapies; and case-by-case flexibilities for chemistry, manufacturing, and controls (CMC) requirements.

Unfortunately, a number of recent negative regulatory actions related to late-stage CGTs have undermined the stated goals of HHS and FDA leadership (see Appendix 1). Over the past four months, the FDA has declined to approve multiple promising CGT medicines – including treatments for rare diseases and conditions like Huntington's Disease, Hunter Syndrome, and Epstein-Barr virus-associated post-transplant lymphoproliferative disorder – by issuing complete response letters (CRLs). Particularly concerning is the inconsistent application of regulatory flexibilities for these rare disease products, despite the fact that nearly all of them received the RMAT designation.

In some of these rejections, the FDA changed the evidentiary requirements for clinical trials at the last minute, reversing commitments it had made just months before to bring these medicines forward. This includes raising last-minute questions about whether a surrogate endpoint predicts clinical benefit or taking issue with the use of natural history studies as a control in the clinical trial design.

Randomized, double blind, placebo-controlled trials that are traditionally conducted in conditions with larger and well characterized disease populations are often not appropriate or ethical when considering the challenges and urgency of rare diseases. These CRLs represent a troubling trend where well-established principles of regulatory flexibility have been sidelined in favor of methodological rigor. In fact, the rejection of natural history studies as a valid control runs counter to the Plausible Mechanism Pathway draft guidance just released by the FDA.

Dating back to last year, communication with sponsors has been poor and external engagement has also been lacking. For example, in the past the FDA has assembled a group of outside experts through an Advisory Committee to offer an independent opinion, to hear from patients and families about their experiences with the drug and the condition it treats, and to help resolve scientific disagreements.³ In 2025, however, the FDA held 65% fewer Advisory Committee meetings for prescription drugs, biologics, and related topics than in 2024, reducing opportunities for external expertise and patient insights to inform FDA decisions, and thus raising questions not only about the adequacy of FDA staffing but philosophical changes.

Historically, collaboration between regulators, researchers, industry, and patients – through transparent knowledge sharing and scientific exchange – has helped drive progress in rare disease treatments while maintaining rigorous standards.

Regulatory inconsistency impacts rare disease patients and the U.S.'s biopharmaceutical leadership

Nearly 900 ongoing clinical trials in the United States are testing CGTs. Each one represents tremendous hope for millions of other patients and their families – not only for those suffering with rare diseases, but also common ones like heart disease, Parkinson's disease, and diabetes. We are concerned that – if not corrected – these patterns of uncertainty risk patient access to life-saving treatments, and this will undoubtedly have a disproportionate impact on rare disease patients. For patients with degenerative conditions, delays in access to treatments caused by FDA's recent regulatory inconsistencies can result in irreversible changes to their functionality or even death. Many rare disease patients simply cannot wait a decade for new trials to be conducted.

These actions that slow the development of urgently needed rare disease therapies also come at a time when China is racing to eclipse the US as the global leader in CGTs. For the first time, in 2025, the Asia-Pacific region surpassed North America in clinical trials for CGTs.⁸ And, during the second half of 2025, clinical trials for CGTs grew 20% in China, compared to only 8% in the United States. Clear and predictable regulatory pathways are essential to maintaining U.S. competitiveness in biomedical innovation and for Americans with rare diseases and other high unmet medical needs. Without a serious course correction, U.S. patients will increasingly be denied access to transformative therapies even as these medicines become available to their counterparts in other countries.

ARM recommends several remedies for late-stage rare disease programs

1 in 10 Americans have a rare disease, with 70% of rare diseases beginning in childhood. Of the more than 30 million people living with one or more rare diseases in the United States, 15 million (or 50%) are children. More than 90 percent of the estimated 10,000+ rare diseases still have no cure.⁹ Parents raising children with rare diseases face challenges in managing their daily lives as they navigate caregiving roles and uncertainties about the life-course of disease for their children. Their hope is anchored on developers, risking capital and potential for profitability, to innovate cures.

To bring these cures to fruition, innovative breakthroughs like CGTs require not only regulatory flexibilities that address the unique challenges associated with their development, but also a consistent and predictable framework for regulatory oversight. ARM urges a common-sense course-correction at the FDA that puts patients first, addresses regulatory inconsistencies, improves communication, and remedies shifts in guidance that put late-stage rare disease

8 Alliance for Regenerative Medicine. Reasons to Believe: Innovation, Access, and Sustainability in CGT. January 2026. <https://alliancerm.org/wp-content/uploads/2026/01/ARM-CGT-Reasons-to-Believe-January-26-2026.pdf>.

9 See National Organization for Rare Disorders. Get to Know the Facts about Rare Disease. December 2025. NRD-2332 RD Fact Sheet_FNL - v2; Global Genes. Numbers: Rare Disease Facts. <https://globalgenes.org/rare-disease-facts/>.

programs in jeopardy. The FDA has commonly used the following approaches in approving dozens of CGTs over the last decade:

1. Sponsors who were previously aligned with the FDA urgently need a path forward. The FDA should honor the commitments it originally made to companies and patients about what evidence would be acceptable for approval. To facilitate, sponsors should be granted an expedited Type A meeting, with FDA leadership present, to resolve these issues.¹⁰
 2. To prevent unnecessary patient access delays, the FDA should leverage post-market commitments to further establish efficacy after approving the therapies.¹¹ Through post-market commitments, the FDA can gather additional data from patients after approval to further verify the strong signals that these medicines work.
 3. Upon request from the sponsor, the FDA should assemble a group of outside experts, known as an FDA Advisory Committee, to transparently review these therapies and listen to testimony from patients about the benefits-risk considerations for a therapy.¹² If a sponsor requests an Advisory Committee meeting, one should be granted.
- We ask the Committee to work with the White House, HHS, and its agencies to ensure that the regulatory flexibilities Congress has authorized are meaningfully and consistently used by the FDA to provide patients with rare diseases access to life-saving therapies like CGTs.

The past decade has shown that a modernized regulatory framework, clear and predictable pathways for sponsors, and open engagement with stakeholders are essential to maintaining the U.S.'s leadership in biomedical innovation. The consistent application of regulatory flexibilities is critical for

patients with rare diseases and other high unmet medical needs, where delays in development and approval can mean the difference between life-saving treatment and no treatment at all.

As evidenced by the many powerful testimonies of patients and their advocates heard throughout Rare Disease Week on Capitol Hill, rare diseases profoundly impact the quality of life of affected individuals and their families. The CGT sector holds great promise for transforming the landscape of rare disease treatment by offering the innovative, targeted, and potentially curative therapies these patients deserve. We thank you for your continued focus on improving the lives of those living with rare medical conditions, for some of whom CGTs may be the only treatment option.

ARM strives to be a resource for this Committee. We look forward to working with you to develop additional policy solutions that bring safe and effective regenerative medicines to patients. For questions, please contact ddavenport@alliancerm.org.

10 PDUFA VII Commitment Letter / FDA Draft Guidance 2023, Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products

11 FDCA § 506(c) (21 USC 356(c)), Expedited approval of drugs for serious or life-threatening diseases or conditions / 21 CFR 601Subpart E, Accelerated Approval of Biological Products for Serious or Life-Threatening Illnesses

12 Consistent with FDA's longstanding practice under 21 CFR Part 14 and Federal Advisory Committee Act (FACA)

Sincerely,

Mark Battaglini
Chief Strategy Officer
Alliance for Regenerative Medicine

Caroline DeBerry – March 5th, 2026

Written Testimony

Thank you to Chairman Rick Scott, Ranking Member Kirsten Gillibrand, and members of the Senate Special Committee on Aging for examining how regulatory processes at the Food and Drug Administration affect the development and availability of treatments for rare and complex diseases. The Committee's hearing announcement highlights concerns that regulatory processes can unintentionally delay patient access to innovation.

I submit this statement as a survivor, female small business owner, and leader with an over 20-year, successful career in government and policy; the below includes suggested improvements for how the United States develops and evaluates medical innovation.

Personal Perspective: Living with a Rare, Lifethreatening Condition

I have been diagnosed with both anaphylactic allergies as well as Mast Cell Activation Syndrome / Disorder (MCAS / MCAD) - which is a rare, lifethreatening condition affecting the immune system and often exists with other rare conditions such as POTS and EDS.

Mast cells are immune cells located throughout the body—including the skin, digestive tract, lungs, blood vessels, and nervous system—and they help coordinate protective responses when the body detects a threat.

In MCAS, mast cells release chemical messengers too frequently or too intensely. These chemicals—including histamine and other inflammatory signals—can affect multiple organ systems at the same time.

Because mast cells exist in so many tissues, symptoms can involve several body systems simultaneously. These may include skin reactions, gastrointestinal symptoms, cardiovascular problems, breathing difficulties, among even more symptoms - and can be lifethreatening. Epinephrine has saved my life more times than I could count.

I have never let allergies or MCAS control my life or hold me back, and I am blessed that, after many years of insufficient treatment, I am now on an effective but complicated and very expensive protocol that does allow me more freedom and improved health but will not cure MCAS. Just this past week, I had to share the disheartening news with a worried grandfather whose granddaughter likely will be soon diagnosed with MCAS that the treatment protocol is not easy and that there is no cure. I have had similar, challenging conversations with other MCAS survivors.

As this committee is very aware, we MCAS survivors are not the only ones - many people live with rare, complex diseases for which treatment options do not exist or remain limited and expensive. Why Regulatory Efficiency Matters for Patients

People facing insufficiently treated conditions cannot afford unnecessary delays in the development and evaluation of therapies. Throughout my career, I have heard many stakeholders—including

patients, clinicians, and researchers—express concerns that regulatory uncertainty, evolving regulatory expectations, and procedural delays can slow access to promising treatments. Congress has previously provided the FDA with mechanisms intended to accelerate innovation, including pathways that allow regulatory flexibility when strong scientific evidence supports potential benefit. But more must be done. I know FDA Commissioner Marty Makary, MD, and respect him for his goal to help people such as me by empowering and accelerating innovation. However, Congress can help too by working more with the FDA and passing additional legislation with needed reforms.

Opportunities to Improve the Innovation Pipeline

Speaking as both a rare disease survivor as well as a policy expert - I want to share the below practical reforms proposed by 1Day Sooner, an impressive nonprofit that advocates for people who participate and want to participate in high-impact medical studies, particularly human challenge trials. These reforms will empower innovation while maintaining high standards of safety and data integrity. First, many obstacles slow down clinical trials. Phase 1 studies carry manufacturing burdens designed for commercial scale, multi-site trials undergo duplicative institutional review board (IRB) review, and innovative designs face unpredictable regulatory pathways.

Second, improving the structure of clinical trial infrastructure—such as platform trials and master protocols—could allow multiple therapies to be tested efficiently within shared research frameworks.

Third, expanding decentralized clinical trial models can make research participation more accessible. Telehealth visits, remote consent, home nursing visits, and the use of local laboratories can expand participation while maintaining high-quality data collection.

Fourth, maximizing the value of clinical and regulatory data would allow knowledge generated in one study to benefit future research. Modernizing databases such as ClinicalTrials.gov and improving transparency around regulatory decisions would strengthen the scientific ecosystem.

(For more information, please visit: <https://www.1daysooner.org/clinical-trial-abundance>.)

Conclusion

We survivors rely on regulators to protect safety while also ensuring that promising, innovative therapies can move efficiently through the development process. Policies that reduce unnecessary delays, improve transparency, and support responsible innovation

will help ensure that survivors of complex and rare conditions have meaningful opportunities for better treatment options.

For people like me living with conditions such as Mast Cell Activation Syndrome and other rare disorders, accelerated innovation in medical science is not just a policy issue. It is a necessity to empower us to have healthy futures.

Bio:

Caroline DeBerry is the founder and CEO of Tenagrity® Solutions. Caroline has been involved in government, policy, and public service for over 20 years - having been a VP, chief officer, senior congressional staffer, senior federal employee, small business owner, and international best-selling published author.
For more information, visit www.tenagrity-solutions.com/about.

Joyce Kullman – March 5th, 2026

Written Testimony

Statement for the Record
U.S. Senate Special Committee on Aging
2/26 Hearing "How FDA Bureaucracy Stifles Innovation"
On Behalf of Vasculitis Foundation
Chairman, Ranking Member, and Members of the Committee:

On behalf of Vasculitis Foundation and our community of patients with vasculitis and their families, thank you for the opportunity to submit this statement for the record with our strong support for the Maintaining Investments in New Innovation (MINI) Act. Vasculitis is a group of rare autoimmune diseases that cause inflammation of the blood vessels and can restrict blood flow and damage vital organs or tissues. While there are no cures for Vasculitis, there are now 11 FDA approved treatments to help improve quality of life for patients living with the disease. Unfortunately, these available treatments do not treat all of the 20 different types of Vasculitis, so more research and development is needed to address the gaps in available treatments to ensure that one day every vasculitis patient has a better quality of life.

Vasculitis Foundation applauds the Senate Aging Committee for focusing on how to remove regulatory barriers to accelerate access for patients with rare diseases like Vasculitis to safe, effective and innovative new therapies. In addition to joining with the rare disease community's support for implementation of FDA regulatory flexibilities, we strongly support the MINI Act, a bill to encourage the development of genetically targeted technology (GTT) that holds tremendous promise for treating rare diseases like vasculitis.

We are excited that several biopharma companies are currently researching and testing how GTTs could potentially treat some subtypes of vasculitis with a targeted RNA strand technology.

However, this is fragile new market which is significantly impacted by regulatory/pricing policy changes, including the Inflation Reduction Act's (IRA) Medicare drug pricing. The MINI Act would make a minor modification to the IRA to allow GTTs to be categorized as large molecule drugs rather than small molecules, giving them an 11 rather than 7 year timeframe after FDA approval before being subject to Medicare drug pricing; doing so would help GTT companies recoup the heavy upfront costs of developing these new treatments.

On behalf of vasculitis patients, including many who are in the aging community that you serve, we respectfully request your co-sponsorship of the MINI Act as a meaningful way to support the development of GTT medical innovation that can mean a world of difference for so many patients in the rare community.

Respectfully,

Joyce A. Kullman, President
Vasculitis Foundation

Kristen Wheeden – March 5th, 2026

Written Testimony

Submitted by: United Porphyrins Association (UPA) on behalf of the EPP and XLP patients

Chairman Scott, Ranking Member Gillibrand, and Members of the Committee:

Thank you for convening this important hearing. I want to begin by adopting the question Chairman Scott posed in his opening remarks: "Is the FDA doing everything Congress intended it to do to quickly get safe, effective treatments to patients with rare diseases who cannot afford to wait?" We are a rare disease community that cannot afford to wait, and recent disappointment in an FDA review only underscores the urgency of this work.

We submit this statement on behalf of individuals and families affected by **Erythropoietic Protoporphria (EPP)** and **X-linked protoporphria (XLP)**. These are rare, genetic diseases that often begin in childhood and cause severe, rapid-onset pain triggered by visible light. Patients describe it in the bluntest terms that it feels like they are "**being burned alive**" by the sun. The pain can be excruciating and overwhelming within minutes, and it is not something you can simply "push through." What makes this especially cruel is that visible light is sunlight - it is everywhere. Avoiding it can mean avoiding life itself. And because EPP and XLP can look "fine" on the outside in the moment, the disease is often dismissed or misunderstood at school, at work, and even in healthcare settings. Yet the impact is constant and unmistakable: families plan every day around risk, spend heavily on protective clothing and specialized vehicle tinting, and still live with unrelenting vigilance just to get through ordinary moments.

Chairman Scott spoke powerfully about time: "Time means independence." For people with EPP, time means the ability to experience life. It means walking from a parking lot to a front door without fear. It means attending school consistently, keeping a job, sitting at a child's soccer game, and saying yes to ordinary moments that build mental health, social connection, and identity. EPP patients cannot afford to "wait" in a generic sense because this disease is seasonal. Spring and summer are especially difficult as months of the highest restriction, isolation, and repeated pain events. Delays are lived in missed milestones and escalating anxiety, especially in children and adolescents.

That is why the Committee's focus on clarity, predictability, and Congress's intent matters so deeply to the porphyria community.

In the U.S., the only FDA-approved therapy for EPP is SCENESSE (afamelanotide), a bi-monthly implant indicated to increase pain-free light exposure in adults with a history of phototoxic reactions. Beyond that, care relies on strict light avoidance and practical protections, which are burdensome and imperfect. There is a clear unmet need, especially for adolescents, for broader access across the community, and for disease-modifying treatments that address the underlying biology, rather than a "band aid."

Several investigational therapies are in development:

- Disc Medicine's bitopertin, an oral small-molecule that inhibits glycine transporter 1 (GlyT1), is in a Phase 3 confirmatory trial **was recently reviewed under the accelerated pathway after receiving**

an FDA Commissioner's Priority Review Voucher.

- Dersimelagon (MT-7117), an oral MC1R agonist, recently reported positive topline Phase 3 results in EPP/XLP.
- PORT-77 is being studied in an early Phase 2a trial

On February 13, 2026, Disc Medicine received a Complete Response Letter (CRL) declining Accelerated Approval for bitopertin for EPP. Public reporting indicates the FDA acknowledged robust lowering of protoporphyrin IX (PPIX) in Phase 2 studies and the biological rationale for PPIX as a biomarker but concluded the Phase 2 program did not demonstrate a clear association between percent change in PPIX and the sunlight exposure-based endpoints used in those trials and requested Phase 3 results prior to approval.

Here is the patient-centered concern: EPP patients and families have described real-world, functional benefit from therapy in language that is not abstract. They describe life opening up, fear easing, participation returning. Yet when lived experience and patient-reported function do not appear to carry meaningful weight alongside biomarker change, patients experience it as being told that the life they are living does not "count" as evidence of clinical benefit. The result is more waiting, more suffering through seasons that reliably bring harm, and more erosion of trust among the families who have volunteered for research and carried out trial burdens in a rare disease with extremely low prevalence.

This is not a request to weaken safety standards. It is a request for consistent, transparent, and predictable application of the tools Congress created for serious and life-threatening rare diseases, including clearer expectations for how surrogate biomarkers must connect to functional endpoints in Accelerated Approval decisions, and how Patient Experience Data is incorporated when patients describe meaningful, lived benefit.

We respectfully urge Congress to:

1. conduct oversight on FDA's application of Accelerated Approval for rare disease therapies, including evidentiary expectations and consistency across programs;
2. promote greater transparency when a CRL is issued under Accelerated Approval, including clear public explanation of what evidence was persuasive, what was not, and what is specifically needed next; and
3. reinforce incentives and policies that sustain rare disease development, including stability in programs that accelerate review for rare and pediatric conditions.

EPP families are doing their part. They enroll in trials. They provide patient experience data. They show up again and again. What they need in return is a system that protects safety while also acting with urgency, common sense, and respect for the reality that patients cannot afford to wait especially when a safe, efficacious therapy that has life-changing real-world impact.

Respectfully submitted,

EPP and XLP Patient Community and the United Porphyrins Association

Jamie Sullivan – March 5th, 2026

Written Testimony

Supplementary Patient Stories

Shared with the EveryLife Foundation for Rare Diseases to Inform the

United States Senate Special Committee on Aging Hearing on

“From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation” February

26. 2026 – SH-216



The EveryLife Foundation for Rare Diseases invited the rare disease community members to reflect on the personal impact of recent FDA therapeutic development regulatory delays.

Submissions have been de-identified to omit personal information, such as name and location.

Section One – Represents submissions from communities who have been directly affected by regulatory delays over the last year.

Section Two – Represents submissions from across the rare disease community, reflecting additional experiences living with rare diseases.

Section One

MPS II (Hunter Syndrome)

Submitted from primary family member

When I was 15 years old, I watched my 13-year-old brother take his last breath and be taken away from our home in a hearse. He had Hunter Syndrome (MPS II). The weeks leading up to that moment started with trips to the hospital, watching him flatline and be revived, bringing him home on life support, and eventually watching my parents make the decision to remove him from life support. "Awesome God" still rings in my head and brings me to tears as we sang it to him as he breathed his last. The faces of my family members etched in my brain as a deafening silence crushed us. I watched my dad disappear while he tried to find distractions. My siblings fell into their own bad habits to cope. I stayed home from school for a week trying to plan my brother's funeral while my mom crumbled in despair.

Now I am 32, and my only child was just diagnosed with the same disease that took my brother's life. He's not yet 2 years old, and I see the delays beginning. This sweet, energetic toddler has to go to the hospital once every single week for the rest of his life to be poked with a needle and sit still in a room for 4-7 hours while medication is pumped into his body. A medication that can't stop the disease from getting worse, and it can't fix the damage that's already been done. All it can do is slow the progression of physical ailments.

The medication does not cross the blood brain barrier, so it does nothing to preserve his cognitive ability. He's 19 months old. Any word he once said, he no longer says. I may never hear my son say, "I love you". We gave up our hobby of off-roading because it's not safe for him. He may never have a hobby of his own, or a job, or a girlfriend, wife, or kids. He may never even see adulthood. The life expectancy in severe cases is 10-20 years old.

Every time I look at my son, I see him dying in my arms like my brother did. We need better treatments and we need them now. My son is 19 months old, has been on the current available treatment for 6 months, and I'm seeing decline. Japan has a treatment that crosses the blood brain barrier, and a one-time gene therapy has been created and shown to be successful in clinical trials but was denied by the FDA. We don't have time to wait. I'm already watching my son move closer to death every day.

Submitted from secondary family member

I met my future brother-in-law in 2008. He was in his later phases of life living with the rare disorder, Hunter's syndrome. He had lost the ability to walk and feed himself, so my future in-laws would move him around in his specially made wheelchair. They were also tasked with feeding, bathing, and cleaning him. His care was 24 hours a day, seven days a week as children with this condition rarely sleep.

My mother-in-law was a home maker which helped as I do not know how two working parents could care 24/7 for a child living with these symptoms. He used to speak several phrases before the condition worsened, though at the stage I met him I unfortunately never had the opportunity of hearing his voice. I never had the chance to see him use sign language as his limbs only moved when he experienced a seizure. I never saw him walk or play as he was secured to his specialized wheelchair for his safety.

Doctors could do little to help mitigate the painful symptoms associated with this debilitating condition. Back then, there were talks of new medications circulating, awaiting approval, in addition to rumored research for possible treatments. The science and approvals never caught up, nor were passed in time and, consequently, were unavailable to patients like my brother-in-law. He passed at just 13 years old in April 2009. I had only known him for those brief 9 months. During those months, I witnessed multiple hospital visits, seizures, and stress.

I am now married to his sister, and it is a tragedy that he was not at our wedding with the rest of our friends and family. Fast forward years later, my sister-in-law's first and only child, has the same condition, Hunter's syndrome. She and her husband both work full time and care for him 24/7 with the assistance of my mother-in-law, as she helps the best she can with her schedule. We love my nephew dearly as we did my brother-in-law. When you watch someone lose the ability to speak, walk, and then eventually pass away, heart wrenching is not strong enough of a phrase. It is excruciating.

With news of a one-time treatment using a gene therapy called, RGX-121, we were optimistic that our nation will take the path forward and approve this treatment for our nephew. This hope, unfortunately, came to a halt in recent days with the news of the FDA not approving this groundbreaking gene therapy. We were so close to receiving approval for this life-changing treatment.

We always hoped and prayed that as time moved forward so would the treatment for this rare condition. Now, we have data, research, and the medical technology to help children with Hunter's syndrome by using this gene therapy. RGX-121 is a one-time treatment, so it will not be a continual process which makes it cost efficient and provides better care for patients. Other advanced nations, such as Japan, have begun treating their patients with gene therapy. The United States was once the medical center of the world. We had the best treatment facilities, cutting edge research, and people flocked from all over the world to bring their children here to receive the best

healthcare. We have the financial success that most nations dream about, so the budgets are available. These funds need to be routed through the appropriate departments. This studied and reviewed gene therapy must be passed for these children's sake, their family's sanity, and for the future of this country's well-being. We, as a people, have a moral duty to fund all healthcare issues including lesserknown disorders. This medicine would also serve to help other children across the globe. With the United States' market and influence in the medical industry, once this gene therapy is approved and used for treatment here, it will become available to all children worldwide.

Every child deserves a chance to live a healthy and loving childhood.

[Submitted by additional family member](#)

To the Senate Aging Committee;

I am representing the community of those affected by the rare disease

Mucopolysaccharidosis Type II (MPS II), otherwise known as Hunter's Syndrome, in support of the proposed gene therapy, RGX-121 (clemidsogene lanparvovec). In the following excerpts, I will discuss my family's experiences with losing my brother to Hunter's, along with the newfound journey of my sister who now has a son with Hunter's. Additionally, I will go further into detail about how this life-altering gene therapy will have positive outcomes not only for our family, but to all families that have a child with Hunter's Syndrome.

I have been both a sibling and now an aunt to an individual with Hunter's Syndrome. Growing up with my brother, and presently my 1.5 year old nephew, whom was diagnosed with the disease just this last summer in 2025. In a family of 5 children, I am the middle child with two older brothers, a younger sister and what was once our youngest brother. He was born with Hunter's Syndrome in 1996, and would have turned 30 this February.

Unfortunately, his predestined disease only allowed him to make it to 13 years old, back in 2009.

My parents were unaware of my mother being a carrier of this genetic anomaly, seeing as Hunter's Syndrome is an X-linked genetic disorder. My brother's diagnosis was made known when he was 2-3 months old, with doctors making it significantly clear that this was a very rare disease & his lifespan would be cut notably short due to it. Without a treatment or cure that could cross the blood brain barrier, the missing link to his DNA would ultimately be his demise. At the time, only being 5 years old myself, I remember my parents telling us four kids that he was special & we didn't know how much time we would get with him on Earth. But that we would treat him just the same as any other child, and give him the same life experiences possible. And that we did.

Everyone knew him, mainly because in his younger more able days he loved to rip off his diaper and hightail it down the street with my mom chasing after him—as he laughed in a guttural, pure sort of way. He was a gentle bliss of a human, despite the downfalls of his condition. He knew no different, as did we. He had a twinkle in his eye that let you know he understood feelings and emotions, even if he couldn't speak it outwardly. Especially in his younger years, he could run with all of us kids along with surrounding neighbors, he could throw and kick a ball like a pro, and ride

his big wheel tricycle into the sunset. My mom definitely had her hands full, but he had a way of making your heart even more overfilled with joy without even trying. Unfortunately this made his decline as he aged that much more apparent and heart wrenching to watch before our very eyes, as his spark of life slowly fizzled out as the disease progressed throughout his innocent body.

Some of the downfalls of my brother's disorder lasted the entirety of his life, not just during the swift decline in later years. He spent his life in diapers with messy bowel movements that were never solid. Even though I never heard my parents complain, he slept in my parent's bed for all 13 years of his life. This was primarily so my mom could keep watch over him 24/7, as he also did not sleep through the night in younger years. This even evolved to long nights of watching Barney in the living room, where my mom would lay half awake on the carpet with her arm around him as he sat up watching into the wee hours of the night. If I woke up in the middle of the night, I remember the soft glow of the television down the hallway & would come out to join them. I remember my mom giving him nightly breathing treatments, the sound of the machine humming is a heavy reminder of one of the many ways my mom did all she could to bring comfort to her child. I remember occupational therapists and speech therapists coming to our home to work one-on-one with him, some more patient with his diagnosis than others.

One thing was for sure, my mom and my brother were inseparable. She never let him out of her sight, aside from the few times she allowed him to be apart of some special needs school programs in his younger years when he was active. Unfortunately, even many of the special education teachers were not proficient in dealing with such a specialized child, and it ended in him communicating with us that he was being abused by them. He could say few words, but did learn some basic sign language to help communicate. My mom never entrusted anyone with him after that.

As time went on, the more nonverbal he became as he aged. He went from being a lively wild child full of spunk and joy riding his big wheel, to a quiet sedentary teen as he lost all his mobility. He began losing his balance before the age of 10 and eventually had to have a specially made walker, and eventually a custom wheelchair where he resided most of his days. He suffered from debilitating seizures, heavy mucous production (some families opt for tube feeding), as well as breathing treatments to help reduce the potential for pneumonia (this would eventually be the means by which took his life). Given the limited knowledge on MPS II back then, my mom did all that she could for him. In his last week of life, we knew it was his time. It seemed like hundreds of people who had been impacted by my brother walked through our front door to pay their respects as he laid there calmly and quietly analyzing each one. He held on for his final visitor, his home helper. My mom told him teary eyed, "It's okay, you can go now" as he took his last breathe. Then, as if the heavens lit up, the darkly lit bedroom was glowing with golden rays of sunshine and his sparkling blue eyes lit back up as he smiled his final goodbye.

Losing a family member leaves a heartache no one can heal, and outliving your own child is something most parents will never have to be concerned with. There is a feeling of hopelessness and deep sadness when you are told your child may only live a certain number of years. It is clear

that my mom was his around-the-clock caregiver, so his absence struck her the hardest & she has never fully healed from his passing. Our entire family has a special place in their heart for my brother, and can easily get choked up talking about memories of him. There are numerous emotions that accompany this sort of loss, the "what if's", along with each family member feeling their own sense of guilt and regret, longing to see their loved one yet being thankful they are no longer suffering from such disease. It has been 17 years since his passing, and simply writing this while reflecting on his life has taken me weeks to finish due to the heavy hearted nature of this topic. With how gut-wrenching and painful the healing process has been after almost two decades, any sort of lasting solution to save children with MPS II is essential. Prevention by means of treatment of those diagnosed with Hunter's is a must, as well as saving their families from having to go through this in the same way that my brother and we did. I believe we should stop at no obstacle, by all means necessary, to make this dream a reality.

Our family's life with my brother was not always negative or sad—he played a significantly important role in not only our lives, but with everyone he met. He touched the souls of everyone he laid eyes on, and in his younger years, when he still had facial expressions, he had a smile that could melt a stone cold soldier down to their boots.

His special happiness brought a peace to the challenges that his life presented. Adjustments usually had to be made to make life work better for our situation, but it never seemed like that much of an issue in the moment.

However, recalling past memories, it is apparent there were quite a few sacrifices we made to have him present in anything we did together as a family unit. Average households got to take flights on vacation, whereas we were advised not to take him on a plane. Our friends got to go out to dinner regularly, whereas it was a common occurrence that he had a buildup of mucus & choked violently anytime he ate—disrupting surrounding tables, and many people acting openly disgusted that we would bring him out in public. Some people even voiced their opinions to us, as if we didn't have the same rights and freedoms to be there. We never even were able to fulfill most childhood dreams to go on a family trip to Disneyland, because it was deemed as unsafe for him to go on any of the rides. All of this to say, even though our "normal" may have been different than the average family, we were able to conduct our lives in our own version of normal.

What had become our normal sometimes puzzled passerby's who didn't always understand his condition and ailments. As a child, I remember asking my mom why other children and more distinctly, why grown adults, would stare blatantly at him when we were out in public. To me, he was just my baby brother. But to the average person, he was... different. With

Hunter's Syndrome there are features that go along with having the missing enzyme in their DNA. Some key physical attributes such as "coarse" facial features along with large heads and abdomens with a short stature to name a few.

Nevertheless, we didn't let any of this get in the way of having time with family and we knew no different than having him along for every memory while he was here. He will forever be a blessing in our life, and I wish the options available and, hopefully soon to be available, were around when he still had a chance. He may have lived the course of his life, but my baby nephew has just begun his. With the studied and successful treatments of RGX-121, this new therapy is able to cross large necessary enzymes across the blood brain barrier—something we waited for all of my brother's life. I believe there is a significantly higher possibility of my nephew being able to live a long, prosperous & cognitively capable life—given that a treatment such as RGX-121 has achieved the unthinkable.

Understanding the specifics on how Hunter's Syndrome inhibits those affected may also help emphasize the importance of treatments available and the timeliness that this medicine can be made available. Hunter's Disease is a deficiency in the enzyme iduronate-2-sulfatase (IDS), meaning that this missing enzyme has the primary job to breakdown complex sugars (glycosaminoglycans). Without this important enzyme, the sugars build up & consequently wreak havoc in the affected individual's organs, bones, & joints. This build up leads to progressive physical and cognitive decline, including aforementioned coarse facial features, enlargement of organs (organomegaly), joint stiffness, and developmental delays, usually appearing between ages 2 and 4.

This is why the gene therapy RGX-121 is so important. It is a one-time AAV9-based treatment developed by Regeneron to specifically treat Hunter's Syndrome. It aims to deliver a functional iduronate-2-sulfatase (IDS) gene to the central nervous system to treat neurological manifestations. This single dose treatment targets the cognitive and behavioral impacts of Hunter's, which the current available standardized enzyme replacement therapy cannot address. The IDS gene is delivered using the NAV AAV9 vector, enabling cells in the central nervous system to produce the missing enzyme that causes Hunter's Syndrome. NAV AAV9 (Adeno-associated virus 9) is a leading gene therapy vector from Regeneron's proprietary platform, which is well-known for its capability of crossing the blood-brain barrier (BBB). By crossing the BBB efficiently, genetic enzymatic material can be delivered to the central nervous system and peripheral tissues. NAV AAV9 is famously used in treating spinal muscular atrophy (SMA) and is widely adopted for treating various genetic diseases due to its high transduction efficiency and tissue-targeting capabilities.

Ultimately, the CAMPSITE trial (NCT03566043) has been investigating safety and efficacy of RGX-121 therapy in patients with MPS II. Despite positive data, in February 2026, the FDA issued a Complete Response Letter (CRL) for the Biologics License Application (BLA), requiring further analysis, thus to our dismay has postponed the approval of the gene therapy. The primary target for the treatment are males aged 4 months to 5 years old.

Given that majority of children with MPS II have the life expectancy of 10-20 years, every minute counts. The sooner these children can receive treatment, the less damage they will undergo by improving the quality of their life while increasing the number of years they can live a healthier life. The cognitive and physical damage eventually costs these children their lives, just like it did to my

baby brother. Most do not make it into their twenties even with precautions such as special diets, which may lessen the build up of sugars. With the missing enzyme in their DNA, their bodies eventually lose the battle.

Until now. For the first time, there are new treatment options being discovered. Enzyme Replacement Therapy (ERT) is currently available in the United States, that of which my 1.5 year old nephew has been undergoing weekly. The reality of ERT is that an implanted medical port had to be put in place in his chest, we call this his "Iron Man". Meaning that he had to be put under anesthesia as an infant, which already came with its own risks. Not to mention the detrimental risks that a port itself has, with infection being the most common concern especially with a toddler. The first signs of infection in or around the port would be a fever, meaning that any time he spikes a fever he must be rushed to the children's hospital—which is an hour away. Sometimes toddlers get sick & have a fever for more than 24 hours. But if his fever persists, he must return to the hospital to check for infection of the port by means of culture sample—that of which takes 72 hours for the sample results to grow a bacteria culture if present. All of these precautions and tests, then add another hour long commuting time to receive his weekly enzyme infusion into his port. This includes keeping an active toddler busy in a hospital room, while his chest is connected to an IV. The visit all together usually is about 5-6 hours, along with the 2 hour round trip from home to the hospital.

It should be made known that children with Hunter's do not have normal sleep patterns. Just to simply take a nap, my sister has to bounce on a yoga ball with her 33-pound son as a means of calming him down enough to fall asleep in her arms for an hour or so. Night time sleeping is just as erratic and typically ends with both my sister and him exhausted with less than a few combined hours of rest each night.

Between the lack of sleep, potential port infection complications, and weekly treatments—the need for an alternative upgraded treatment option for my nephew is more evident than ever, as is likewise for all the other families affected by a loved one with Hunter's. Though the enzyme replacement therapy has been a decent option to begin with, unfortunately, it does not cross the blood brain barrier to halt the cognitive decline of Hunter's Syndrome. However, this is what sets apart the treatment we are requesting be approved at the earliest convenience. The RGX-121 treatment does cross the blood brain barrier & with a single treatment can give children like my nephew, the best chance at the most normal life possible. His life is in the hands of your discretion to pass and approve this treatment. Please don't let him down. Thank you for your time and consideration on this matter.

[New submission]

I have two sons with MPS II, Hunter Syndrome, the severe form. One of our sons was diagnosed at 2 years old when I was carrying our 3rd son. Both sons had unexplained respiratory distress at birth, staying in the NICU for 17 days each, starting the difficult and terrifying journey to diagnosis. Our first born was diagnosed at 2 saving his soon-to-be born brother from late diagnosis, even 2 years old is too late. Our youngest began the approved treatment at 3 months old and has enjoyed a fantastic

quality of life. The disease has been much harder for our older son, especially in the beginning when development is so critical. He lost his ability to speak. Both boys participated in clinical trials on different timelines. The younger boy started a clinical trial at 2 years old to treat the central nervous system. This trial went on for years and did not meet its endpoint and therefore was never available to our older son, who did not qualify. Our younger son has enjoyed a fantastic life so far with a bit of joint pain but normal height and the opportunity to attend high school in our community.

Our oldest was selected for a trial at 12 years old that also treats the brain and CNS with a different technology that attaches the enzyme to a blood brain barrier penetrating molecule carrying much needed enzyme to the brain. During the trial, he was able to be potty trained, is still alive, attends a school for autism, and has a tranquil, happy life! His brother needs the treatment that our oldest is on, but it takes years to even get to the approval stage, often more than 5 years. Even then, these treatments have to meet impossible standards to be approved, which change depending upon the administration and mood of the approvers. If you think of it from a child's perspective, it is a huge time commitment. You endure PK blood draws around the clock, multiple tests you don't understand, especially if you are not verbal, all to try to compare you to the rest of the American population. It is asking too much, but the children comply because it saves their lives, and that the results will save their brother and the many other men and boys with Hunter Syndrome.

Our youngest has been in a trial for 90% of his life to date and thinks of the medical teams as his family. But this time could have been spent living if treatments were not withheld, delayed, extended, denied, canceled, etc. Please make helping them live and treat their disease easier so that they may enjoy life. We hold hope for their futures and innovation that leads to functional cures!

[\[New submission\]](#)

We have an absolutely adorable little 4-year-old boy in our family with

Mucopolysaccharidosis type 11, AKA MPS 11. This is a rare, progressive, life-altering, and life-limiting disease.

Children with MPS 11 are likely to begin losing basic functions before the age of 10. This could mean the ability to walk, talk, play, just to name a few.

Our little guy is currently receiving the benefits of being in a clinical trial. This has helped him develop more like a child without MPS. If his treatment is delayed, he may lose these skills which will leave him more isolated. This can impact his ability to enjoy the life healthy Children can take for granted. Most children with MPS don't make it to their 20th birthday, with some not even getting to see double digits. Not to mention, the quality of life during those years can be so limiting.

I could go on and on about the physical challenges facing Children with MPS, but I would be remiss if I didn't mention the emotional impact this disease has on his family. For his parents it is heart wrenching and requires Herculean effort to face each day with a smile for the sake of the child MPS along with any siblings they might have. The Grandparents' heart aches for the child but have to watch their own children walk through life with a heavy heart not knowing what each day will bring. For the siblings it is confusing and often times difficult for them to understand why they can't always get the attention they need because their parents are busy caring for a sibling with

special needs. For the extended family, it is a feeling of helplessness because we don't always know how to help.

On paper our little guy can be a statistic, but to the family he is the whole world. He truly is a ray of sunshine, an inspiration because of how bravely he faces each day and the light of so many of our lives.

[New submission]

My godson was diagnosed with a rare genetic life altering and terminal disorder two years ago. At two years old he was diagnosed with MPS II. This diagnosis was terrifying for his parents and loved ones. MPS II comes with a host of symptoms and complications. When he got the diagnosis of short life expectancy, the clinical trials that he is in have been a beacon of hope. We have seen him progress and developed beyond what was expected. With continued access, my godson and other kids with MPS II have a chance and hope for a better life as they battle their condition which carries a limited life expectancy and devastating developmental disabilities.

[New submission]

A little over a year ago, my life looked completely normal. We had three thriving boys, and I was nine months pregnant with our daughter. No family history of genetic disease on either side. Our youngest needed hearing tubes and a small hernia repair, but nothing unusual. He had a little bit of a speech delay, and I suspected maybe a mild bit of ASD, but nothing severe enough to pursue testing. All and all, we were healthy, thriving, and living the American dream.

Then I saw a little girl on TikTok who looked exactly like my son. She was dying from a terminal neurodegenerative disease. Her parents had believed she was perfectly healthy, too — until social media connected the dots. Something in me quietly shifted that day.

I sought reassurance from six different physicians and a pediatric clinical geneticist. One by one, each of them told me my son was healthy and developing normally. That I was worrying about nothing. That if he started to regress, we would “deal with it then.” But in neurodegenerative disease, “then” is too late. I could not ignore what I had seen. So, I ordered my own carrier screening test, and through that process, I unraveled his diagnosis myself.

There was no roadmap. Most of the doctors we encountered had never even heard of this disease. When the results came back, I was not handed a treatment plan. I was handed the responsibility to save my child's life.

I had to move immediately. With neurodegenerative disease, time is brain. Every month without treatment means irreversible damage. I had to locate specialists, find a clinical trial, and fight for access, all while knowing any delay could cost my son his future.

My son, now almost five years old, has Mucopolysaccharidosis II — MPS II (Hunter syndrome), a rare pediatric neurodegenerative disorder. Children with MPS are missing a critical enzyme responsible for breaking down toxic cellular waste called heparan sulfate. Without that enzyme, heparan sulfate accumulates in the brain and body, leading to progressive physical and neurological decline. Without treatment, life expectancy is typically in the mid-teens. There is one treatment approved by the FDA, but it cannot cross the blood-brain barrier. Despite receiving therapy, most children still pass away from neurological complications before the second decade of life.

I found a clinical trial for a brain-penetrating therapy that delivers a synthetic version of the missing enzyme and crosses the blood-brain barrier. This drug is already approved in Japan with robust data. But time was not on our side. The trial was almost full and projected to close at the end of the month. As an enrollment requirement, children had to receive 12 consecutive weeks of the FDA approved therapy, elaprase, before they could be screened. Against all odds, somehow a spot remained open as my son received his weekly elaprase treatments, and we made it into the trial. When I opened the email confirming he was accepted and randomized to be treated with the drug instead of the placebo, it was the greatest moment of my entire life. My son is now receiving this treatment, and he is thriving. Every week, I pack up my children and fly out of state to give him the chance to fight. The chance to save his life.

The difference in him is remarkable. He is not just holding steady; he is progressing. He is catching up to his neurotypical peers. For the first time since his diagnosis, his doctors have told us that with this treatment, a near-normal lifespan is within reach.

For a disease that once came with a teenage expiration date, that is nothing short of extraordinary.

But even after beating all the odds, we are living in fear that we could lose access. Not because the science failed. Not because companies stopped fighting rare disease. But because of regulatory inconsistency.

For more than 30 years, the MPS community has fought for the FDA to recognize heparan sulfate as a valid biomarker — our only meaningful measure of disease progression. The FDA agreed. Trial designs were negotiated over a decade. Accelerated Approval pathways were discussed and aligned. Sponsors invested hundreds of millions of dollars. Then, after completion of trials, the FDA reversed course. In a recent Complete Response Letter, the agency questioned the reliability of heparan sulfate — the very biomarker it previously agreed to use — criticized trial designs they had accepted and rejected applications despite strong clinical data and visible patient benefit.

This is not an isolated case. Many rare pediatric neurodegenerative therapies are experiencing similar outcomes. Accelerated Approval was created precisely for:

- Small patient populations
- Serious and irreversible diseases
- Situations where traditional large, randomized placebo trials are infeasible

Yet ultra-rare pediatric genetic diseases have seen minimal utilization.

Meanwhile, standards appear to be shifting mid-stream:

- Biomarkers previously accepted are being reconsidered.
- Natural history comparisons are being rejected after prior agreement.
- Trial designs and expectations are changing after sponsors have already invested years and resources.

For small biotech companies, this unpredictability is existential. Companies developing lifesaving therapies are beginning to withdraw from the space because they cannot absorb the regulatory risk.

The economic cost is staggering. Thirty million Americans live with a rare disease. The annual U.S. economic burden exceeds \$1 trillion. Delaying treatment does not save money — it increases lifetime dependence on Medicaid, disability services, and eliminates future workforce participation.

But this is bigger than dollars.

Biotech companies that have invested millions into rare disease therapies are going bankrupt after these rejections. I personally know of ten companies with strong clinical data that have had to hand their programs to nonprofits and walk away because funding ran out.

If this continues, we will lose the very companies fighting to save our children.

Innovation will not disappear. It will move, and other countries are already preparing to receive it.

For families like mine, that does not just mean economic loss. It means losing access. It means watching breakthroughs happen somewhere else while our children decline.

In rare pediatric neurodegenerative disease, waiting is not neutral. It is watching your child slip away in front of you.

Last week, on a private call among MPS parents, a father's voice broke as he said something that will stay with me forever: "I wish my little boy had cancer. At least then we'd have a chance to fight."

We have submitted letters. Our physicians have met with FDA officials repeatedly. Advocacy leaders have walked the halls of Congress and even visited the White House. We have done everything asked of us. Yet rejection after rejection continues.

I am writing this from my son's hospital bedside. He will require weekly infusions for the rest of his life simply to survive. We have accepted that reality. What we cannot accept is losing access to the treatment that is keeping him alive because agreements are no longer honored.

We are not asking for shortcuts. We are asking for consistency. For enforcement of existing law. For regulatory reliability. We are asking for our right to try.

In the wealthiest, most innovative nation on earth, no child should lose their life because the system meant to protect them cannot keep its word.

We are closer than ever to rewriting the future of this disease, and all rare diseases. Please don't let my generation become the next group of MPS mothers who stand at gravesides instead of graduations.

[New submission]

Submitted by grandparent

I am a representative for the MPS II {Hunter Syndrome} community. This is a rare, progressive, and life-limiting genetic disease that mainly affects boys.

My grandson was a healthy baby. That changed when it was discovered that he had Hunter Syndrome. This is caused by a deficiency of the enzyme iduronate-2-sulfatase. This leads to an accumulation of glycosaminoglycans, especially heparan sulfate, throughout the body and the

brain. Over time it continues to build up, damaging the organs, bones, airway, heart, and the central nervous system.

I want you to know our boy. Not just his disease. He dreams of amazing adventures. There are no mountains too high to climb, no ocean too far to sail across, no star he cannot reach. He is a Super Hero Boy! His Dreams are bigger than Life and his Imagination brings them all alive.

He shines bright - he wants to do it all. To meet every person he encounters and they in turn feel his glow. His personality is his gift, his laughter, his dancing, his stories and his joy no matter what he has gone through. He is my Hero and my Best Guy. How lucky am I to be his Gra!

Yet there is more to his story. Hunter Syndrome is relentlessly progressive in the neuropathic form, severe, children experience:

- Developmental delays than cognitive regression
- Speech and communication loss
- Behavioral changes
- Airway obstruction and recurring infections
- Cardiac valve disease and skeletal deformities

Many of these boys lose the skills they had. Their independence shrinks as their words fade away. Life expectancy is often in their teens. Time is a neurological function. In six months, language can disappear. In a year there can be serious cognitive decline and loss of mobility.

With so many days spent in a treatment bed for him, movies create a different world. I know someday he will direct and produce his own stories. I hope I will be a part of them. His imagination takes him into jungles, exploring mountains, and walking shorelines for treasures. So many steps are waiting to be taken. The World is waiting for him to take it by storm! To Fly, to soar, to create, to grow, to be Super Hero Boy!

Yet the world never just hands us something without a catch. His catch is so large and so unknown. My grandson has Hunter Syndrome, a genetic disorder causing Heparan Sulfate, what is known as a GAG, to accumulate in his body and brain. A simple explanation is that debris builds up within him. With the new medical trials that are now taking place, he would have the chance for the quality of life every child should have.

Currently there is an approved FDA therapy, but it has serious limits. Elaprase (idursulfase), an enzyme replacement therapy given weekly by infusion. It is able to help with treating systemic symptoms. It can improve endurance, reduce organ enlargement, and stabilize some physical complications. This all matters, but it does not cross the Blood-Brain Barrier. It does not address the cognitive decline that comes with the most devastating form of Hunter Syndrome. Children can receive Elaprase for years and still lose their personality, language, and memory.

This is the central unmet medical need - a therapy that reaches the Brain.

Promising blood-brain barrier penetrating therapies have been developed to address neurological disease. Regulatory uncertainty and delays are holding this back. The questions about already established biomarkers like cerebrospinal fluid heparan sulfate and shifting expectations and the

evidence needed to demonstrate neurological benefits. The impact is immediate when late in the development or approval process the standards are changed. This slows the trials and investment backs away. The real crisis is what happens to the children as they then decline. Delay leads to irreversible loss. In progressive neurological disease, success comes with stabilization.

In six months, he could lose his speech. In one year, his world could shrink away, measurable cognitive drop, worsening airway and cardiac disease, loss of independence with his life skills. Once he suffers these losses, his neurons will not regenerate and bring them back.

For Hunter Syndrome children and their families, Time is not an abstraction. It is the difference between preserving who our sons are or watching them disappear.

Regulatory delays are not administrative. It is Childhood, it is memories, it is their brain cells.

Will you support us in our quest to make this happen? Will you help us make sure that Super Hero Boy's Story has a happy ending? My grandson and the other Super Hero Boys are counting on you.

Submitted by additional family member

I represent families in the MPS II (Hunter syndrome) community — a rare, progressive, and life-limiting genetic disease that primarily affects boys, including my son.

Hunter syndrome is caused by a deficiency of the enzyme iduronate-2-sulfatase, which leads to the buildup of glycosaminoglycans — especially heparan sulfate — in cells throughout the body and brain. Over time, that accumulation damages organs, bones, the airway, the heart, and, in the severe form, the central nervous system.

Children with the neuronopathic form experience developmental delay followed by cognitive regression, loss of speech, behavioral changes, airway obstruction, cardiac disease, and skeletal deformities. Many boys lose skills they once had. Words disappear. Independence fades. Life expectancy is often in the teens.

There is an FDA-approved therapy, Elaprase (idursulfase), a weekly enzyme replacement infusion that treats systemic symptoms. It can reduce organ enlargement, improve endurance, and stabilize some physical complications. Those benefits matter. But Elaprase does not cross the blood–brain barrier. It does not address the cognitive decline that defines the most devastating form of Hunter syndrome. Children can receive treatment for years and still lose language, memory, and personality. That is the central unmet need: a therapy that reaches the brain.

Promising blood–brain barrier-penetrating therapies have been developed to target the neurological disease process. Yet our community has faced regulatory uncertainty, including disputes over biomarkers such as cerebrospinal fluid heparan sulfate and shifting expectations about what evidence is required to demonstrate neurological benefit. When approvals are delayed or standards change late in development, the disease does not pause. Children continue to degenerate while the FDA keeps moving the goalposts.

In a progressive neurodegenerative disorder, stabilization is success. Delay is irreversible loss. Six months can mean my son loses two-word phrases. A year can mean measurable cognitive decline, loss of toileting independence, worsening airway disease, or new cardiac complications. Neurons do not regenerate. Skills rarely return once lost.

For families like mine, time is not abstract. It is brain cells. It is memory. It is childhood.

[New submission]

When my son was two, my husband received a call from my son's ENT: "We need to see your wife and you in our office this week." Something was wrong. He had had routine ear tube surgery, and all had gone well. There was something that the doctor didn't think I was strong enough to handle. In his office, I heard those three letters for the first time: "MPS." And in a few seconds, my dreams and expectations for my family, for my son, were shattered. My baby boy was going to die.

As soon as we got home, I went for a long run. I ran so fast that I couldn't breathe, and then I fell on the ground and cried. I don't know how long I was there. But eventually, I picked myself up and headed home, determined to do what I needed to save my son's life.

As any parent would, I searched and found the best doctor in the country for MPS. We packed up the car and headed there. He said my son needed to start enzyme replacement therapy (ERT) immediately. But he cautioned us that the standard ERT would not cross the blood-brain barrier, so my son would continue to suffer brain damage until eventually he passed in his teenage years.

The doctor offered a sliver of hope. He told us that the only trial addressing the cognitive decline of severe MPS II was on hold by the FDA. We waited two long years – watching to see if my son was losing skills, sleeping next to him, so I could hear him breathe, wondering how I could continue to live when he passed away.

My son finally entered the Intrathecal Enzyme Replacement trial at age 4. I knew going into the trial that this wasn't a cure. I didn't expect him to regain the skills he had lost. All I hoped for was stability, slowing down the progression of the disease, and keeping my boy alive.

The FDA did not approve the intrathecal drug, but the pharmaceutical company and the FDA agreed that the boys in the trial could continue receiving it. Each month, for the past 143 months, he is sedated and receives the enzyme he is missing directly into his cerebrospinal fluid through a lumbar puncture.

At 15, my son can still do things I never imagined he could. He is stable. He and I go on threemile walks together. He is still feeding himself and breathing without assistance. He completes 50-piece jigsaw puzzles and runs to his school bus by himself every morning.

The dose in the intrathecal trial was too low and not given often enough, but the drug did slow down his progression and has stabilized him. It gave him more time to run on the beach, chase the dog, and laugh at Curious George.

Other boys have not been as fortunate as my son. They did not get into the intrathecal clinical trial he was in, so their disease progression continued.

I will never forget the agonizing wait in the recovery room on that Friday in 2014 to see if he would be randomized to the drug or the control group. When the nurse came out and told me he was

randomized to drug, I burst into tears. She gently touched my shoulder and said, "I don't think you heard me correctly. I said he would be getting the drug." I heard her correctly, but to me, her words came out, "your child is going to live."

I rushed out into the waiting room to tell my friend, "He is on drug! he is on drug!" As we hugged and cried, another mom sitting there asked me softly, "Is that for the MPS II trial?" I answered excitedly, "Yes, it is!" She replied, "My son has MPS II also." I asked her, "Is your son in the trial?" She said, "No, he is too old to qualify."

Her son would have to wait. But the drug was not available in time for him, and he died. Not because there was no treatment, but because he was too old. Imagine, as a parent, knowing there is a drug that can help your child, but not being able to receive it because someone who has never met your child decides your child is too old to receive treatment and isn't worth saving.

My goal for him was always to keep him alive long enough for something better to come along. Something better is here. For MPS II, we have two drugs up for approval. I have seen the kids taking the drugs, talking, singing, and laughing. They are stable. That's all I want for my son.

These drugs will change the trajectory of MPS II forever. We haven't had a new drug approved for this disease since 2006 -- twenty years without innovation. Our MPS II community is anxiously awaiting approval for tvidenofusp alfa. We have been patiently trying to keep our kids alive, so they can experience the benefits and have more happy days. This drug needs to be available to every boy with MPS II, regardless of their age. Please don't discriminate against our older boys. They also deserve treatment and a chance at life.

[New submission]

Submitted by parent

My son is four years old. He is funny, determined, and full of life. He is also living with Mucopolysaccharidosis type II, or MPS II, a rare, progressive, and life-limiting disease. When you receive an MPS II diagnosis, you are not handed a hopeful roadmap. You are told to enjoy what your child can do today... because there will come a day when he will lose those skills. A day when walking may stop. When words may fade. When pieces of him will be taken away right in front of you in just a few years. You're forced to embrace the mindset of packing in a whole lifespan in just a hand full of years before preparing to say goodbye forever.

That is what delayed access to treatment means to me.

My son is part of a clinical trial. As his mother, I fully understand the risks. I understand the unknowns. I understand that research carries uncertainty. But what people need to understand is this: the alternative is unfathomable.

Without intervention, MPS II had already begun to steal his development. Before treatment, the disease limited nearly every skill a typical two-year-old should be building. We watched him struggle to form words. To coordinate his movements. To keep up.

Since receiving treatment, I have watched something extraordinary happen. He can form words. He can talk. He can run. He can make friends. He can build meaningful connections. For most families, those milestones are expected. For us, they are everything.

This is what quality of life looks like for a boy with MPS II. It is not perfection. It is possibility. It is time. It is siblings getting to know their brother. Really know him, before the unthinkable day when we may have to say goodbye.

Delayed access to treatment is not an administrative issue. It is not paperwork. It is not policy. It is children losing abilities they may never regain. It is families watching time slip away while waiting. It is young brothers and sisters being asked to process more grief than many adults ever have to face.

Children with MPS II are losing their lives with every delay. And families like mine are fighting. We are sacrificing time, emotional strength, and countless hours in hospital because this is the only chance our child has to keep walking, to keep talking, to keep being here as fully as possible.

When we talk about access to treatment, we are talking about time. And for families like mine, time is everything.

[Submitted by parent](#)

Right now, he is four.

Right now, he is in the living room lining up his trucks like they're heading into some kind of mission. He runs, not fast, not steady, but with everything he has. When he falls, sometimes he laughs. Sometimes he just looks at me.

Confused.

Like I'm supposed to explain something.

Most of our days look normal from the outside. Cereal. Cartoons. Toys everywhere. "Dad, watch this!" shouted from the other room like it's urgent.

And I watch. I always watch.

But our mornings start earlier than most families.

Because his doctor is far. Far enough that we wake up in the dark to make it on time. We move quietly through the house. Pack bags. Load the car. Try not to wake the other kids too early before they go to their grandparents' house.

They know the routine now.

"Is it Liam's doctor day?"

They ask it casually. But they know something is different.

Once a week they see their grandparents while Mommy and Daddy take their brother to the doctor
"to help him grow big and strong" That's the phrase we use.

And I wish it were that simple.

There are nights we stay up later than we should, too. Talking. Researching. Watching him sleep.
Trying to stretch time. Trying to control something. Trying to feel like we're doing enough.

I've always believed hard work fixes things.

I've built things. Repaired things. When a toy breaks in our house, I look at my kids and say the
same thing every time.

"Don't worry. Anything can be fixed."

I've said it for years without hesitation.

But this...

This can't be fixed.

We wake up early.

We stay up late.

We drive miles.

We sit in waiting rooms.

We ask every question.

We do everything we're told.

And there is still no fixing MPS II.

I can't outwork a genetic disorder.

I can't grind harder and beat it.

I can't trade sleep for progress.

There is never enough time, not in the mornings, not at night, to rewrite what's written in his DNA.

That realization humbles me in a way nothing else ever has.

During the day, though, he's just four.

At the playground, he lines himself up next to kids his age. In his mind, he's exactly the same. He reaches for the same bars. Tries to climb the same ladders. His hands struggle to grip the way he wants them to. His legs work harder than they should have to.

He looks frustrated sometimes. Not defeated. Just confused.

He doesn't understand why his body won't do what he tells it to.

He's only four.

When he finally makes it up a step or jumps a little farther than last week, I cheer like he just won something huge. Because for him, it is huge.

Pride and heartbreak live side by side in those moments.

And then there was the day he looked at his grandfather and said, "Pop, you went to the doctor and he made you better."

He said it so simply. Like that's just how the world works.

You go.

You get fixed.

You come home better.

And then he looked at him.

It wasn't dramatic. It wasn't loud. Just a quiet look that asked a question he didn't fully know how to say.

Why am I not getting better?

I felt that in my chest in a way I can't really explain.

Because how do you tell a four year old that sometimes the doctor isn't fixing, he's managing? That sometimes "better" doesn't mean what we want it to mean?

At night, when the house is quiet, that's when the future tries to creep in.

Not as certainty.

Just as fear.

Fear of losing abilities.

Fear of watching something slip away.

Fear of outliving my child, a sentence that feels wrong even forming in my mind.

My wife and I don't always say it out loud. Sometimes we just look at each other when he struggles. There's love there. There's exhaustion there. There's strength we didn't ask to have.

We worry about his siblings. How this shapes them. Whether they feel the weight of it even when we try to shield them. Whether they'll someday understand the early mornings and the long drives differently than they do now.

But today, they're just kids together.

And today, he's just their brother.

Parenting a child with MPS II means living in real time.

It means celebrating what he can do while quietly grieving what might not come. It means kneeling beside him when he's frustrated and saying, "We'll do it together," even when I wish I could do it for him.

It means learning that love doesn't fix everything, but it shows up anyway.

And here's the part that's hard to say out loud.

There are treatments in trial phases right now. There is research happening. There is real hope, hope that could mean more time, more ability, more life for children like my son.

But time is not theoretical for us.

Every delay is not paperwork.

It is not procedure.

It is not a line item on a calendar.

It is a child losing ground.

It is a father waking up early and staying up late knowing there may be something that could help, but it is still out of reach.

I understand safety.

I understand process.

I understand responsibility.

But progressive diseases do not pause while we wait.

My son does not get those months back.

He does not get those years back.

Right now, he is four.

Right now, he is laughing.

Right now, he is trying.

Right now, he reaches for my hand without looking because he trusts I'll be there.

I can't fix what's written in his DNA.

But you have the power to decide how quickly hope can reach him.

And right now, that matters more than anything.

Please don't let delay be the reason he runs out of time.

Submitted by aunt

My nephew and godson is four years old. Of the eight grandkids, he is the happiest of them all. He is also living with Mucopolysaccharidosis type II, or MPS II, a rare, progressive, and life-limiting disease.

When you receive an MPS II diagnosis, you are not handed a hopeful roadmap. You are told to enjoy what your child can do today... because there will come a day when he will lose those skills. A day when walking may stop. When words may fade. When pieces of him will be taken away right in front of you in just a few years. You're forced to embrace the mindset of packing in a whole lifespan in just a hand full of years before preparing to say goodbye forever.

That is what delayed access to treatment means to me.

My nephew is part of a clinical trial. I understand that research carries uncertainty. But what people need to understand is this: the alternative is unfathomable. Without intervention, MPS II had already begun to steal his development. Before treatment, the disease limited nearly every skill a typical two-year-old should be building. I have watched him struggle to form words. To coordinate his movements. To keep up.

Since receiving treatment, I have watched something extraordinary happen.

He can form words. He can talk. He can run. He can make friends. He can build meaningful connections.

For most families, those milestones are expected. For us, they are everything.

Delayed access to treatment is not an administrative issue. It is not paperwork. It is not policy. It is children losing abilities they may never regain. It is families watching time slip away while waiting. It is young brothers and sisters being asked to process more grief than many adults ever have to face.

Children with MPS II are losing their lives with every delay. And families like mine are fighting.

We are sacrificing time, emotional strength, and countless hours in the hospital because this is the only chance he has to keep walking, to keep talking, to keep being here as fully as possible.

When we talk about access to treatment, we are talking about time. And for families like mine, time is everything.

Submitted by godparent

My godson was diagnosed with a rare genetic life altering and terminal disorder two years ago. At two years old he was diagnosed with MPS II. This diagnosis was terrifying for his parents and loved ones. MPS II comes with a host of symptoms and complications. When he got the diagnosis of short life expectancy, the clinical trials that he is in have been a beacon of hope. We have seen him progress and developed beyond what was expected. With continued access, my godson and other kids with MPS II have a chance and hope for a better life as they battle their condition which carries a limited life expectancy and devastating developmental disabilities.

Submitted by aunt

My nephew is a Rare Gem. He is so unique and so uncommon that he is one of only 500 little boys with the same enzyme deficient genetic disorder. Our family absolutely adores and treasures this gift of a spunky, fun loving, fierce little fighter. Please let me tell you why the FDA needs to approve lifesaving medication for him and the other 499 boys who will simply not survive without this drug.

His genetic makeup is such that he does not have the capability of creating an imperative enzyme that is used to break up waste in every single cell throughout the entire human body. As a result, every cell in his body retains waste and grows in size, eventually causing mobility issues, limited organ function and most especially decreased cognitive function. Almost 2 years ago, my nephew began receiving FDA approved enzyme infusions on a weekly basis to help each cell break up that waste. He receives this drug out of state, so once a week my family must make the trip. We quickly found out that the FDA approved enzyme treatment did not cross the blood-brain barrier. So, while it did improve his mobility and organ enlargement, it did nothing to assist his speech processing, hearing loss, and general cognitive function. As a matter of fact, his general cognitive function only got worse and worse.

Not long after beginning the enzyme treatment, he qualified to partake in a trial of enzyme replacement drug that was not yet approved by the FDA. He has been in the enzyme replacement trial for just shy of a year and a half. This drug that we are begging for FDA approval on crosses the blood brain barrier and effectively administers the enzyme to brain cells, drastically improving my nephew's hearing, seeing, speech, and overall cognitive function.

This drug is imperative to my nephew's survival because without it, there is no other alternative to maintaining the same little boy he is growing to become. Without this drug, his brain function will only decline with no hope for any reprieve. Please approve the Denali therapeutics enzyme drug that crosses the blood brain barrier and keeps my nephew and all the rare gems alive and thriving.

Submitted by grandparent

My 4-year-old grandson has a rare disease known as MPS2, a life limiting, progressive disease that affects every system in the body for which there is no cure. The lifespan for children with this disease is usually until their second decade.

In some ways he is very much like a typical 4-year-old. He loves Hot Wheels and movie nights with his young siblings, playing in the snow, and making sandcastles on the beach. Currently the only available treatment for his condition does not cross the blood/brain barrier, so it does not address the cognitive decline that occurs with MPS2.

For the past two years, Liam has been in a clinical trial testing a treatment that does cross the blood/brain barrier. Since he started this trial, we have noticed great strides in his development. His speech and his physical capabilities have improved dramatically. He can run and jump, ride his bike, and play on the playground. He's full of wonder and questions about everything under the sun. This has given us great joy and hope. Joy that he is doing so well, hope that he will continue to do so.

But for children living with MPS2 that do not have access to this life changing treatment, abilities are slipping away, as cognitive decline sets in. Every delay in the FDA approval process results in lost abilities, lost lives, devastated families. Time is not on our side in this battle against a relentless debilitating enemy, and the current FDA approved treatment falls woefully short.

Families have been watching, desperately waiting for access to meaningful, life-giving treatments for rare diseases - waiting for treatments that can give our children a fighting chance.

[New submission]

My son is diagnosed with MPS II, also known as Hunter Syndrome. He loves playing with his cars, hugging his friends, and has a laugh that shines through his entire body. He is joy. He is light. He is our whole world.

But every single day, I live with the fear that he will lose the skills he has worked so hard to gain — the ability to talk, to walk, to feed himself, to simply play like a child should. With this disease, time is not on our side. Every day is precious, and it is time we do not have to waste.

There are treatments and therapies currently in clinical trials that children like my son desperately need. Delaying approvals does not just delay paperwork — it costs children skills they will never regain. It steals milestones. It steals independence. And ultimately, it shortens lives.

Please listen to our stories. See our children. Remember that behind every policy decision is a child fighting to stay who they are, and a family fighting to give them the best possible quality of life.

Our children cannot afford to wait.

[New submission]

I am writing to you as a grandmother of a spirited four-year-old boy who is navigating the realities of Mucopolysaccharidosis type II (MPS II), a rare and progressive condition that is life-limiting. My grandson is not just a patient; he is a vibrant individual filled with joy, determination, and an unwavering zest for life. Nevertheless, his diagnosis has cast a shadow over our family, revealing the painful truth of a disease that steals skills and abilities, often far too soon.

When we received the diagnosis of MPS II, we were told to embrace every moment and enjoy what he can do today, knowing that there would come a day when he might lose those abilities. It is a crushing reality to confront: the prospect of watching my grandson possibly lose his ability to walk or talk. Delayed access to effective treatment means lost abilities and time — a heartbreaking reality for families like ours.

My grandson is currently involved in a clinical trial that carries risks and uncertainties involved, but the alternative is unthinkable. Before treatment, MPS II limited nearly every aspect of his development. However, since receiving treatment, we have been blessed to see him achieve milestones that we hold dear: he now talks, runs, and forms meaningful friendships. For our family, these aren't simply developments; they are lifelines.

What quality of life looks like for my grandson with MPS II is not a pursuit of perfection but rather striding towards possibility. It means allowing his siblings to know him in his entirety before we eventually face the unthinkable. Delayed access to treatment means watching him lose abilities we fear he may not regain. It means families like ours watching time slip away, with siblings grappling with a grief that few adults ever truly understand.

I implore the FDA to acknowledge that when we discuss access to treatments, we are discussing time—an invaluable currency for families battling rare diseases.

For us, time isn't just about years; it is about the quality of those moments, watching my grandson walk, talk, and grow.

Thank you for your attention to our story and the stories of countless other families like ours. We hope for your understanding and support as we advocate for expedited access to treatment for MPS II, allowing children the opportunity to thrive, live fully, and embrace the lives they deserve.

[New submission]

My friend's son is 4 years old and has MPS II. He is in clinical trials taking risks to himself so that others may have a brighter future. At only 4 years of age him and his family have made decisions, most of us cannot even fathom.

Delays to this treatment are risking the progress made and wasting time people do not have.

Please do not deny access or delay treatments

[New submission]

My son lives with the severe neuronopathic form of Hunter syndrome. Hunter syndrome is a rare, progressive, genetic condition that primarily affects boys. It occurs because the body cannot properly break down certain complex sugars (glycosaminoglycans). These sugars build up in cells and organs, causing damage throughout the body, including the brain.

How Hunter Syndrome Affects Our Life:

Hunter syndrome is not just one symptom. It affects nearly every part of my son's body and development. He receives weekly enzyme replacement infusions to help manage the disease in his body. But the most devastating part is that the current treatment does not cross the blood-brain barrier, meaning it does not protect his brain.

Hunter syndrome can cause:

- Developmental delays
- Cognitive decline
- Speech regression
- Behavioral challenges
- Progressive organ damage

- Hearing loss
- Joint stiffness and mobility limitations
- Shortened life expectancy in severe cases

For families like ours, the most painful reality is neurological decline. We watch milestones stall or disappear. We worry about skills being lost. We live with the fear that time is not on our side.

This disease is progressive. It does not pause while policies are debated.

Current Approved Treatments & Limitations:

There is an FDA-approved enzyme replacement therapy (ERT) for Hunter syndrome called Elaprase. It supports organ function, but it does not treat the brain.

For children with the severe form of Hunter syndrome, the unmet medical need is urgent. The neurological component continues to progress. Families are left knowing that while we are fighting for our children's bodies, their cognitive function may still decline.

There are gene therapies and brain-penetrating treatments in development, treatments that could change the trajectory of this disease entirely.

But they are not yet available.

Regulatory Challenges and Delays:

Our community is facing regulatory uncertainty, requests for additional data, and delays in trial progression and approvals, even when there is more than a decade of research behind some of these therapies.

Rare disease families understand the need for safety and evidence. We want safe treatments.

But rare diseases, by definition, have small patient populations. Waiting for perfect data in a small population can mean waiting while children lose skills, mobility, and cognitive function.

Some therapies have been:

- Delayed due to requests for more data
- Slowed by disagreements about endpoints
- Limited by narrow eligibility criteria
- Stalled after promising trial phases

For a progressive pediatric neurodegenerative disease, delays are not neutral. They are not administrative. They are life-altering.

What Time Means to Us:

Time means everything. In six months, a child with neuronopathic Hunter syndrome can:

- Lose words

- Lose attention span
- Lose motor coordination
- Develop worsening behavioral symptoms
- Experience further cognitive decline

In one year, the difference can be profound. Regulatory delays are not abstract for us.

It is measured in:

- Words not spoken
- Skills not gained
- Memories that may fade
- Opportunities missed

Every month matters. Every quarter matters. Every year matters.

When a treatment that could potentially protect the brain is delayed, families like mine are left wondering if our children will still qualify or still benefit by the time it becomes available.

For rare disease families, time is not theoretical.

Time is neurological function. Time is mobility. Time is independence. Time is life expectancy. Time is our child's future.

And unlike policy timelines, our children's disease does not wait.

[New submission]

Dear Senate Special Committee:

Watching a child progress from being healthy, playful, smiling, and basking in love, to becoming immobile, requiring a feeding tube, multiple surgeries, or possibly even a tracheostomy, is heartbreaking for any parent, relative, or friend.

Our family has witnessed this with Hunter Syndrome in a beloved family group, as one child passed away at the age of 13 years. Another family member is affected by this disease.

[New submission]

I represent the Hunter syndrome community through both professional clinical experience and personal relationships with families affected by this devastating disease.

Hunter syndrome (MPS II) is a progressive, life-limiting disorder that robs people of their health, independence, and often their lives. Even with currently available treatments, many patients endure ongoing neurological decline, chronic pain, frequent infections, cardiac and orthopedic complications, and an immense treatment burden requiring lifelong medical care. Families live with the knowledge that existing therapies slow, but do not stop the disease from relentlessly damaging multiple organ systems.

A gene therapy that addresses the underlying cause of the disease represents more than incremental improvement, it offers the possibility of preserving cognitive function, preventing

irreversible organ damage, reducing suffering, and fundamentally altering the trajectory of a child's life. For newborns and young patients especially, time is critical, as every day without effective intervention allows permanent harm to accumulate.

I urge the FDA to engage experts with deep, practical experience in Hunter syndrome, mucopolysaccharidoses (MPS), and other rare genetic disorders when evaluating investigational gene therapies. Rare disease trials inherently face small patient populations, clinical heterogeneity, and complex, multi-system manifestations. These realities should inform regulatory flexibility instead of becoming barriers to progress.

When evidence demonstrates meaningful improvement in quality of life, reduced disease burden, and strong support from informed patients and families, approval should not be delayed absent compelling safety concerns. For rare, progressive pediatric diseases, regulatory timelines have real human consequences.

Approving gene therapy in a timely manner could mean fewer hospitalizations, less joint pain and disability, reduced cardiac and respiratory complications, preserved cognitive abilities, and ultimately longer, fuller lives. It could also significantly reduce the long-term healthcare burden associated with unmanaged disease progression.

For families facing Hunter syndrome, time is precious and irreplaceable. I ask the FDA to act with urgency, scientific rigor, and compassion to ensure that promising gene therapies are evaluated efficiently and made available without unnecessary delay.

[New submission]

I am representing the Hunter syndrome (Mucopolysaccharidosis Type II) community, a rare genetic disorder that primarily affects young boys and progressively damages nearly every organ system. Children with Hunter syndrome are unable to properly break down certain complex sugars, leading to their buildup in the body and causing symptoms such as developmental delays, breathing and heart problems, joint stiffness, hearing loss, and, in severe cases, neurological decline. While enzyme replacement therapy is available and can help manage some physical symptoms, it cannot fully stop disease progression or effectively treat the neurological impacts, leaving families with significant unmet medical needs. Access to treatments and emerging therapies has been challenged by the rarity of the disease, the difficulty of conducting large clinical trials, and regulatory hurdles that can delay approval of potentially life-extending options. For families, this means navigating a devastating illness with limited tools, racing against time while hoping for advances that may come too late for their loved ones. I'm hopeful that signing this will help my friends in need.

[New submission]

Hunter Syndrome is a rare disease, and watching a child digress in their physical and mental health is heart-wrenching for any family member, or family friend. We saw our daughter in law's younger brother die from this disease, at age 13 years, and knew of his disease progression.

Knowing that there is treatment with the potential to stop the ongoing disease process is a gift for every family member and friend affected by this disease, but not being able to access the needed medication/treatment is beyond our ability to comprehend. Watching an infant, a young child, a teenager, or a young adult progress to death from irreversible changes in their body is something no parent should have to witness.

Please, please consider allowing the treatment, a one-time gene therapy for Hunter Syndrome, to receive FDA approval. Another family member, a young child over one year of age, is also affected by this disease and desperately needs the treatment that is available, the treatment that could be life changing. Please do not allow another young baby to progress to not being able to walk, talk, eat normally, or to end up with developmental delays, severe cognitive impairment, continued respiratory infections, and progress to needing 24-hour a day total care. Thank you.

[New submission]

I have two sons affected by a rare genetic disease called Hunter Syndrome

(Mucopolysaccharidosis Type II, MPS II). It's a systemic disease that affects every tissue and organ, which causes physical disabilities, developmental delays, and eventually leads to organ failures and death in early adulthood. With only about 400 diagnosed patients in the entire country, virtually no one knows about the disease, including many of their doctors. The standard therapy can only partially slow down the disease's progression in physical symptoms and have no effect on developmental delays. There was a clinical trial that was actively recruiting patients shortly after their diagnosis in 2011. However, the stringent enrollment criteria delayed their eligibility for a few years due to impractical trial design, and the endpoints were destined to fail - cognitive improvements are impossible after the onset of cognitive damages. Eventually, they were enrolled but all too late. They are currently both intellectually disabled and are in palliative care. As much as we love them, they present a heavy burden to our family in terms of daily living, financially, physically, and mentally.

In the past 15 years since my sons' diagnosis, science has made tremendous progress. New clinical trials include gene therapy and enzymes that can enter the brain and address brain development symptoms. Our community has engaged in multiple ways with the FDA to communicate what's important to the patient families, and the scientific community has provided undisputable evidence that the surrogate biomarker called Heparan Sulfate is clearly indicative of treatment effectiveness. Unfortunately, the FDA remained stuck in time and refused to grow with science. Their continued skepticism against surrogate biomarkers shows their arrogance and close-mindedness. The members of the current leadership team at the FDA are not fulfilling their duties to the American taxpayers and walked back their stance on accelerated approval based on surrogate biomarkers and chose to ignore the patient community's voice and scientific evidence.

We need the FDA to be held accountable for its actions. We need the FDA to listen to the patient community and understand that clinical science is helping patients at the end of the day, and the endpoints should be aligned with what the patients and families value with most. We need the FDA to be impartial and be science driven, rather than letting the biased view (or even political agenda) of individuals in leadership position to dominate its opinions and review results. It's too late for my

sons, but new patients suffering from rare genetic diseases are born every single moment. We need actions from the FDA to give them a better start of life when the evidence of clinical trials demonstrates effectiveness.

[New submission]

Thirty years ago, we received a brutal diagnosis from a geneticist in Boston that our son had Hunter Syndrome. He was 2 years old. We had never heard of this rare disease and were basically told to "love him while you have him". At the time there were no treatments or therapies for MPS II. Our pediatrician read the diagnosis from a medical textbook and we began a journey we never expected to take.

When he was 8 years old, he became one of the youngest patients to be enrolled in an enzyme replacement therapy clinical trial. While this double blind, placebo study went on, we began to see transformations in him. We knew he was getting the "real deal". His liver and spleen reduced greatly as his stamina increased. We made the trip twice a week for three years...within a few months we were chasing him through the airport terminal as he was off on his own amazing race.

Our son has been getting ERT for over 25 years now. He graduated from college, got his license and landed a job at a pharmaceutical company. All milestones we never dreamed we would see.

The current therapy for Hunter Syndrome does not cross the blood brain barrier however, and we have seen the progression of this disease continue as time has gone on.

He was in a gene editing trial in 2019 that unfortunately did not give us the benefits he'd hoped for. At our most recent visit, we were told of a potential drug that was close to FDA approval that could reach his brain and spine. Those hopes have been dashed away, however, with regulatory hiccups at the FDA. We don't have time on our hands to wait for these approvals as it seems the FDA keeps kicking the can down the road.

We are forever grateful for the research, funding, doctors and families who have given their lives to making a better life for our Hunter boys. We seem to be at a crossroad with recent stalls. We implore your Committee to do whatever can be done to continue to give us hope for the future of our children and keep our dreams alive.

MPS I

My son is now seven years old. He was diagnosed with MPS1, a rare lysosomal storage disorder at the age of nine days. Fortunately, for MPS1, there is an approved treatment: a bone marrow transplant. He underwent chemotherapy and transplant at the unimaginable age of 3 months old. The complications of transplant landed him in the ICU, and he was on a ventilator for almost 2 weeks. Many times, I thought we would lose him.

So many kids do not survive the bone marrow transplant. Even if a transplant is successful, it is not a cure. Patients with MPS1 still undergo countless risky surgeries due to the effects on the skeletal system, heart, and lungs. Children often suffer tremendous developmental delays when diagnosis and treatment occur late. These delays affect their ability to be productive members of society as well.

We need better treatments. Better treatments = less complications. A large percentage of patients with MPS1 are covered under Medicaid insurance due to the debilitation of this disease.

Cost of care rises when better forms of treatment are delayed. Within just one year, my son went from needing no surgical intervention to requiring major hip surgery, back surgery, and now possible carpal tunnel surgery as well. All within a single year. This is because, despite the best treatment, MPS1 continues to progress quickly.

Delays in approval mean suffering for innocent children. Parents unable to work because of worsening symptoms in their children, excess surgeries requiring more parental care, and unfortunately at times, death of an innocent child. Children with MPS1 and other debilitating rare diseases deserve better.

[New submission]

My son was diagnosed with MPS1 Hurler Syndrome shortly after birth as a result of newborn screening - a testament to what scientific advancements can do to change the trajectory of a child with a rare illness if we are willing to commit to harnessing our scientific potential as a nation.

Due to early diagnosis, my son was able to almost immediately take advantage of the two available FDA approved treatments - he started Aldurazyme enzyme replacement therapy at just 5 weeks old and received a bone marrow transplant the day he turned 4 months old.

Each and every day I feel two incredibly opposing feelings about my son's life. I am eternally grateful for the scientists, advocates, and doctors who fought to develop treatments for MPS1 despite it being an ultra-rare condition. His bone marrow transplant will significantly slow the progression of his disease, and ERT, while not protective of his brain, does help to shield his body from some of the effects of his disease. Neither is anywhere near a cure, but I can't help but be grateful he has an opportunity to receive treatment at all. I know all too well this is the exception and not the rule when it comes to rare diseases.

And in the same breath that I thank God for the ability to have some access to treatment to support for my son, I feel anger, frustration, and confusion around why, despite BETTER and SAFER treatments being technically possible (and even in development) on the part of biotech companies and researchers, we were still relegated to a the newest available treatment that, at the time of his birth, was approved by the FDA 20 years ago. How could we not have advanced by this point? Who are we as a country if this is how we support our most vulnerable children?

I lament the lost time I had with my newborn while we left his father and sister behind to live in the hospital and isolate for months to undergo his bone marrow transplant, quite literally risking his life for a shot to extend his life. His transplant course, like most children's courses, was not without complications and came with forever life-altering consequences. He survived, thank God, but the impact emotionally and physically will be with him forever. To add insult to injury, his donor percentage nearly 3 years post-transplant is failing. We're facing the possibility of a second transplant, a second round of isolation and toxicity, and a second test of his ability to survive being brought to the brink of death all because the FDA is limiting our ability to access safer and more effective treatments.

Despite obvious evidence that OTL-101 is both more effective and safer than traditional transplant, my son is not eligible as the FDA requires an unethical, double-blind study against traditional transplant that has ALREADY taken the life of a fellow MPS1 child we met while undergoing the transplant process when they were randomized into the BMT arm. We have decades of data to show us what happens when you put a child through a bone marrow transplant. We know the risks involved, and we have extensive documentation of its shortcomings when it comes to preserving the life and abilities of children with MPS1. To pretend we need a randomized trial is insane, and to withhold OTL-101 while newborns and toddlers continue going through BMT is just plain cruel.

Despite incredible potential for B-cell therapies like those developed by Immunsoft which require absolutely no toxic conditioning and are re-dosable, the FDA will not allow children to benefit from these clinical trials.

We could avoid a second transplant if this option were open to us but, due to his age, it's not.

And beyond that, we've watched as MPS treatments have been delayed or denied in this last year in our immediate and wider MPS community for absolutely unwarranted reasons (RGX121, RGX-111, Tividenofusp alfa, UX111). In many cases these diseases have NO approved treatments whatsoever. We are killing children in full conscious when hope is dangling right in front of these families!

How can I possibly be standing here, watching my almost three-year-old walk, talk, play, run, and jump like any other toddler with a death sentence over his head? How can I possibly be standing here facing another transplant that could take him from us? How can I possibly be standing here knowing he will be subjected to dangerous and painful surgeries, all while his body slowly continues to poison itself until his eyes can no longer see through the clouding, his body can no longer hold him up, and his brain can no longer communicate the way it does in this moment, until eventually, his entire body can no longer sustain life?

How is that the case? In large part it's because the FDA is communicating to the researchers and biotech companies that could save my child's life that they are not valued. That regulatory technicalities matter more than children without hope. That death is a sacrifice we have to make so we can have just a little more time to sort through the research on biomarkers that's already been approved.

And if people don't matter to you, maybe dollars do. Newborn screening coupled with a definitive treatment could protect these children from years of Medicaid funded treatment, extensive disability, and an inability to contribute financially to society. If that's where your line is drawn, then it's not too late for my son. Get him the treatment he deserves, and he'll repay this society beyond your wildest dreams. At this moment he's still young enough that his potential is unlimited. Make him wait a few more years and you'll lose your future dollars while I lose my son.

What are you waiting for!? The choice is yours.

Sanfilippo Syndrome

My daughter has MPS Sanfilippo Syndrome. She is 4 years old and was diagnosed at age 2.5 with a rare genetic condition (1 in 70,000 births) causing debilitating effects on the body. But the most marked effect is progressive and fatal cognitive decline. Children with Sanfilippo will suffer Brain Damage Leading to loss of all their functional skills and is often times characterized as childhood Alzheimer's. Research has shown that brain damage becomes irreversible by the age of 3. There is currently no approved treatment.

Recently, Ultragenyx received an incomplete Response Letter from the FDA related to their BLA resubmission. Tough news after a year of unnecessary delays. The data show that the treatment is successful, and the earlier kids have access to it, the better. Time is crucial, and we pray that the FDA will keep their commitment to accelerate approvals."

[New submission]

My two daughters have MPS IIIB. There is no FDA cure or approved treatments. The rare disease community is urgently asking for your help and flexibility approving gene therapy and enzyme therapy for these kids. Their neurodegenerative diseases do not pause; it continues to cause regression and cognitive decline.

[New submission]

From a parent to a child with Sanfilippo Syndrome and an advocate with the Cure Sanfilippo Foundation

A delay of 6 to 12 months means losing parts of my son that I will never get back. Every single second matters for him. Not months. Not weeks. Seconds.

I have already watched him lose so much in such a short period of time. He used to sing in the car. Now there is silence. He used to talk. Now the only word he consistently says is "daddy." And I live with the fear every single day that one day, he will stop saying it. I won't know when the last time was. I won't be prepared for it. It will just be gone. That is what time does to children like mine.

A delay of 6 to 12 months means 6 to 12 more months of watching my son slip away from me. It means more moments where he seems lost. More moments where he cannot communicate. More moments where I see pieces of him disappear. It means his brothers losing their little brother piece by piece. It means our family living with the pain of watching someone we love fade in front of our eyes while we wait for help that may come too late. Every second matters because every second is time I may never get back with my son as he is today. A delay is not just time on paper. It is time that this disease takes my son from me.

A better quality of life means I don't have to keep watching my son drift further away while I stand there unable to reach him. There are moments now where I look into my son's eyes, and I don't know if he fully understands or recognizes what's happening around him. I talk to him, and I don't know if he can respond the way he wants to. I see him struggling, and I see the frustration in him. And as his dad, there is nothing more painful than knowing he's still in there, but I can't fully reach him anymore.

A better quality of life means he doesn't have to live in that place of confusion. It means he can feel comfort instead of frustration. It means he can feel safe, peaceful, and connected to us instead of slowly slipping further away. It means his brothers don't have to grow up watching their little brother lose more of himself. They deserve to have real moments with him. They deserve to hear his voice, see his smile, and feel like their brother is still there with them—not just physically, but emotionally.

For our family, it would mean relief from the constant heartbreak. Right now, every day feels heavy. Every day feels like we are waiting for the next piece of him to be taken. A better quality of life would mean fewer of those losses. It would mean more peace for him and more peace for all of us. It would mean he could live with comfort, dignity, and love, without this disease continuing to take more from him than it already has. He has already lost so much. A better quality of life means he doesn't have to lose everything.

I need you to understand that this is my son's life, and I am the one who has to watch him die while waiting for decisions I have no control over. Every day that passes, Sanfilippo Syndrome takes more from him. I am not reading about it. I am living it. I see it in his silence where his voice used to be. I see it when he seems lost. I see it when he struggles with things that once came naturally to him. And while this is happening, I am forced to wait. Waiting for people who have never met my son, who will never know his laugh, his smile, or the way he says "daddy," to decide whether he gets a chance.

You are not the one who has to sit down with his brother, who is in kindergarten, and try to explain why his little brother is changing. You are not the one who has to answer questions no parent should ever have to answer. You are not the one who has to watch the confusion and sadness in his brother's eyes while trying to stay strong yourself. That choice should not belong to someone who has never looked into my son's eyes. That choice should belong to me.

I am his father. I am the one who loves him. I am the one who has to hold him, comfort him, and live with whatever happens. I am willing to accept the risks if it means giving him a chance. I am willing to fight for him with everything I have. What I am not willing to do is stand by and watch him die while waiting for permission to try to help him.

You have the power to give families like mine a chance. You have the power to move with urgency. You have the power to recognize that time is something children like my son do not have.

Please do not make families like mine wait while our children disappear in front of us. He deserves the chance to fight for his life. Because while you are deciding, I am watching my son disappear.

[New submission]

For me and my child with Sanfilippo Syndrome, time means loss of words, increasing headaches and aggression, loss of mobility, worsening gi issues, toileting accidents. His personality is fading with every passing day.

A chance at a better quality of life would mean the ability to live past his teenage years, retention of mobility and ability to continue eating all his favorite foods by mouth, remembering all the family members he loves by name.

When it comes to risk from therapeutic options, there are not many risks worse than this terrible progressive disease itself. We are hoping every day to hear that the therapy that could save Merrick's life will finally be accessible to him. We are willing to move to raise money, to go into debt—anything to get him this treatment.

We wish the FDA felt the same urgency to save my son's life that we do. Every day we hope to hear good news that could turn the tide for this disease. With AI tools, science breakthroughs will continue to progress more and more rapidly, and the FDA needs to figure out how to speed up their own processes for the good of everyone.

Duchenne Muscular Dystrophy

I am the mother of a 25-year-old young man with Duchenne muscular dystrophy. Diagnosed at 18 months, we were told that there was nothing they could do. No treatments other than steroids, and to just "open the door and let them be."

We did just that. My son has thrived. He has had amazing opportunities to be in the school band, played in a steel drum band, scouts, achieving Eagle Scout rank, graduating from college with a degree in hospitality management. We are extremely blessed to live in such a community that is so caring and inclusive.

If you are not aware, Duchenne is caused by the lack of dystrophin production in muscles, caused by a mutation in their DNA. What you may not be aware of is that there are many different mutations. My son has a duplication of exons 8-12. There are no research or trials for him.

I'm asking you to review the current legislation and reevaluate current guidelines for trials and research. For example, a trial that produces only a small amount of dystrophin for our boys that can maintain their pulmonary or cardiovascular health may not seem like a significant endpoint for the trial, but for these men/boys it can be life altering.

Our family appreciates your time and consideration of rare disease awareness. Just know that we are out here, as members of the community you serve. Hopefully thriving and always aware of what your voice could mean when combined with ours.

[New submission]

Submitted by parent

Our son has Duchenne muscular dystrophy (DMD), which is the number one genetic killer of boys worldwide, affecting 1/300 births boys with the disease, girls unknowingly carriers. This is the largest gene in the body with the highest spontaneous mutation rate, like in our case, and over 30% of all cases. Boys with DMD don't have the structural protein dystrophin, so their muscles begin to deteriorate affecting all of their muscles including his heart, diaphragm, and eventually affecting all their muscles.

Boys with DMD usually die in their teens or early 20s. After over 2 decades of my son participating in a clinical trial for PTC 124, Ataluren, the FDA decided not to approve it this past week, even though it is safe and had better endpoints than Elevidys, the gene therapy drug the FDA approved last year even though several boys had died. Ataluren allowed my son to graduate from college, live on his own 5 hours from his family, work for the Governor, and as a HS social worker. At 34 1/2 he makes the 17 hour trek each year to a children's hospital where he is the oldest DMD patient. This clinic has over 800 DMD patients.

There is no question this drug is responsible for him to breathe on his own. Unfortunately, there are no other drugs for a premature stop codon mutation, his mutation. Without this drug, he will decline and die. This oral drug is safe with hundreds who have been on the drug. This drug is approved in over 50 countries.

There are very different evaluation criteria at CDER, where Ataluren was evaluated, than CBER, where Elevidys was granted approval.

By denying this drug for our son, the FDA is creating a type II error, and boys will die needlessly.

Submitted by other family member

I am writing on behalf of the young men affected by muscular dystrophy, including my brother-in-law. The FDA is denying access to the drug Ataluren, and I am requesting they reconsider. This drug has allowed him to pursue a career as a social worker, live independently for a portion of time, and has given our family the beautiful gift of having him as "Uncle" to our two young sons who ADORE him. This medication has helped him to continue breathing on his own—a privilege many of us take for granted every day. DMD has taken so many things from my brother-in-law. Please don't take the one thing we have that has helped him. Please reconsider continued access for all boys with muscular dystrophy as they too deserve the same chance at a fulfilling life.

Submitted by cousin

My cousin was diagnosed with Duchenne's muscular dystrophy when we were both young. I still remember seeing the heartbreak my aunt and uncle went through upon learning about his future as an individual diagnosed with the disease. Throughout nearly his entire life, he has persevered through trial after trial so that he could live as normal a life as possible. In spite of it all, he has been able to graduate from college with a master's degree in social work; giving him the opportunity to share his unique life experience with high school students.

None of this would have been possible without Ataluren. My cousin would not have survived or succeeded for the past 34 years; this is the only drug currently available that treats the decline associated with a premature stop codon.

Real-world data supports this drug's effectiveness over the past 20 years. By choosing to deny Ataluren for use by patients with Duchenne muscular dystrophy you are condemning my cousin and many others. I am pleading with you to reconsider this decision.

Submitted by cousin

My cousin has Duchenne muscular dystrophy. After over two decades participating in a clinical trial for Ataluren PTC 124, the FDA decided not to approve it this past week. This drug allowed him to graduate from college, live on his own, five hours from his family, work for the Governor, and as a HS social worker. At 34 1/2 he makes the 17 hour trek each year to a Children's Hospital where he is one of the oldest with DMD out of 800 patients.

There is no question this drug is responsible for him to breathe on his own. It is a travesty that the FDA considers that ad hoc data and not relevant. Other INVASIVE drugs in which boys have died with a similar p-value have been approved. This FDA ruling will have adverse effects on future DMD clinical trials. Unfortunately, there are no other drugs for a premature stop codon mutation. Without this drug, my cousin's health will decline. This is a safe oral drug approved in 50 countries.

Please consider the approval of this drug. It will extend the life of my cousin and maintain his improved quality of life. He has spent his life in service of others. He is an amazing man. He and others just like him deserve the opportunity to benefit from this drug. I humbly beg you to get approval for Ataluren.

Submitted by aunt and uncle

Our nephew was diagnosed with DMD as a preschooler and accepted into a trial for the drug Ataluren. It has been a life changing drug that enabled him to graduate from college with a master's degree in social work and share his skills while working with high school students. Without Ataluren, Jacob would not have survived or succeeded for the past 34 years. This is the only drug currently available that treats the decline associated with a premature stop codon.

We ask that you please reconsider the FDA denial of Ataluren for use by patients with DMD. Real-world data—our nephew' life story—supports this drug's effectiveness over the past 20 years.

Submitted by cousin

My amazing, intelligent, and funny cousin, was diagnosed with DMD as a preschooler and accepted into a trial for the drug Ataluren. It has been a life changing drug that enabled him to graduate from college with a master's degree in social work and share his skills while working with high school students. Without Ataluren, he would not have survived or succeeded for the past 34

years. This is the only drug currently available that treats the decline associated with a premature stop codon.

I ask that you PLEASE reconsider the FDA denial of Ataluren for use by patients with DMD. Real-world data—my cousin's life story—supports this drug's effectiveness over the past 20 years.

[New submission]

Submitted by parent

We are writing today to tell you about our son's experience with Ataluren (Translarna) manufactured by PTC Therapeutics. This oral small-molecule treatment allows for stopcodon read through to produce dystrophin in patients, like our son, with nonsense mutations which leads to a diagnosis of Duchenne muscular dystrophy. Recently, the FDA was unable to resolve differences in data interpretations with the manufacturer, causing the new drug application to be withdrawn.

Duchenne muscular dystrophy is a genetic disorder that causes progressive muscle weakness and primarily affects boys. It is caused by a mutation in the dystrophin gene, which normally produces a protein that helps protect and strengthen muscle cells. Without sufficient dystrophin, muscle fibers become damaged and are gradually replaced with fat and scar tissue. Diagnosis usually occurs in early childhood, between the ages of 2 and 5. As the disease progresses, weakness spreads to more muscles, and many require a wheelchair during their early teenage years. Over time, Duchenne affects the heart and breathing muscles. Although there is currently no cure, treatments such as corticosteroids, heart and respiratory care, and newer gene-targeted therapies can help slow progression and improve quality of life.

Our son was diagnosed with Duchenne in November 2013, four months after his first birthday. We knew shortly after the time of diagnosis that Ataluren was the medication he needed for his type of mutation. Unfortunately, at the time they were only enrolling boys over the age of 7 for any trials. We were told that an FDA approval was hopefully around the corner. Three years came and went, and while there was no approval, PTC was starting a safety study for children under the age of five. We immediately started researching sites and were selected to enroll. Eleven days before his fourth birthday, he received his first dose of Ataluren. Within the first six weeks we saw a positive change in his strength and mobility and haven't looked back since.

Our son is still ambulatory at the age of 13.7 years. In the past year, his Cardiac MRI, Pulmonary Function tests, and bone density scan results were all within a normal range. All his physicians marvel at how incredible he is doing compared to his peers of the same age and diagnosis. They are all very encouraged about how Ataluren has delayed the onset of the typical pathology of Duchenne. Other than a medical stroller and mobility scooter (to use long walking distances, like at an airport or theme park), he has no assistive devices. Remarkably, our son participates in PE for 60 minutes 5 days a week. While some of the activities are modified for his safety (no pull-ups, push-ups, etc.), he is still able to claim that PE is his favorite time of the day. A few months ago, he came home excited to share that while playing flag football he caught a pass and ran 20 yards to score a touchdown!

When our son was diagnosed in 2013, we were told by one neurologist to go home and give him the best life possible because by the age of 7, his mobility would start to decline. Another neurologist told us not to give up hope that there were so many things in the pipeline for Duchenne, so much more than there had ever been before. During what was one of the most terrifying times in our lives we are grateful for that second neurologist's advice. We knew there was something out there to help slow this terrible disease. Ataluren was that "something" for our son. We have no doubt in our minds that Ataluren and the age at which he was able to be first dosed is the reason he is still running and jumping today. It is the reason his heart, lungs, and bones are still healthy. The safety profile of Ataluren is also a major benefit of the drug. He has never suffered any side effects while taking this drug for the last 9 years.

In addition to our own observations and experiences, results from the most recent clinical trial show a 3.5-year delay in loss of ambulation. Ataluren is also found to be safe and generally well tolerated. The most recently approved gene therapy Elevidys has shown promise biologically but its impact on motor function is still being investigated and safety concerns have led to liver complications and even death. This makes the denial of a new drug application for Ataluren even more confusing and frustrating. Our son does not qualify for Elevidys because his mutation is on exon 9 which is part of the exclusion criteria. Patients receiving Elevidys with mutations in exons 8 or 9 have the risk of severe immune-mediated myositis. This is a severe, life-threatening autoimmune reaction where the body's T cells mistakenly attack the skeletal muscle.

Currently, my son's access to a safe drug, Ataluren, is being denied. However, a drug that would potentially have a life-threatening outcome is approved. With the FDA's decision, he is in a lose-lose situation. There are no other options for him besides the standard of care.

Without Ataluren, his life will change dramatically. He will require more assistance with everyday tasks such as dressing, bathing, and eating. His favorite activities, like playing basketball in our driveway and football with his friends at school, will be stolen from him. His easily accessible middle school for an ambulatory teen will now be faced with daily obstacles. His future depends on a treatment that is safe and helps preserve his function. Ataluren is that treatment. Please help our son stay on Ataluren; his life depends on it.

Thank you.

Submitted by grandparent

I would like to address this committee about my feelings and opinions about my grandson, who has nonsense mutation Duchene muscular dystrophy. This is a very rare form of this terrible disease and he has been on Ataluren since age 4 with remarkable results. I am a retired physician.

He was diagnosed at an early age with Duchene muscular dystrophy and was not able to ambulate and perform other tasks requiring muscle strength. His treating pediatric neurologist informed his parents that he would be in a wheelchair by age 6. Since beginning Ataluren, not only has he been able to ambulate and perform normal tasks for his age (currently almost 14), but he attends junior high school and only uses a wheelchair for long trips. His quality of life has vastly improved since on Ataluren from what had been predicted.

The FDA has denied approval for this drug despite evidence from clinicians that it has definitely helped children with this rare genomic form of this disease. It is my opinion that the trial did not reach statistical significance because of the small number of participants.

Regulatory delay in the production and dispensing of Ataluren will definitely, in my medical opinion, quickly hasten the worsening of his condition, which will ultimately lead to an earlier demise. This would be unforgivable!

Submitted by grandparents

Our grandson was diagnosed with Duchenne muscular dystrophy at just two years old. We were told to expect a steady and devastating loss of strength, independence, and ultimately, life. Today, at 13, he continues to defy those expectations.

For over nine years, he has been taking Ataluren. His physicians consistently express surprise at his strength and function compared to untreated boys his age. He remains ambulatory, relying only partially on assistive devices during fatigue, and maintains strong pulmonary function and normal bone density. His doctors firmly believe Ataluren is delaying the progression of his disease.

Clinical trials involving nearly 800 patients have shown that Ataluren can delay loss of ambulation by approximately four years and slow pulmonary decline by two years. In a fatal disease with limited treatment options, those years represent precious time — time walking, breathing, and living with greater independence. The drug's safety profile has been remarkably favorable, and it is approved in more than 50 countries.

We have witnessed its benefit not as an abstract data point, but in the life of our grandson. Without access to this treatment, our grandson's decline will accelerate. The physical losses are inevitable in Duchenne — but the timing matters. Every preserved year of strength profoundly affects his quality of life and emotional well-being.

We respectfully urge reconsideration of approval for Ataluren and greater flexibility in evaluating therapies for rare, fatal diseases with significant unmet need. For families like ours, this is not policy — it is time, hope, and the chance for our grandson to remain a little stronger for a little longer.

Our grandson is not a statistic. He is a child fighting a relentless disease. We are asking for the opportunity to keep fighting with him.

Submitted by family friend

My friend's 13-year-old son has Duchenne muscular dystrophy. His mom and I are very close, we are co-workers and neighbors, and our kids are close in age. I'll never forget my daughter hitting her physical milestones and her son was not. He was diagnosed with DMD at one. My friend was told he would be in a wheelchair before the end of elementary school. She sought alternative treatments, and he was put on a study for Ataluren.

He began hitting his milestones, he played chase with the other kids, and he continued to thrive. Now at 13, he's still standing and thriving with the help of this drug, walking the halls of middle school with his peers. None of this was expected, but Ataluren is the cause. Please approve it for

his special case. He has a bright future ahead of him and deserves to receive the treatment he needs. Ataluren is a necessity for him. Thank you for your time.

Submitted by teacher

The kids call me Coach. I have been my student's physical education teacher since he was 5 years old. He suffers from DMD (Duchenne muscular dystrophy). He is now in his 8th grade year, and I am witnessing each day how the drug Ataluren has halted the progression of this muscular disorder in this young man. Not only is he mobile, he is active! I was acutely aware to expect him to be wheelchair bound by the end of his elementary school days. I am here to tell you that I have not seen a decline in his physical abilities at all. Not one day! I have only seen improvements and gains in his physicality and motor skills.

We have recently learned that Translarna, the maker of the remarkable and effective medicine Ataluren, which my student takes, has ceased production because of FDA nonapproval. This is outrageous. It works! Please come to our school and watch him run and catch a football thrown at him from 30 yards! And then watch him return the throw on target with a perfect spiral EVERY TIME!! More importantly, come and watch him WALK to and from class each day in the hallways with his friends like a normal kid. Please! Please come and see the reality of this kind of data. Those affected by this are too few, apparently, to obtain enough data for approval. This too is outrageous! Change your scope, please! This is my plea to those who make the big important decisions that affect the lives of everyone in this community... come and see us! We will show you!

Submitted by teacher

I am a teacher and one of my former students has DMD. He's now 13. Through his treatment with the drug Ataluren, he is defying the natural progression of this disease. He can still do PE class. He can throw and catch a ball and do things that all 13-year-olds should be able to do. My heart breaks at the thought of this life changing medication is now gone. That all of the progress he has been able to have is now threatened. Duchenne may be a rare disease but the boys and men who have it matter. They deserve to be able to have medication that makes their life better.

[New submission]

I am a 32-year-old man living with nonsense mutation Duchenne muscular dystrophy (nmDMD), a rare and progressive genetic disease. I have no financial relationship with the manufacturer of Ataluren and receive no compensation for sharing my story.

I was diagnosed with Duchenne muscular dystrophy just before my first birthday. Duchenne gradually weakens every muscle in the body—first the legs, then the arms, then the muscles that support breathing and heart function. It is the most common fatal genetic childhood disorder, affecting 1 in every 5,000 boys born each year. Currently, there is no cure. Steroids may slow progression but do not stop the disease and can have significant side effects. Fewer than half of individuals with Duchenne live beyond their late twenties.

Throughout my childhood, this illness shaped my daily reality. I couldn't run and jump with my classmates. After walking or standing for ten minutes, my muscles would become so tight that I would collapse into a chair, unable to bend my legs. Night splints, orthotics, physical therapy, and occupational therapy were part of my life for as long as I can remember. By sixth grade, I could

only reach my bedroom by crawling up the stairs. My parents renovated our home to give me a ground-floor bedroom and a wheelchair accessible bathroom. By the end of grade school, I relied on a motorized scooter to navigate much of my world.

In ninth grade, I enrolled in the Translarna (ataluren) 007 study. My life changed in ways that my family and I never imagined possible.

After starting the medication, I began gaining strength and endurance. Though I had taken steroids for many years, they only really slowed the progression of my disease and caused negative side effects like weight gain. It wasn't until starting Translarna (ataluren) that I noticed that I was getting stronger. Halfway through high school, I stopped using my motorized scooter. My senior year, I completed a mile-long hike with my family—something that, just a few years earlier, had been unimaginable. After high school, I began exercising regularly, lost 35 pounds, and completed a 5K race. Today, I am fully ambulatory and live independently with my dog, a fifty-pound labradoodle whom I am physically strong enough to manage and routinely walk for a mile or more. I have experienced no negative side effects from medication.

In 2017, I traveled to Washington, D.C. to testify before the FDA Advisory Committee Meeting regarding ataluren. Ultimately, the FDA did not approve the medication, citing insufficient evidence of effectiveness. But in rare diseases like mine, the measures used in clinical trials do not always capture meaningful improvements in real people's lives. For me, this medication has been truly life changing.

Now, after further regulatory setbacks, the manufacturer of ataluren has stopped pursuing FDA approval. As a result, access for patients like me in the United States is uncertain. I recognize that I may be an outlier, but the benefits of this medication are undeniable. I worry what would happen to me if I'm unable to continue taking it.

Time is not abstract in Duchenne muscular dystrophy. Six months can mean the difference between walking and needing a wheelchair. One year can mean losing the ability to climb stairs, to stand from a chair, or to lift your arms. Once lost, those functions do not return. Delay is not neutral – it is decline. When I was little, I expected that having muscular dystrophy meant I would steadily lose the ability to walk, to breathe, and, ultimately, to live. I watched other boys in my muscular dystrophy support group follow that path. After starting this medication, my life trajectory changed. Instead of planning for decline, I began building a future. Instead of losing independence, I gained strength and stability.

My older brother is a physician who understands the natural course of Duchenne. He has watched my trajectory closely and has seen how, after beginning this treatment, my course diverged from what medicine predicts for this disease. He says this change is extraordinary.

I respectfully ask the Committee to consider how regulatory processes could better take into account the real-world experiences of patients with rare, progressive diseases. For patients like me, access to treatment is not theoretical—it can mean the difference between walking and needing a wheelchair, between having hope and facing inevitable decline.

For individuals with Duchenne muscular dystrophy, time is muscle. And muscles, once lost, are gone forever.

[New submission]

I submit this testimony as an individual living with Duchenne muscular dystrophy, a rare muscle-wasting disease, and as a representative voice for countless Americans affected by rare illnesses and chronic conditions. Our community faces unique challenges in accessing life-changing therapies, and we urge policymakers to recognize and address these barriers.

Adding to these challenges, the FDA held the Ataluren file for approval for over 18 months and refused to include the STRIDE data in its review. Ultimately, the FDA indicated it would not review the application based on the totality of the data provided, forcing the drug company to withdraw it voluntarily. This decision has left patients and families in limbo, unable to access a therapy that has demonstrated safety and life-changing efficacy.

We are born into a world with the potential to offer us greater opportunities, yet we are too often marginalized. If the FDA is truly committed to supporting Americans with rare diseases, it must adapt its policies to recognize the unique realities of our population.

Specifically, the agency should reconsider how it evaluates drug efficacy for rare diseases, acknowledging that small cohort studies can still yield significant, life-changing results.

Without FDA approval or continued compassionate use, patients will face rapid decline, loss of essential abilities, and preventable suffering and deaths. I urge the FDA and lawmakers to act swiftly to secure ongoing access to Ataluren and similar therapies for all who need them. Hope for a better life should not be a fleeting platitude—it must be a tangible promise, backed by responsive policy and regulatory action.

Thank you for your attention and commitment to improving the lives of Americans with rare diseases.

[New submission]

My 26-year-old son has Duchenne muscular dystrophy. When he was diagnosed at age 2, life expectancy was mid-to-late to teens, but advancements in the standard of care allowed him to attend and graduate from college and survive well into his twenties.

Duchenne is all-encompassing, continuing to rob my son of his independence and agency. He lost his ability to walk at age 12. He uses a BiPAP machine to help him breathe at night. He wakes multiple times nightly and calls me to reposition him. He lost his ability to raise his elbows and arms last year, so he is no longer able to feed himself. Recently, his hands have become weaker, making it difficult for him to use his wheelchair joystick for too long and interfering with using his computer mouse.

Although he earned a bachelor's degree in computer science, he is unable to obtain consistent employment because he is easily fatigued and needs to take frequent breaks to reposition in his chair. My son's ongoing, compounding losses in his physical abilities has led to much anxiety and

depression—living at home with his mother, completely reliant on her for all daily cares—as his peers are thriving in careers, getting engaged and married, etc.

Since he was diagnosed in 2001, many therapies have entered the pipeline that potentially could benefit him. The most significant is Ataluren (originally named PTC-124 and later named Translarna when conditionally approved in Europe), developed by PTC Therapeutics. Ataluren was the first drug for Duchenne that saw clinical trials with Duchenne patients. He was in that trial in 2006. Participation required many 7-hour drives, countless blood draws and clinical testing, as well as two muscle biopsies.

Because of Duchenne's complexities and progressive nature—it affects ALL muscle groups and systems in the body—identifying data points to show the drug's efficacy has proved difficult. After FDA's initial denial, PTC continued to hone its trial design and allowed Nick to enter into an extension study, requiring additional invasive muscle biopsies and blood draws. FDA denied it again. PTC continued to offer the drug to patients in an extension study for two decades as they worked to develop the necessary data for the FDA. However, after 20 years, the FDA is still not persuaded, so PTC has ended its pursuit of approval.

Ataluren is not a miracle drug. It doesn't "cure" Duchenne. But I believe it has played a role in my son's pulmonary function. Yes, he does use a BiPAP and his cough strength has weakened; however, his rate of decline seems significantly delayed compared to others his age with Duchenne. Stopping Ataluren is devastating for him.

Obviously, PTC's struggle with approval for Ataluren is an extreme case in terms of time delay. But all time is precious with a disease like Duchenne that daily robs patients of their mobility, independence and self-direction. Clearing hurdles to drug approval is essential for ensuring maximum quality of life for our community.

Thank you for your help.

[New submission]

I am the parent of an 18-year-old son living with Duchenne muscular dystrophy (DMD). Duchenne is a rare, progressive, and fatal neuromuscular disease. I am submitting this statement to share what regulatory decisions and treatment delays mean to families like mine who live every day with the consequences.

Living with Duchenne

Duchenne causes ongoing and irreversible muscle loss. It is a genetic condition often diagnosed in early childhood due to gross motor delays. Patients gradually lose the ability to walk, then lose

strength in their arms and hands, followed by declining heart and lung function. Life expectancy is significantly shortened, and quality of life steadily declines despite best supportive care.

My son was diagnosed as a young child. Over the years, we have watched him lose abilities one by one; walking, standing, climbing, lifting. Today, at 18, he depends on assistance for most daily activities. Every year brings noticeable decline. Time is not neutral in Duchenne.

Treatment Experience and Access Barriers

There is no cure for Duchenne. The few available therapies are meant to slow progression, not stop or reverse it. My son participated for five years in a clinical trial. During the trial, he tolerated the drug well and remained more stable than expected for someone with his disease progression.

After the FDA approved the therapy using the Accelerated Approval Pathway, our insurance continued to deny coverage—not because the drug was unsafe, but because my son is now older than the age group studied in the trial despite already having received the therapy for years. This is a common experience in the Duchenne community: patients who survive longer and need treatment most are often the ones who are denied or lose access.

Trial Design and the Reality of Older Patients

As boys with Duchenne get older, they are frequently excluded from clinical trials like my son, who currently does not qualify for any ongoing trials. This is not because patients cannot benefit, but because it becomes riskier and harder to show large, statistically significant changes to traditional endpoints.

What gets lost in this process is what matters most to patients and families. For my son, maintaining the ability to use the toilet on his own, feed himself, adjust his arm position and use his phone makes a real difference in his independence and dignity.

These changes may look “small” on a chart, but they are enormous in daily life.

When trials and regulatory decisions focus only on endpoints that favor younger patients, older individuals are left behind. Their benefits may be harder to measure, but they are no less real.

Regulatory Uncertainty and Its Impact

Recent regulatory actions including delayed reviews, complete response letters, and uncertainty around trial outcomes have created fear and instability for Duchenne families. Communications from the FDA regarding trials not meeting primary endpoints raise serious concerns about continued access to therapies that patients are already relying on. These are not abstract policy decisions. Every delay has consequences. Duchenne does not wait for new trials, new endpoints, or regulatory alignment.

What Time Means for My Son

My son will graduate from high school soon and has been accepted at premier institutions to pursue his college education. In six months, my son could lose more function and struggle with basic self-care. In a year, further respiratory decline could permanently change his health and independence. These losses are irreversible, making achieving his dreams impossible.

For families like ours, regulatory delay is not just delay—it is loss of function, loss of ability, and loss of time we cannot get back.

I urge this Committee to consider regulatory approaches that better reflect the realities of progressive rare diseases: flexibility in trial design, recognition of patients' lived experience and continuity of access for patients who age beyond trial populations. Waiting for perfect data should not come at the expense of the people living with the disease today. For my son, time matters. Every decision made affects what he will still be able to do tomorrow.

[New submission]

I have a 21-year-old son who lives with progressive heart failure. He barely survived three life threatening episodes in 2025. Yet, between ICU stays, he is a thriving honor roll student who just wants to live like other college kids. Duchenne muscular dystrophy has stolen his arm and leg muscles, and now his heart and breathing muscles are in peril. Duchenne progressively destroys skeletal, cardiac and respiratory muscles, leaving teenagers' breathing abilities weakened to the point of needing ventilators, and hearts weakened to needing pacemakers, and ultimately, stopping.

While some newer genetic therapies are showing promise in a select few younger patients with Duchenne, none have specifically rescued or stopped progression in the heart. There is an extremely high unmet need for teenagers and young adults with DMD. A therapy that helps the dystrophic heart is urgently needed by the entire Duchenne & Becker muscular dystrophy community, not specific to ages or mutations.

Our hopes have been pinned on Deramiciel (CAP-1002) from Capricor Therapeutics. We had hoped for an Accelerated Approval by FDA in August of 2025, based on very encouraging Phase 2 data. FDA was also reportedly impressed with the cardiac data from a Phase 2 trial and understood the incredible breakthrough that this therapy represents to the entire Duchenne community and guided the company as such. However, with delays at FDA, apparently new staff did a complete U-turn on the review of the investigational therapy, cancelled an Ad Comm meeting and issued a CRL, despite their earlier advice given to the company. We were shocked and devastated by this delay.

While the company has time to resubmit their data to the FDA, my son does not have time. He continues to lose cardiac and respiratory muscle function every day. Since the delay, this hardworking college student has now been prescribed to use a daytime ventilator attached to his wheelchair. We've gone over a cliff I had hoped we would never see. Can someone still attend college on a daytime ventilator, or even leave their house? Can they still talk, speak, breathe and laugh?

We live in fear of the flu season. Even mild colds can push DMD patients to the point of no return. Deramiciol (CAP-1002) represents the retaining of strength to stay alive. In December alone, my family lost 3 friends in their young 20s to DMD, dying suddenly due to cardiac failure -- young lives that could have potentially been saved by Deramiciol -- we will never know.

Heart function in Duchenne is a matter of life and death, and therefore the review and potential approval of Deramiciol is a matter of life and death. Delays and misdirection by FDA are costing young lives. Please help.

Tay Sachs

This is affecting the Tay Sachs community. My daughter qualifies for a trial, but we are being faced with a 1:3 placebo rate, which means I would have to take her off her compassionate-use medication to go on the trial, while risking a 1:3 placebo rate. My child is 13 and her life expectancy is 15 years old. I don't have 18 months to gamble with a placebo.

Eosinophilic Esophagitis

I am representing the eosinophilic esophagitis (EOE) community as the parent of a child living with this chronic immune-mediated disease. It has profoundly affected his life through daily abdominal pain, difficulty swallowing, food aversions, anxiety around eating, restrictive diets, and social isolation, all of which significantly lowered his quality of life even though the condition is not typically life-limiting.

For years we relied on elimination diets, steroids, and repeated endoscopies while waiting for better options, and those delays meant ongoing inflammation, fear of choking, emotional distress, and disrupted school participation. But now that dupilumab (Dupixent) has finally received approval from the U.S. Food and Drug Administration, he is in remission. His stomach pain and inflammation have improved, his allergies are also improving, and he can eat with less fear. This treatment is not a cure: access barriers and variable responses remain, and we still manage chronic symptoms and monitor his nutrition and mental health. Time in rare disease is not abstract because six months can mean prolonged pain, nutritional compromise, and worsening anxiety around food, and a year can mean cumulative physical and emotional loss during critical developmental years. So, regulatory delays translate directly into months of suffering and missed milestones, which is why this approval is so meaningful to our family and why my son, now finally feeling better, hopes to return to school soon and reclaim the normal childhood experiences that EOE once took from him.

Limb Girdle Muscular Dystrophy

Limb Girdle Muscular Dystrophy 2I/R9 is an ultra-rare, progressive muscle-wasting disease that ultimately leads to loss of ambulation, respiratory complications, and cardiac failure.

My 18-year-old daughter, was diagnosed with LGMD2I/R9 at the age of two. Since then, she has endured profound physical and emotional losses. She falls frequently and can no longer rise from the floor independently. She is unable to transition from sitting to standing without assistance, which means she cannot use a traditional bathroom or sit in a standard classroom or restaurant seating without someone physically lifting her. Recently, she shared that the constant vigilance and planning required just to get through each day is mentally and emotionally exhausting.

My daughter has already undergone two major surgeries, a spinal fusion, and an Achilles tendon lengthening, to address severe contractures caused by this disease. She experiences extreme fatigue and pain when she pushes herself beyond her limits. And yet, despite her strength and resilience, LGMD2I/R9 continues to take more from her each year.

For the past 15 years, our family and our foundation have worked tirelessly to support research and drug development. Despite this commitment and progress, there are still no FDA-approved therapies for LGMD2I/R9. Several clinical trials are underway, offering hope to our community. However, difficulties with funding have halted progress in a promising gene therapy program that could significantly impact patients like my daughter.

Time is not a neutral factor for our community. This disease is progressive. Every month without treatment means further muscle loss, decreased independence, and irreversible decline. Every day that passes carries the risk of a fall that could result in fractures, respiratory failure, cardiac complications, or permanent loss of remaining muscle function.

My daughter, and so many others like her, do not have time to wait.

Niemann-Pick

My son had Niemann-Pick type C (NPC) disease and died at the age of 20. NPC disease is a fatal, genetic, neurodegenerative disease that causes progressive deterioration of the nervous system resulting in dementia, seizures, disrupted sleep patterns, behavioral disturbances, fine and gross motor problems, and learning disabilities. The disease takes away your ability to walk, talk, swallow, eat, and breathe.

The NPC1 gene was discovered in 1997 after decades of research. Then it took 27 more years of research before the FDA approved the first treatment for neurological symptoms of NPC disease in September of 2024. There needs to be multiple drugs approved by the FDA to address all the symptoms of NPC disease.

There are multiple challenges and regulatory delays surrounding FDA approved treatments for NPC disease.

1. Drug trials for common diseases like high blood pressure and asthma can include thousands of participants. The size of the trial makes it easier to achieve better randomization and see statistical significance of the drug's efficacy
2. Trials are much more difficult for rare diseases, particularly because symptoms and the rate of disease progression in the patients is often highly variable
3. The cyclodextrin trial for NPC disease (my son was in this trial) included just 56 children and young adults with a broad range of disease symptoms, which limited the interpretation of the results
4. Rare disease drugs need another pathway to approval by the FDA. They cannot follow the same pathway to approval as common diseases
5. We need to modernize clinical trial designs
6. Include natural history controls and natural history comparison groups
7. Rely on surrogate or intermediate endpoints for rare genetic diseases
8. Allow Accelerated approval for ultrarare genetic diseases with primary disease biomarkers based on clear biology for treatments aimed at the underlying cause
9. Issue a guidance in compliance with original FAST bill (FDASIA) to ease the excessive burden on qualification of primary disease cause biomarkers
10. Accelerated approval shortens the time it takes to drug approval, while allowing for longer timeframes to collect confirmational data
11. Randomized placebo-controlled trials for a disease with irreversible brain or muscle disease are unethical. No placebo-controlled trials for these diseases.

Niemann-Pick type C disease relentlessly takes away your ability to walk, talk, swallow, eat and breathe as time marches on. Regulatory delays mean your ability to swallow or walk slips away. Having longer timeframes to collect confirmational data after a drug is approved gives patients with neurodegenerative diseases access to medicines that can slow or stop the progression of their disease and buy them time with their families. Rare disease drugs need another pathway to approval by the FDA. They cannot follow the same pathway to approval as common diseases.

[New submission]

I am the mother and sole caregiver of my 4-year-old daughter.

I represent the Niemann-Pick disease type C community.

Niemann-Pick Type C is an ultra-rare, progressive, neurodegenerative genetic disease affecting approximately 1 in 100,000 individuals. In the United States, there are only about 943 diagnosed cases.

It is terminal.

It is fatal.

There is currently no cure.

Many children with early-onset forms do not survive into adolescence or early adulthood.

The disease is often described as "childhood Alzheimer's." Like Alzheimer's and other neurodegenerative conditions, it causes gradual and irreversible loss of brain function. But in my daughter's case, that decline began in early childhood.

My daughter was born healthy. She walked. She talked. She laughed. She said "Mom."

Then she began to regress.

Niemann-Pick Type C is caused by mutations in the NPC1 or NPC2 genes, preventing the body from properly transporting cholesterol within cells. Toxic accumulation damages the brain and nervous system over time.

Symptoms vary widely, which frequently delays diagnosis. In our case, it took nearly two years to receive answers. During that time, we watched her lose skills while moving from specialist to specialist. Many providers had never encountered the disease.

By the time we received the diagnosis, progression had already taken hold.

Today, she can no longer walk, talk, or swallow independently. She has lost voluntary movement in her limbs. She is aware. She is present. But she is increasingly trapped inside her own body.

Last year, what was expected to be a brief hospital stay became a two-month hospitalization after she took a sudden turn for the worse.

This is what terminal neurodegeneration looks like in real time.

In six months, a child can lose speech.

In a year, a child can lose mobility.

Decline does not wait for process.

There is no approved cure to stop this disease. Supportive care may manage certain symptoms, but it does not halt progression. The unmet medical need is profound.

As her caregiver, I live with the reality that the clock is not on our side.

Time, for us, is measured in functions.

Time is whether she can still swallow safely.

Time is whether she can still move her hands.

Time is whether she still recognizes my voice.

When research funding slows, when regulatory pathways stall, or when advisory committee meetings decrease — as seen in 2025 with significantly fewer meetings for prescription drugs and biologics — families like mine feel that delay immediately.

Because regulatory delay is not neutral.

For a terminal disease, delay means decline.

The work of this Committee matters. Pediatric neurodegenerative diseases and adult neurodegenerative diseases share biological pathways. Investments in one advance progress in the other.

I cannot change her diagnosis.

But Congress can ensure that the pace of research and regulatory review matches the pace of disease.

For families living with terminal neurodegeneration, time is everything.

And once it is lost, it cannot be returned.

Thank you.

ALS

We lost Mom to ALS 29 years ago last month.

The prognosis seemed outrageous then, and it is all the more outrageous today. There is still no known cause, and the treatments are not very effective.

A dear friend I lost to ALS talked about the ALS Clock. It runs relentlessly fast. Healthcare delivery simply doesn't keep up. Research moves at the speed of concrete. Surely there are ways to speed up the deliverables without compromising the scientific truth.

We want therapies that work. We also want to stop this relentless destruction of vibrant human beings.

I was diagnosed with ALS mid-2025 and am now really starting to lose control of my body. Before the disease, I was an active equestrian, long walker, and generally in great health. Not only is it disheartening to have a terminal illness, but the lack of approved treatments to extend life without trach/feeding tube is horrifying. This disease really strips away who you are along with your dignity since ultimately you will have to rely 100% on others for care (not a good thing for a previously independent person who likes to be in control). I feel like there are far more people trying to live with this disease than I ever thought --- all relying on help to maintain their lives. Please help this community out by funding further research with a goal of curing this disease or at least converting it to a 'chronic' one.

[New submission]

I am paralyzed from ALS, a rare disease. This results in a large uncompensated caregiver burden on my family. While there are approved treatments, they are not effective at stopping the disease progression. The current clinical trials disqualify the vast majority of people living with ALS.

The FDA could be more involved in Expanded Access Protocol therapies, which recently have shown positive medical evidence in conjunction with clinical trials. The FDA provides minimal funding for ALS research, while many identified disease ideas go unfunded.

Please provide the FDA with directions and funding for ALS Research, CTs & EAPs.

Spinocerebellar Ataxia

I am 43 and living with Spinal Cerebella Ataxia. My sister died at 48 and my father died at 56. There are no approved treatments for my condition. The FDA regulations don't seem to reflect the essence of time, and what it means to me as a rare disease quickly degenerates my abilities. I need ends to justify the means in this situation.

My disease is harsh and hope is hard to find when my government organizations seem to be misleading research, so medicines are denied. The triruzole drug seemed like it had followed all the rules and was being fast tracked towards approval only to be denied. This is not about a

company making money or not about the population of voters being denied access to the first drug that was proven in studies to slow the progression of my SCA3 rare disease. Please have compassion-based ideals and firmly understand that the disease is worse than the medicine, and we are all looking at a shortness of time.

[New submission]

I have Spinocerebellar Ataxia type 3 (SCA3), a hereditary degenerative disease. Each day my balance and coordination worsen, or I notice something new that I can no longer do. Recently, I noticed that I can no longer jump or coordinate to do a jumping jack. This disease has been known and researched for 30 years, yet there is still no treatment or cure. Rather, some medicine, Troriluzole has been proven to help, but we cannot get it because FDA red tape prevents its approval. The neurologists have nothing to offer us and tell us to exercise a lot, but our bodies are losing the ability to move well.

My mother who died from complications related to SCA3 always told me, "Even if you get it, a cure will exist by your time." Now, I fear that I will have to tell my children (who have a 50% likelihood of getting it) the same thing.

[New submission]

I have a SCA3. There is no cure for it. It is disheartening when you hear of a possible treatment for it, only to hear that the FDA has rejected the medication. Whatever their reasons for rejecting it, there is still no cure, so what is the harm. There will be a day when I am unable to type this. I am restricted to wheelchairs now. Unable to drive, traverse the lawn let alone woods. I used to work for Verizon installing and repairing communication lines. I was up and down ladders and utility poles every day. Now I can't stand being unassisted.

[New submission]

I was 42 years old and absolutely terrified. My body was doing something strange. I embarked on a four year journey to find a neurologist that was able to help me. In the interim years, I was subjected to countless blood tests, MRIs, spinal tap, and multiple nerve conduction studies. All this to find that I have Spinocerebellar ataxia. Unfortunately, there has not been enough research to specify exactly what I have. Although this is incurable, I would like to be able to pinpoint my diagnosis. This is not possible without more research being done.

[New submission]

I was diagnosed with SCA 6 Ataxia several years ago -- and have been in a trial program with Biohaven Pharmaceutical for the past year. The drug offered is to "slow down the progression" of the disease. The FDA has not approved the drug for distribution, however, to my knowledge this is the only drug available for those suffering with SCA 6 Ataxia. On my 70th Birthday my PGA handicap index was 12. I was enjoying life as a part-time employee, playing golf, riding bikes, traveling with our Airstream and being an active grandparent. Now I am preparing my home for a

wheelchair ramp, adding a lift to our mini-van, and waiting for a cure! Help is REQUIRED! Life has radically changed for me, my wife, my children and our grands. WE Need ACTION! Thanks.

[New submission]

I have a form of Spinal Cerebellar Ataxia, specifically SCA5. I have a de-novo mutation of the gene which means that neither of my parents have the disease, but I have passed it to at least two of my children. My two girls, now in early adulthood (22 and 24), are experiencing gait and balance issues. My youngest son (21) has not presented at this time, and we have not tested for the gene because there are no cures or trials for this rare disease.

I currently use a walker because this disease causes issues with my balance and gait. I am beginning to experience some slight difficulties with speech as well. I am 54 and am much more concerned with finding a cure that can halt or slow down the progression for my children. My oldest is getting married and I'm concerned with navigating life as a young mom and being able to handle a child.

I am working with a researcher on the disease and am learning how archaic the process is. I have learned a bit about AlphaFold and some of the tremendous benefits AI can have on research and drug development. Especially in reducing the time and more importantly the cost of drug development. However, I am concerned that bottlenecks in the FDA process will negate these benefits. I am very concerned because my disease and the disease that affect my children is progressive and every delay means that they will face some of the things that I am experiencing as an adult. I am not as worried for me as I am for my children and urge the committee to do whatever is necessary to move this forward.

[New submission]

One year ago, I was diagnosed with Spinocerebellar Ataxia type 3 (SCA3), a rare, progressive, and currently incurable neurodegenerative disease. I am facing a future of steadily worsening balance, coordination, speech, and daily functioning. Without medical intervention, I am destined to end up in a wheelchair with complete reliance on caregivers.

I am a wife and a mother of two daughters, and I inherited SCA3 from my father. My father had no chance of treatment for his SCA3, as there was none available while he was alive. I witnessed how the disease stole his ability to walk, to feed himself, to speak intelligibly, and to swallow food without choking. His mind remained intact, but his body was failing. SCA3 eventually claimed his life. What echoes in my ears is one of the last understandable words that he spoke as he lay dying in the hospital. That word was "help." Distressingly, there was no help to be had.

As a doctor who witnessed how SCA3 first affected my father, I understood the implications when I unexpectedly stumbled one day. Over the following year, frequent muscle cramps became alarming occasions when I would take an extra step to catch myself from falling. I became wary of uneven ground and fearful of walking up or down stairs without railings. I was only 51. I made a

bucket list of all the things I wanted to do in the next 20 years or so before I lost the ability to walk, to hold a pen, or to communicate well. The thought that my daughters had a 50% chance of inheriting this crippling disease from me kept me up at night.

However, I was given new hope 10 months ago when I started taking VYGLXIA (troriluzole), an investigational drug developed by Biohaven, through the FDA's Expanded Access (compassionate use) program. In clinical trials, Biohaven showed that troriluzole has the potential to slow disease progression by 50-70%. Astoundingly, within 3 months of starting the medication, my physical exam reflected improved balance and coordination. By 6 months, I was more confidently walking in a straight line and climbing up and down stairs without assistance. In the last 10 months, my symptoms have stabilized and I have many more good days than bad ones. I know troriluzole will not cure me, but it is my only lifeline to a better future — maybe even one without a wheelchair.

Disappointingly, in November 2025, the FDA issued a Complete Response Letter to Biohaven's New Drug Application for troriluzole. Fortunately, Biohaven remains committed to working with the FDA to find a path forward. I am fearful that I and many others will lose access to troriluzole once the Expanded Access program ends. This affects not only me, but the thousands of other spinocerebellar ataxia patients across the country who are on this medication. My biggest fear, however, is that my daughters will not have access to troriluzole if they should need it.

I respectfully ask that you contact the FDA and express your strong support for the expeditious review and approval of troriluzole for spinocerebellar ataxia. Your advocacy could make the critical difference in bringing the first disease-modifying therapy to those affected with spinocerebellar ataxia.

Thank you for your commitment to improving the lives of those living with rare and serious diseases. While there was no disease-modifying treatment for my father when he was dying from SCA3, you can help give me, and thousands of others who are fighting this dreaded disease, a chance to enjoy their best lives for as long as possible.

[New submission]

To whom it may concern:

I'm a 47-year-old male with SCA Type 1. There are currently no treatments for this disease. It is an extremely rare progressive, inherited neurodegenerative disorder caused by a CAG trinucleotide repeat expansion in the ATXN1 gene, typically inherited in an autosomal dominant pattern. It causes imbalance, lack of coordination (ataxia), slurred speech, and dysphagia, usually starting in the 3rd or 4th decade, with a 10–30-year lifespan post-onset.

Bottom line, there's no money in research/curing this disease, so I'm at the mercy of my government through a subsidy. The FDA recently denied approval for a drug called Troriluzole, which has very promising potential delaying the onset of symptoms by an average of 60% with real

world data. Meaning I'd live long enough to die of something else. After the denial, the company developing the drug was forced to put it on the back burner so to speak, as they couldn't keep investing money into something that may not have a return. The drug is still available through the Expanded Access Program and may be my only hope for any kind of quality of life over the next 20 years. They have another hearing with the FDA soon to discuss a potential path forward. I have 3 children.

My hope, even if I don't get it, would be to have it available to them. Judging by how the disease is passed on, I would bet at least 2 out of the 3 are carriers. My Grandfather took his own life due to the disease. My Father is 70 and is very close to being in a wheelchair and needing a feeding tube. My children have witnessed his decline over the past 10 years and will likely have to deal with mine as well. I've begun experiencing symptoms, as have several cousins of mine. Time is of the essence. Thank you for taking my statement.

[New submission]

Good day, I was diagnosed with Ataxia last year. As you know this is a quickly degenerative inherited disease that impacts the quality of life (I have no balance, prone to falls, shrinking brain, no control of extremities, slur speech and more) I have left as a man of only 50 years old, a full time employee for the municipality I work for and a proud father of 3 school age children. My father and my son suffer from this disease severely and it hurts to know that there is no cure at the moment. However, a company by the name of Biogen just concluded some successful studies with a pill that the FDA did not approve even though their clinical trials showed success within the subjects they recruited. Unfortunately, I cannot get the pill Biogen designed because of all the regulatory decisions. I am imploring to please approve Biogen's treatment for Ataxia so that I may live longer and live a better-quality life. FDA— please approve Biogen's pharmaceutical treatment for Ataxia so that my father, who is now dying at 72 because of this disease, my son is now completely disabled, myself and others an opportunity at a slightly better life with treatments targeting Ataxia. Thank you and I hope you can bring some hope to those of us who are in the dark.

Chronic Inflammatory Demyelinating Polyneuropathy

I represent the rare disease community of people living with Chronic Inflammatory

Demyelinating Polyneuropathy (CIDP), and I stand alongside those impacted by GuillainBarré syndrome (GBS). These are autoimmune diseases where the immune system attacks the peripheral nerves — stripping away the protective myelin sheath and disrupting the body's ability to function.

For many people, CIDP is described as a "motor neuropathy" that causes weakness and sensory loss.

But for me, it did more.

CIDP did not just attack my ability to walk.

It attacked my autonomic nervous system — the system that controls the things your body is supposed to do automatically, like regulating heart rate and blood pressure.

My heart began misfiring. My rhythm became unstable. My body could no longer reliably control something as basic — and life-sustaining — as a heartbeat.

As a result, I now live with a pacemaker.

At 60% pacing, my device is not optional — it is supporting a heart that cannot consistently regulate itself. What started as an autoimmune neuropathy progressed into cardiac instability. This is something many people do not realize can happen in the GBS/CIDP spectrum.

CIDP affects quality of life in profound ways. Weakness. Fatigue. Nerve pain. Instability. Periods of paralysis. Loss of independence. And in cases like mine, autonomic dysfunction that can impact the heart, blood pressure, and overall safety.

CIDP may not always shorten lifespan directly — but untreated or poorly controlled disease can lead to permanent nerve damage, severe disability, and life-altering complications. Six months without adequate treatment can mean muscle atrophy. A year can mean irreversible nerve damage. Autonomic involvement can mean emergency interventions.

There are FDA-approved treatments, including IVIG, corticosteroids, plasma exchange, and subcutaneous immunoglobulin therapies. These treatments can slow progression and restore strength for some of us. They have given me stability at critical moments.

But they are not cures.

Many patients require lifelong infusions. Some do not respond to first-line therapies. Others lose response over time. Access can be delayed due to insurance barriers, prior authorizations, step therapy, or questions about diagnostic criteria. Because CIDP is rare and heterogeneous, clinical trials are small and complex. There have been ongoing debates about appropriate endpoints, biomarkers, and what level of evidence is “enough.”

For patients like me, those debates are not theoretical.

Regulatory delays are measured in nerve loss.

In muscle loss.

In independence lost.

When a decision is delayed by six months, that may mean six months of progression. In autonomic involvement, that can mean dangerous instability. Nerves do not regenerate quickly. Some damage cannot be undone.

Time, for me, means:

Six months — the difference between walking independently and needing assistance.

One year — the difference between working and permanent disability.

Delay — the difference between a stable rhythm and a life-threatening one.

I never imagined that a rare autoimmune neuropathy would lead to me needing a pacemaker. But rare diseases do not follow neat textbook boundaries.

I share my story because patients cannot afford prolonged uncertainty. We cannot afford regulatory gridlock. We cannot afford to wait while our nerves are under attack.

In rare disease, time is not just a policy variable.

Time is nerve function.

Time is autonomy.

Time is independence.

Time is life.

[New submission]

Do you like to wake up in the morning feeling pain free, full of energy, and ready to start your day? I wish that was my reality, but it is not. I have lived with a rare disease for 31 years since the age of 28. I have Chronic Inflammatory Demyelinating Polyneuropathy (CIDP). I am 1 in 100,000.

Each morning, I wake up sore, stiff, and in pain. I have been on IVIG - intravenous immunoglobulin gammaglobulin for 25 years. As a patient of a rare disease community, the FDA is important. We need you to allow research for these rare conditions to continue. Without research we will not develop new and improved medicine to improve our quality of life. Medicine is expensive. More research allows patients and doctors options. Without medicine, I would lose my quality of life. I cannot go longer than two weeks without my medicine. I rapidly declined. Walking, daily life skills, and being a productive member of society decrease rapidly. Regulatory delays mean that I will end up in a wheelchair sooner or even totally dependent on others for my care. How would you like to live with that prognosis?

Huntington's Disease

I am at risk of living with Huntington's disease and live with family members who tested gene positive. I am submitting this testimony to share my concerns about current FDA regulatory decisions and their impact on the Huntington disease (HD) community.

Huntington's disease (HD) is a rare, inherited, and ultimately fatal neurological disorder. Often striking in the prime of a person's life. It causes a progressive decline in a person's ability to think, move, and function independently. If one parent has HD, their children have a 50 percent chance of inheriting HD. There is currently no treatment that slows or stops the progression of HD. It progresses from symptom onset to death over approximately 15 years often beginning in the prime of life.

As a child, experiencing a parent with HD was traumatizing, tragic, and painful. Not only did I lack a maternal figure, I had to watch someone, someone who I should've known but instead as a stranger, deteriorate before my eyes. I couldn't explain what was happening or relate to any of the peers or adults in my life. It was isolating. Even after her passing, seldom do people understand the trauma I lived with as a child. In the present, the ever-impending doom of my brother's sickness as well as my own potential sickness, looms over my daily life like a thick fog. I can never be at peace. I never will be at peace. This is the experience of many children of HD parents like myself.

My brother participated in a clinical trial. This trial occurred hours away and was worrying to experience even from a distance. There was an overlying anxiety over his physical and emotional wellbeing.

People living with HD and their families are willing to take risks to stop the progression of the disease. Nearly three-quarters of respondents to the 2024 HD SA HD Symptoms and Treatment Impact Survey said they would accept treatment risks to gain five years with no disease progression, and almost 35% were willing to accept risks for even three years of halted progression.

When FDA policies are unclear, inconsistent, or unpredictable, it creates additional barriers for therapies that may represent our only hope. I am concerned about lack of transparency in decision-making for HD therapies, inconsistent application of regulatory standards, and failure to adequately account for the realities of small patient populations. I respectfully urge the Committee to direct FDA to:

- Consider benefit/risk tolerance of people living with Huntington's disease when making decisions about trials for HD treatments and cures.
- Utilize natural history studies for rare disease trials.
- Be clear and transparent about its decisions related to HD trial decisions, including recent statements about uniQure's AMT-130.

Thank you for the opportunity to submit testimony for the record. I appreciate the Committee's attention to the needs of rare disease patients and families. For our community, innovation is not optional — it is survival. It represents more time, more independence, and more life.

[New submission]

I am gene-positive for Huntington's disease. I cared for my father as he declined and eventually passed away from this disease in January 2021. I now live knowing that Huntington's disease is progressing inside me.

I am also a clinical research participant.

Over the years, I have participated in a therapeutic clinical trial and in several observational studies, including contributing to the natural history research that helps define how Huntington's disease progresses over time. That natural history data is not abstract to me - it represents blood draws, cognitive testing, travel, vulnerability, and time given freely in the hope that it will help build a pathway to treatment.

Patients like me enroll in these studies because we believe in science. We believe in partnership. We believe that if we do our part, the system will work with us.

Huntington's disease is a fatal, inherited neurodegenerative disorder with no diseasemodifying treatment. Time is everything. Time is cognitive function. Time is independence. Time is the ability to be present for your children — to help with homework or teach them how to ride a bike.

Recent regulatory decisions affecting rare disease therapies - including incomplete response letters, refusals to file, and shifting expectations for trial design - have had destabilizing consequences across patient communities.

For diseases like Huntington's, traditional placebo-controlled trials are uniquely difficult. Our population is small. Our disease is progressive and irreversible. Natural history data and external controls are not shortcuts; they are tools built from years of patient contribution and scientific rigor.

When regulatory expectations shift late in development, it does more than delay a submission.

It calls into question whether the years patients have spent contributing to natural history databases will truly be recognized and utilized as intended.

We are not asking for lower standards or shortcuts. We are asking for:

- Consistent application of accelerated approval pathways Transparent and predictable regulatory expectations
- Scientific flexibility appropriate for fatal neurodegenerative disease
- And meaningful incorporation of patient experience into risk-benefit decisions

I have sat in research visits answering memory questions, knowing that one day I may not be able to answer them. I have contributed to natural history studies designed to map the decline of my own disease. That data exists because patients like me were willing to document our progression in the hope that it would shorten the path to treatment, not extend it.

When a delay happens in Huntington's disease, it is not neutral.
Delay is decline.

Delay is an irreversible loss of brain cells.

Patients have done their part. We show up to studies. We give our data. We accept risk. We build natural history datasets so that innovative trial designs can be possible. We are asking that the regulatory framework meet us with the same urgency and consistency.

Thank you for holding this hearing and for examining how FDA processes affect real families like mine that are facing progressive, fatal rare diseases.

[New submission]

I represent the Huntington disease (HD) community, which is a rare, neurodegenerative disease that impacts motor, cognition, and behavior. There are no treatment options and the average lifespan is 10-20 years since symptom onset. I witnessed my mom battle this for 17 years before passing away over 10 years ago. Because of the genetic component, each child of a parent with the disease has a 50-50 chance of inheriting it. I decided to go through testing and found out I also carry the gene, and I'm guaranteed to get the disease unless there's a treatment in time. I tested over 15 years ago and now I'm racing against this invisible clock as I get closer and closer to potentially developing symptoms.

More recently, there's been some promising research from a company called uniQure who's working on an investigational gene therapy for HD. They demonstrated clinical benefit in outcome measurements that are meaningful to patients and families. They previously agreed with the FDA on using an external control arm through a natural history dataset instead of placebo since it's not ethical to make a patient go through a brain procedure. However, the FDA is no longer in agreement, and the HD community is running out of time as people will continue to get worse.

Every moment matters as the HD community specifically told the FDA in a recent PFDD meeting. We want to continue to build memories with our loved ones rather than having them lose their independence day by day.

Prader-Willi Syndrome

I am a constituent of West Virginia and have a 7-year-old daughter with Prader-Willi Syndrome (PWS). West Virginia has always been her home, and she received a diagnosis of PWS at 2 weeks old. PWS is a rare genetic disorder affecting approximately 1 in 20,000 individuals, and for decades families have navigated it with almost no FDA-approved treatment options. It begins at birth with failure to thrive and quickly becomes a lifelong medical and developmental challenge requiring intensive therapies, constant monitoring, and extraordinary vigilance. In 2000, growth hormone became the first FDA-approved treatment—a milestone that changed outcomes for physical development but did not address the full complexity of the disorder. Then, twenty-five years later, in 2025, a second approval came: Vykat for hyperphagia, the hallmark, and most life-threatening symptom of PWS. Hyperphagia is not overeating by choice; it is a relentless biological drive to eat without ever feeling full, leading to severe obesity, diabetes, hypertension, and premature death. Two

approvals in twenty-five years is progress—but it is not enough. PWS is multifaceted, involving cognitive delays, behavioral dysregulation, anxiety, rigidity, and metabolic instability. Families cannot wait decades between breakthroughs. We need accelerated research, additional FDA approvals, and treatments that address the full spectrum of symptoms—not just one.

I see two realities and issues that policymakers can easily overlook. The first is that parents are taking steps for earlier interventions (therapies and these few approved treatments) and individuals with PWS are living longer than before. Secondly, their caregivers are also aging alongside them. Parents who have managed complex medical regimens, locked kitchens, prevented life-threatening food access, and de-escalated neurological behavioral episodes for decades cannot do so forever. There is not an individual with PWS who can live fully independently without structured support, yet as parents age, the system offers few sustainable options. Institutions have rightly closed, but closure without replacement leaves families in crisis. We need support both in-home for as long as our loved ones can remain there, and highly supported residential communities that preserve dignity, provide medical oversight, and ensure safety when parents can no longer serve as primary caregivers. It's a both/and. The life expectancy for individuals with PWS still hovers in the low twenties, largely due to complications of hyperphagia. Twenty is too young. If we are serious about extending lifespan, FDA approvals must continue, treatments must expand, and long-term care infrastructure must evolve in parallel. Our loved ones deserve more than survival—they deserve longevity, stability, and the promise that when we age, they will still be protected.

Hereditary Xerocytosis

I'm a Registered Nurse. My mother-in-law, daughter and husband have Hereditary Xerocytosis. At this point, my daughter is in stable condition. My husband, however, has elevated liver enzymes, jaundice, fatigue, and iron overload as a result. My mother-in-law has daily severe fatigue, symptomatic anemia requiring transfusions, and jaundice. This affects them in completing activities of daily living.

Residing in a rural area, one of the biggest obstacles is finding a physician knowledgeable in the illness. I am unaware of any approved treatments for the disease. Time for us is everything. My loved ones live with a high risk of aplastic anemic crises. I hope for a cure or suppressing treatment & gene therapies for my daughter's lifetime. What a gift it would be for her to be able to become a mother knowing she can avoid passing on this hereditary illness.

Pyruvate Dehydrogenase Complex Deficiency

I am writing as a parent to a sweet, three-year-old girl who is currently living with Pyruvate Dehydrogenase Complex Deficiency (PDCD). On September 4, 2025, Saol Therapeutics shared a press release stating that the U.S. Food and Drug Administration (FDA) will not approve Saol Therapeutic's New Drug Application for SL1009 (DCA) for Pyruvate Dehydrogenase Complex Deficiency (PDCD) in its current form, outlining specific observations that must be addressed before potential approval can be reconsidered. We were fortunate to receive her diagnosis in utero. Because of that, she began the ketogenic diet on the first day of her life.

From birth, everything has been carefully measured and medically managed. We also knew time is a gift with her, as life expectancy with PDCD is early childhood. Despite early intervention and around-the-clock care, she is nonverbal and non-ambulatory. She lives with profound neurological and physical disabilities that impact every aspect of her daily life.

She cannot speak to tell me how she feels. She cannot walk to explore the world. She depends on us for everything. And yet, she is the sweetest, strongest little girl you could ever meet. She is joyful. She is determined. She deserves every possible chance at life.

I have spent years advocating for PDCD to try and help save our daughter and give her the best chance at life possible. We have been anxiously awaiting any type of therapy or drug for her for three years, and this news is devastating to say the least. Right now, someone living with PDCD has a life expectancy of early childhood, and we are in a race against time to get a drug approved to extend and improve their quality of life.

However, DCA has given us hope and my daughter was able to start the drug in November of 2025 through an Expanded Access Program.

Since starting DCA, we have witnessed meaningful changes:

- Increased energy
- Improved appetite
- More voluntary movement
- Greater engagement with her surroundings
- And for the first time, she began to wave

That wave may seem small. For us, it was monumental. For a child who is nonverbal, it was connection. It was communication. It was hope.

DCA remains under regulatory review. The possibility that Expanded Access could be restricted or that approval could be delayed due to another clinical trial requirement is frightening beyond words. For children with PDCD, time is not an option as disease progression does not pause.

In rare pediatric diseases, even the smallest milestones matter. A wave matters. Increased energy matters. Engagement matters. Traditional clinical endpoints may not fully capture what progress looks like for children like my daughter. For our community, perfection cannot be the enemy of progress. When therapies show safety and real-world functional improvement—even small ones—those gains should matter.

My daughter was not given a generous timeline when she was diagnosed. Every month she is stronger, more engaged, more connected is a gift. Removing access or delaying flexibility risks taking away progress that her fragile body fought so hard to achieve.

She cannot advocate for herself. I am asking you to help ensure that children like her are not left behind by a system that moves more slowly than their disease. We hope the right voices make it to the FDA and meetings with Saol to come up with a plan moving forward for full approval given there have been no safety concerns with the results.

Thank you for standing with rare disease families and children who cannot afford to wait.

[New submission]

I am writing on behalf of my son who was diagnosed with Pyruvate Dehydrogenase Complex Deficiency. He was diagnosed at the age of 5 after many years of testing and lack of answers.

This mitochondrial disease affects his energy levels. At times he loses motor function in his legs, leaving him unable to walk or stand. These episodes come with extreme fatigue at times leaving my son, a now 8-year-old boy unable to act as his peers at times.

We are blessed. Many patients with PDCD have cognitive delays, feeding issues, and some die from this condition. There is no cure for PDCD and as it is a rare genetic disease, it is not screened for with newborn screening. We spent 3 years and an unmeasurable amount of money and time to try and figure out what was causing Miller's symptoms. There is not currently an approved treatment for PDCD, though DCA has been proven in some trials to lessen symptoms. The FDA would not approve DCA for the treatment of PDCD and closed further trials.

My son has been on a ketogenic diet since he was diagnosed to keep his symptoms at bay. He loves baseball and it is hard as a parent to watch him struggle with something he loves because of a condition that has no treatment. Since diagnosis, he has participated in speech, physical, and occupational therapies. His medical shakes that he requires as part of his ketogenic diet are not covered by Blue Cross Blue Shield insurance, therefore, we pay for those out of pocket. Funding and clinical trials for children like Miller are necessary. These kids deserve a life lived fully.

Other Mitochondrial Diseases

I am representing the mitochondrial disease community, specifically families of children with extremely rare genetic forms such as COXPD4, a life-threatening mitochondrial disorder that affects energy production in every organ system and has shaped my daughter's entire life through chronic fatigue, muscle weakness, neurologic symptoms, gastrointestinal challenges, and significant mental health impacts that fluctuate with her metabolic stability. Many children with mitochondrial disease do not survive to adulthood, and while our daughter is nearly there, her path has required constant vigilance, complex medical care, and extraordinary financial and emotional effort just to maintain stability and function.

With no FDA-approved cure available, treatment is limited to supportive care, metabolic supplements, and alternative therapies such as neurochiropractic care that have helped her tremendously but are expensive and often not covered by insurance. This leaves families to rely on grants, out-of-pocket costs, and relentless advocacy simply to preserve quality of life.

Regulatory and research challenges for ultra-rare conditions like COXPD4 include small patient populations, limited clinical trial feasibility, and disagreements about appropriate outcome measures, all of which slow the development and approval of targeted therapies while children continue to decline or face life-threatening metabolic crises. For us, time is everything because six months can

mean the difference between stability and regression in cognition, stamina, or psychiatric symptoms, while a year without disease-modifying treatment can mean irreversible loss of function that can never be regained. So, regulatory delays are not theoretical—they represent lost abilities, increased medical fragility, and ongoing uncertainty about survival.

Although we feel deeply grateful and privileged that through hard work and grants we have mostly been able to afford the supplements that keep her stable, the reality is that many families cannot, and a true cure would mean the world to our family and to the many children with mitochondrial disease who are still fighting for the chance simply to reach adulthood.

Invasive Fungal Disease

I am representing the invasive fungal disease community, specifically families affected by CNS mucormycosis (*Apophysomyces variabilis*) – a rare, aggressive fungal infection that can spread from the sinuses to the brain.

Mucormycosis is often misunderstood, under-recognized, and rapidly fatal if not treated immediately. Survivors are rare. Families navigating it often feel invisible.

My Story

What began as what appeared to be orbital cellulitis from a routine sinus infection progressed into a life-threatening brain infection.

Mucormycosis is an angioinvasive fungus—it invades blood vessels, cuts off blood supply, and causes tissue death. In my case, it spread from the sinuses to the skull base and brain.

The impact included:

- multiple hospitalizations
- prolonged ICU care
- five brain surgeries, including emergency neurosurgical intervention
- skull base osteomyelitis (bone infection)
- venous sinus thrombosis
- brain herniation
- six months of toxic antifungal therapy with amphotericin B
- permanent hearing loss caused by life-saving medication
- ongoing neurological recovery

Recovery is slow and uncertain. Brain healing takes months to years. Monthly PET scans still show osteomyelitis throughout my skull base. Fatigue, cognitive slowing, and emotional trauma are part of my everyday.

Mucormycosis carries high mortality when it reaches the brain. Survival is medically remarkable, and the aftermath reshapes daily life.

There is no FDA-approved therapy specifically for mucormycosis.

Treatment relies on:

- antifungal medications such as amphotericin B
- aggressive surgical removal of infected tissue
- prolonged hospitalization and intensive monitoring

These medications are toxic and difficult to tolerate. They can damage the kidneys, cause permanent hearing loss, disrupt electrolytes, and produce severe systemic side effects. Treatment is grueling and even with treatment, mortality remains high when the brain is involved.

There are significant unmet needs.

Current treatments:

- are decades old
- were not specifically developed for mucormycosis
- do not reliably penetrate necrotic or infected bone
- require prolonged IV administration
- carry substantial toxicity

There are limited clinical trials for rare fungal infections. I am dependent on compassionate use programs, investigator-initiated protocols, or extrapolated evidence from other fungal diseases.

Because mucormycosis is rare, research funding is limited. Diagnostic tools are also inadequate. There is no rapid, reliable blood test for early detection. Diagnosis often requires biopsy, for me, progression had already occurred by then. Earlier recognition and targeted therapies could have changed everything.

Rare invasive fungal infections face unique barriers:

- small patient populations make traditional clinical trials difficult
- lack of standardized endpoints for ultra-rare infections

- uncertainty around acceptable evidence thresholds
- limited commercial incentive for pharmaceutical development delays in diagnostic innovation

Patients with mucormycosis can deteriorate within days. Regulatory timelines operate in months or years.

For rapidly progressive infections, time is survival. When treatment development stalls, patients are left with outdated, toxic options. When diagnostics are delayed, infections are misidentified until irreversible damage occurs.

With mucormycosis, time is everything.

Six weeks of misdiagnosis allowed the infection to invade my brain.

Days can mean the difference between localized disease and catastrophic neurological injury.

Brain healing continues, but deficits are permanent.

For our family, time is measured in MRIs, surgical dates, antifungal infusions, and waiting for scans to show stability.

Regulatory delays mean another person may lose their hearing. Another patient may lose cognitive function.

Another parent may not survive.

We need faster diagnostics.

We need targeted antifungal therapies.

We need regulatory flexibility for ultra-rare, high-mortality infections.

We need recognition that invasive fungal diseases are not fringe...they are emerging global threats.

Every day matters! Because when a rare infection reaches the brain, time is no longer on your side.

Section Two

I was diagnosed with SCA7 (Spinocerebellar Ataxia Type 7). My mother and maternal aunts had this condition as well as my grandmother. In my generation, my brother and I were unlucky to have

gotten it out of a 50% inheritance chance; we are very unlucky. Oh, less I forget, my cousin had SCA7 and died because she was not able to care for herself and since her mother was also battling it, she could not help and watched her daughter, my cousin, die.

The thing with this condition is that each generation is worse than the previous. My mom's symptoms started around 40 years; mine is starting around my late 20's; I'm 29 this year. I am very unstable when I walk; my vision is bad; I stumble a lot. I randomly walk into people. They find it weird and so do I; I try to avoid them but my body does the opposite. My cerebellum is shrinking; I get a jolt of shock when I stand for too long and I pass out. My brother, who is 36, has all my symptoms but worse. He says he is "shy." Why? Because you were strong and all of a sudden people come and help you; it's embarrassing. I completely understand him. He does not know of my diagnosis; he is not strong enough for his let alone mine. My mother does not know of my diagnosis either. The lifespan for this is maybe 20-30 years. Since it affects the muscle; eventually, breathing becomes difficult and the heart stops.

Currently, my mother is bed bound (she can't walk/stand/see/feed herself) and I am her caregiver, but I am also sick. I worry about myself. I do not have a husband nor kids to do what I am doing for my mom. I have no one. My brother forcefully got married, so no woman rejects him when he can't walk. Every year that goes by, we get worse; time has never been more precious to us than it is now. As I care for my mom, I see my future, and when I see my brother, I see my path to my future, and it is painful. It depresses me each time I think about it.

A treatment I heard about was Troriluzole. I have contacted the manufacturer to see if they can help. They pointed me to a doctor. She has been ignoring me and there is no one to help me. No neurologist can help. Every help points me to the same doctor who ignores me. I even joined an exercise group at the Ataxia Foundation, but the people there were seniors; I didn't belong. I pray to God for the approval of Troriluzole, so that I do not have to get it prescribed by this one doctor who I cannot seem to access. I am fighting to get better even if it means delaying symptoms. I have not enjoyed life. I wanted to become a doctor but chose to work at NIH to further research for SCA related neuropathies. I sacrificed my future; that is how bad I want this.

Troriluzole is 50-70% efficient. SCA7 is among the rare neurodegenerative diseases. When I look up SCA7, small information exists. I get other SCA related neuropathies instead, yet, because the backbone of all SCA neuropathies are similar, Troriluzole targets that. Troriluzole needs more FDA approval. I hope with complete FDA approval, more than 1 doctor can prescribe it, so I have a broader network of doctors to work with instead of the one at JHU who ignores me.

Troriluzole may not help my mother, nor aunts, but it can help my brother and I. We may have 10-20 years added because of this drug. It is my hope that it gets approval, so we can get the help we -- my brother and I -- need.

[New submission]

I have CRPS (Complex Regional Pain Syndrome). I have been fighting this war for around four decades. I have tried many treatments. However, the treatments that are offered are too late for me. It took me 20 years before I found out what my diagnosis was.

Doctors did not believe this condition exists. I am still told that I am making this up. No one can be at a pain scale of 10 and still smiling/laughing. But, crying and screaming gets a person nowhere and it hurts a lot less by smiling. Laughing is getting to the point of hurting too much. Research on this "disease" is basically not heard of in the US. However, countries overseas have come up with some positive treatment ideas. Those treatments cannot be done here. They are not approved by the FDA.

It gets very disgusting when the treatments that are allowed are for people who were diagnosed within the first 10 years of initial onset. I was already behind the eight ball, at 20 years. There are no treatments offered for someone like me. I struggle every day. I can't find an employer who is willing to take a chance on me.

Even with my scooter, I have huge issues with going out in rain/snow and cold/hot temperatures. Weather patterns, I feel a few days before one hits. How bad I hurt usually means it will be rough front. The deeper the low pressure is, the more I hurt. I am not making this up. It is not in my head. Please believe me. Is that too hard to do? I guess it still is. I can see it in your body language.

[New submission]

Please help patients with chronic illness requiring controlled medications matter again! Why are we the ones left paying a high price for actions of other people? My life is destroyed losing medication that gave me a productive life. Over policy, not my individual health needs! They don't matter at all anymore! Patient suicide jumped 400% since 2016, this doesn't matter to you? Preventing addicts from getting a few "safer" pills matters more than patient lives?? It's pushed patients to turn to illegal drugs to relieve intolerable pain because Drs turn them away, is that what the goal is?? Kill off as many people with chronic illness as possible? Because that is what people think, genocide by denying vital medication! The added health issues from ongoing physical stress caused by pain cause easily 100,000 more deaths than overdose does!! And you could care less!!

[New submission]

In 2022, at the age of 66, my blood pressure suddenly became treatment resistant after a decade of blood pressure being controlled by one medicine. I also developed constant pulsatile tinnitus. After several months of trying different medicine combinations, a combination of 4 medicines stabilized my blood pressure. I had undergone a multitude of tests to determine cause, and an MRA showed bilateral renal artery stenosis. The goal was to keep my blood pressure in a healthy range and monitor kidney function via bloodwork.

Prior to 2022, I had always been a physically active person. I am a 3rd degree Black Belt in Taekwon Do and won a World Championship in weapons at age 51. When my blood pressure went haywire, I became extremely fatigued and lost almost 20 pounds of muscle mass because my appetite simply vanished.

I worked at regaining healthy weight and tried to stay active, but I would have drops in blood pressure during any kind of excursion. Loss of physical activity was, and still is, a daily mental challenge.

This year, 2025, I began retaining a lot of fluid and had a sharp uptick in shortness of breath and fatigue. My cardiologist referred me to a vascular surgeon who did a Doppler ultrasound on the renal arteries which showed significant stenosis, and it was determined that stenting was required. On February 17, the procedure was started and when the camera approached the left renal artery, the giant monitor showed the classic string of beads associated with Fibromuscular Dysplasia. The right artery presented the same structure. The vascular surgeon let me know that he preferred not to stent until he could consult with the nephrologist.

As it turns out, none of my local physicians have had any FMD patients, so I reached out to FMDSA to find a medical team that could help me. They told me about a specialist I could see. The doctor ordered additional scans and discovered FMD in my iliac, coronary, and carotid arteries in addition to the renal arteries. He also had me added to the FMDSA registry, which is an important tool for gathering detailed information for use by researchers.

I have added a therapist to my medical team to help me learn new coping mechanisms for the anxiety I have about living with FMD. My old coping mechanism of good, hard work out in the gym is a thing of the past. 24/7 pulsatile tinnitus is also hard to live with. I miss silence. Therapy is helping and I am so grateful for FMDSA.

[New submission]

My friend's son is a real-life superhero. He is kind, funny, resilient, and lights up every room he is in. He is also fighting a rare genetic condition. He is part of a clinical trial that has shown incredible improvement in his day-to-day life. He needs this trial. My best friend needs her son. His brother and sister need him. This is more than devastating. The FDA needs to approve these treatments. These children deserve and chance.

[New submission]

ALS is 100% fatal and terminal with 0 treatment options and a prognosis of 2-5 years. It does not discriminate against age or gender. I am a 33-year-old stay-at-home mom of a 4 year old. It could happen to anybody, including you.

[New submission]

Please provide more funding for research, especially diagnosing, of the disabling disease of gluten ataxia.

[New submission]

I have lived with Dystonia and Ataxia all my life. I have other debilitating issues as well, but these 2 are the rare ones that cause havoc in my daily life. There is no cure, just a few things to try to get

relief. Botox was designed for Dystonia but it's too expensive for us patients and our Dr's to have. Hollywood people enjoy the medicine because they have reduced their wrinkles but us who need it for relief can't afford it.

I hope this helps people understand that these rare diseases are not easily diagnosed or treated. Thank you for your time.

[New submission]

My time has passed, so has my children's, but my grandchildren and great grandkids have an opportunity of beating this awful disease. I urge each and every one to help our future generations to eradicate rare genetic conditions. Your unborn child or grandchild or great grandkids could suffer from a rare disease. Wouldn't it behoove you to help in so many ways to help them.

[New submission]

I have had Spinocerebellar Ataxia for 4 years. It's been a great struggle living with and doing daily activities. I've been going from doctor to doctor and because this is, we're not a lot of people who are educated and have ways to help me out. All I can do is exercise and physical therapy. I just hope there will be a cure approved soon for all of us that have this.

[New submission]

I got disabled with this rare disease called Ataxia. I am using a study medication called TRORILUZOLE, that is helping me a lot. Please get this FDA approved.

[New submission]

My son was diagnosed with a rare disease, Langerhans cell histiocytosis, when he was 4 years old. There is no known cause or cure. His treatment was considered experimental because it was considered an orphan disease and had very little funding for research. It is vital that rare diseases get funding at a similar ratio as more well-known diseases, as the victims should be considered no less important and need hope. Thank you.

[New submission]

Being in the sixth generation of a family which has been plagued by this horribly debilitating disease, whose mom (2014) & brother (2017) passed away. As well as grandparents, great grandparents, many aunts, uncles and cousins over the decades.

I think the FDA has to be open to new drugs for not only SCA3, but all the related ataxias.

I currently have been taking Troriluzole for at least 6 months, under an expanded access protocol EAP.

I was part of the original trial for this drug back in 2020.

While it is not a cure, I certainly have had a slow progression of the disease.

Please reconsider the drug use and trials for all of us.

[New submission]

My son has DMD. It is a devastating disease we live everyday. Every day is a day we deal with fear. Fear that he will fall and break his hip, fear that he won't be able to live past his 20's and a fear that limits your capacity to live a life with hope. Currently, he is in a clinical trial that is helping him. My son wouldn't be able to walk at 19 if he wasn't on the drug. Please consider all outcomes from real people that are dealing with this devastating disease. If a drug helps just one person then it's a success. I urge you to really listen to the DMD community with compassion and love. Thank you for taking the time to read this.

[New submission]

My 10-year-old son has Batten Disease CLN3. There is no FDA-approved treatment or cure. There have been drugs that showed promise but were never able to make it through the requirements to become approved. My son's disease causes waste to build up on the cellular level, and that waste causes cell death. That cell death causes a progressive loss of skills, blindness, cognitive decline, seizures, until all abilities are lost and the cellular death causes early death in the late teens to early 20s. Every day that passes without a treatment or cure is another day closer to losing my son.

[New submission]

Ataluren

It is literally needed to save my nephew's life!

I am a physician, educator, and have seen what can happen when people fail to get needed meds first hand.

Let's move forward to help people, not hurt them by denying.

[New submission]

I am 41 years old. I have 2 healthy children, and I've been diagnosed with muscular dystrophy. I've been to many MDA clinics to usually hear the same thing, that there is no cure, and you don't qualify for any treatments. But the only problem I have with that is that I'm 41 years old and I would like to see my children graduate. It's horrible for the children to see their parents died from this miserable disease. Just because the doctor won't give you Compassionate Use. Or Right to Try.

We already have CRISPR-Cas9 for 41 years. I've been chasing a cure with my parents since I was a child. I have been to many MDA association clinics I've been to... flying back and forth, wasting a lot of money and getting harder every time.

[New submission]

I was a kindergarten teacher. Teaching was what I was meant to do.

I had serious sinus infections, fatigue, and pain in my hands and feet. I went to the doctor that did a CT scan that revealed a mass in my left lung. This hospital discharged me with an appointment to see a Rheumatologist in six months. I went home, but a week later was much worse. My family drove me to a university medical center. It was during the covid pandemic so I was alone in the hospital. No family allowed. Doctors did a kidney and lung biopsy to diagnose me with Granulomatosis with Polyangiitis. My fingers changed colors due to the lack of blood flow. The nurses could not get readings on the oximeters. They would use every finger. In June 2021, my index finger on my left hand and my pinkie finger on my right hand were amputated.

First, doctors gave me Viagra to increase my blood flow so I would not lose more fingers. Insurance would not cover this since I was a female. It cost my mom \$800 for a 15 day supply. I started with 60 MG Prednisone which caused me to have mobility problems. It also caused me to gain 60 pounds. This was tapered to end before my finger amputations. Cytoxan infusions were every month for six months to kill my white blood cells. In my disease, the white blood cells attack normal organs by stopping blood flow. I have stage three kidney disease because blood was stopped to my kidneys. After my amputations, Rituxan infusions were scheduled every six months. My insurance does cover some of the cost of these infusions. I would be dead if it did not.

The infusions are \$27,000 every six months. Rituxan was too expensive. My cost after insurance paid was \$800. I asked my doctor to switch me to Ruxience which has a total cost of \$20,000. My cost is about \$400. These infusions are every six months for the rest of my life. There is no cure for my disease.

I did enter remission in 2021 during my Cytoxan infusions. If I do not get these infusions, I would flare causing my disease to become active again. Blood flow will stop going where it is suppose to go in my body. Who knows what part of the body I would lose if I did not have my infusions? I may have to be put on dialysis in the future. Many people with my disease have to get nose surgeries due to build up in their nose. I hope to stay in remission to prevent that from happening. I have my nose cleaned out by my ENT once a year. It cost \$800 for that procedure.

I take medications for high blood pressure, reflux, and depression. Since my purpose in life has been taken away due to this disease, my mental health does need help. I have found a new purpose in advocating for myself and others with my disease. In the future, I hope there will be other treatments for this disease. I hope for a cure.

Avery Roberts – March 5th, 2026

Written Testimony

March 5, 2026

The Honorable Rick Scott & The Honorable Kirsten Gillibrand
U.S. Senate Special Committee on Aging 628 Hart Senate Office Building Washington, DC 20510

Re: From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation Hearing – Statement for the Record – Cure CMD
Chairman Scott, Ranking Member Gillibrand, and Members of the Senate Special Committee on Aging:

On behalf of Cure CMD, I thank you for the opportunity to submit a statement for the record. Congenital muscular dystrophy (CMD) is a group of ultra-rare neuromuscular diseases, with no approved treatments or cures at this time. Each subtype affects only a small number of individuals, but collectively, CMD profoundly impacts the lives of children and families worldwide.

Cure CMD appreciates the opportunity to submit this statement on behalf of the congenital muscular dystrophy (CMD) community. Each subtype of CMD is ultra-rare, and currently, there are no approved treatments or cures. Families and patients rely on innovation, expert guidance, and access to clinical trials to pursue hope for therapies.

Cure CMD has funded more than \$4 million in research across 70 projects, assembling some of the brightest scientific minds from around the world to identify treatments and optimize care for CMD. We provide educational resources and support to families navigating this journey, ensuring they have every opportunity for a successful future. Most importantly, the voice of the affected community is at the heart of everything we do.

We are grateful to Congress for creating tools that enable the FDA to act with flexibility and speed for rare disease therapies. These include the accelerated approval pathway and advisory committees, which provide essential input from external experts and patients. However, in 2025, advisory committee meetings declined, while the FDA issued at least 23 Complete Response Letters (CRLs) explaining why rare disease therapies were delayed or denied. Advisory committees are essential—they bring external expertise, promote transparency, and give patients a voice in shaping the science that directly impacts their lives and clinical trial endpoints. For ultra-rare conditions, where trials are small and data are complex, this dialogue is critical to ensuring fair and informed regulatory decisions.

We are also concerned that the Rare Disease Innovation Hub, established by Congress to encourage cross-center collaboration at the FDA, currently has only one full-time staff member. Without adequate resources, the Hub cannot fully achieve its potential to streamline processes, share expertise across centers, and consistently engage the rare disease community.

Cure CMD encourages continued Congressional oversight to ensure that all regulatory tools are used effectively and consistently, that advisory committees remain a central component of FDA decision-making, and that the Innovation Hub receives the support it needs. By leveraging existing tools, maintaining transparency, and amplifying patient voices, we can accelerate the development of life-saving therapies for families affected by ultra-rare conditions like CMD.

For questions regarding the above viewpoints
Sincerely,

Avery Roberts
Community Engagement Coordinator Cure CMD

Jessica Haywood – March 5th, 2026

**Written Testimony
Statement for the Record**

Submitted for the U.S. Senate Special Committee on Aging Hearing

"From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation" February 26, 2026

For families with children who have [Sanfilippo syndrome](#), a terminal type of childhood dementia, time is not measured in years or presidential cycles. It is measured in lost words, hospital visits, seizures, and skills slipping away. Birthdays are bittersweet because we know there will be far too few of them.

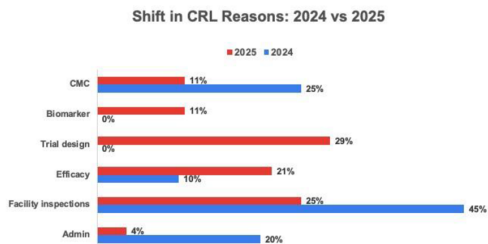
My niece, [Sadie, is almost 10 years old and is full of life despite her struggles with](#) Sanfilippo syndrome. Sadie was diagnosed early, at only 3 months old. Around the same time, the first child was dosed with a gene therapy called UX111. We have been watching this drug's development for Sadie's entire life. We have longed for it to reach approval so she could receive it.

Unfortunately, the application has been delayed twice due to manufacturing documentation, not safety or efficacy concerns. For diseases with a life expectancy of 15 years, accelerated approval and regulatory flexibility must be used. Why is paperwork more important than a 10-year-old's ability to walk?

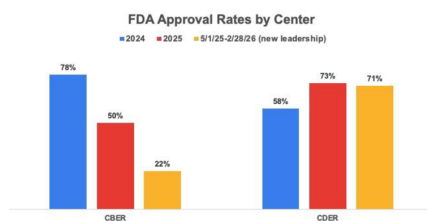
We've spoken to parents of children who have been treated with UX111 at varying ages. Their kids are running when they should be wheelchair bound. They're eating by mouth when otherwise they should have a feeding tube. After seeing such promise, the FDA's rejection last summer was devastating. And we weren't alone, as many rare degenerative disease patients have watched the FDA reject their drugs in recent months.

I've watched Sadie go from spelling her name at age 2, knowing hundreds of words, and speaking in full sentences, to now, maybe only saying one word a day. She's also falling and choking more. I don't want to see any other children or families suffer while waiting on lifechanging treatments to be approved.

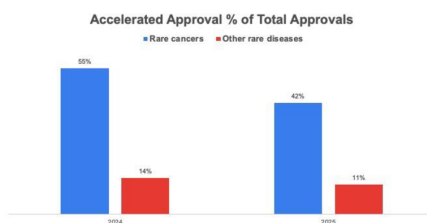
My background is in data analytics, so I have been tracking FDA decisions to better understand what's happening.



In 2024, most CRLs (90%) were due to facility, manufacturing, and administrative issues. In 2025, this shifted to disagreements over the science, with trial design, efficacy, and biomarkers accounting for 64% of rejections, which indicates that the regulatory bar has been raised.



The rare disease delays are primarily in the CBER division, as shown in the chart above. In 2024, 78% of applications received approval. Under new leadership, this has reversed, with 78% of decisions resulting in a CRL. CDER approvals have remained consistent since new leadership took over.



Additionally, while 42 percent of approvals for rare cancers received accelerated approval, only 11 percent of approvals for non-oncology rare diseases did. CBER only approved three new rare disease drugs in 2025, down 75 percent from two years earlier.

The rare disease community's requests to the FDA are simple:

- Maintain commitments to using [disease-causing biomarkers](#) for accelerated approvals.
- Apply flexibility across manufacturing, trial design, and labeling.
- Include the patient voice in all aspects of drug development.

Since UX111 was rejected in July, Sadie has experienced an agonizing increase in agitation and a decrease in cognitive, motor, and verbal skills. We miss her singing and dancing. If this drug is approved quickly for kids of all ages, we have a chance at stabilizing Sadie's disease progression, which is a huge win in any neurodegenerative disease.

We implore you to use Congressional oversight to urgently investigate this situation and hold the FDA accountable. Our kids don't have time to wait.

Jessica Haywood

Peter Mantas – March 5th, 2026

Written Testimony

Subject: Formal Statement for the Record: Urgent Need for Accelerated Approval of AMT-130 for Huntington's Disease

Dear Chairman Scott, Ranking Member Gillibrand, and Members of the Committee:

I am writing to submit this formal statement for the record following the February 26, 2026, hearing regarding the FDA's treatment of rare disease therapies. I urge this Committee to hold the FDA and HHS accountable for their recent reversal on the regulatory pathway for uniQure's AMT-130, a potentially life-saving gene therapy for Huntington's Disease (HD).

I am a lawyer, investor, and founder of Back of the Napkin Bios, a life sciences investment publication. I have met with Huntington's disease patients, advocates and researchers and have conducted extensive primary research into the AMT-130 regulatory pathway.

The FDA's demand for a new, prospective, sham-controlled trial is ethically indefensible and scientifically redundant for the following reasons:

1. **Established Biomarker Precedent (Tofersen):** The FDA set a clear precedent by granting accelerated approval to Tofersen for SOD1-ALS based specifically on a reduction in Neurofilament Light (NfL), determining that NfL reduction was "reasonably likely" to predict clinical benefit. There is no scientific basis for accepting NfL as a valid surrogate endpoint in ALS while dismissing it in Huntington's disease.
2. **Astounding Biomarker Results:** AMT-130 has achieved NfL reductions that defy the natural history of this slow-burning disease. Treated patients saw a mean reduction in CSF NfL of -9% at 24 months and remained -8.2% below baseline at 36 months. In contrast, NfL typically increases by 26% over 24 months in untreated patients. This creates a cumulative spread of nearly 40 percentage points between treated and untreated patients — consecutive negative NfL readings in a treated population against a comparator that is actively rising. In a disease defined by progressive neuronal death, back-to-back negative NfL results against a rising untreated comparator is not a marginal signal. It is the molecular signature of a working therapy. The FDA accepted exactly this logic when granting accelerated approval to Tofersen for ALS. Applying a different standard to AMT-130 in Huntington's disease is scientifically inconsistent and demands explanation.
3. **Slowing the TFC 9–13 "Clock":** The patient population eligible for this therapy — Total Functional Capacity 9–13 — is at a critical juncture where every month of delay leads to the irreversible loss of daily functions like working and living independently. This window closes permanently as patients progress. High-dose treatment led to a statistically significant 60%

slowing of decline in TFC at 36 months compared to matched external controls. According to analysis by Professor Edward Wild of University College London, one of the world's leading HD researchers, treated patients would take 11.7 years to reach the same level of decline that untreated patients reached in just 3 years. A sham surgery trial requiring 5 to 6 years to complete will generate data on patients who have already progressed beyond the eligible treatment window. The trial the FDA is demanding cannot produce timely data on the population the drug is intended to treat.

4. Clinical Efficacy (cUHDS): This therapy met its primary endpoint with a statistically significant 75% slowing of disease progression at 36 months as measured by the composite Unified Huntington's Disease Rating Scale. Treating physicians with direct patient experience have personally informed the FDA that every patient they treated in the trial is progressing slower than age and CAG repeat length matched peers — the most precise genetic predictor of HD progression available. This is not statistical modeling but a direct clinical observation communicated to the agency by treating physicians.

5. The Ethical Crisis of Sham Surgery: Forcing a sham control for a neurosurgical gene therapy is a violation of basic medical ethics. A sham procedure in this context involves drilling burr holes into the skulls of dying patients under general anesthesia with zero hope of benefit. Subjecting HD patients to risks including brain hemorrhage and infection for a fake surgery — when the data is already clear — violates the spirit of the Nuremberg Code's core principle of avoiding unnecessary suffering. The European Medicines Agency has indicated that sham craniotomy is unethical and will not require it. Neurosurgeons will not perform it at scale. IRBs will not approve it without extraordinary difficulty. The trial the FDA demands is not merely burdensome. It is operationally impossible to conduct ethically.

6. Official UK Government Endorsement: Published Today: On March 5, 2026 — the same day anonymous FDA officials told Bloomberg that AMT-130 is a failed product and stone cold negative — the UK Government Office for Science published an official case study on GOV.UK titled "Slowing Huntington's disease: how science advice enabled a breakthrough treatment." The document explicitly describes AMT-130 as producing long-awaited hope for patients, validates the natural history comparison methodology as robust, and highlights the UK's NIHR research infrastructure that supported the external control cohort which is the exact methodology the FDA rejected. This is not a patient advocacy statement; it is an official publication of the British government. The contrast between the UK government calling this a breakthrough and anonymous FDA officials calling it a failed product on the same day demands congressional scrutiny. If the MHRA approves AMT-130 — as current signals strongly suggest — American patients with the same fatal genetic mutation will watch British patients receive treatment while they are told to wait for a sham brain surgery trial that will take six years and has never been ethically conducted at scale.

7. A Broken Regulatory Process: uniQure CEO Matt Kapusta has stated publicly and on the record that in November 2024 the FDA specifically told the company that data from their single-arm study compared to an external control may serve as the primary basis of a submission. The company built its entire BLA strategy around that meeting. The FDA has since stated no documented agreement can be found. A company that received directional guidance from a federal regulator, acted in good faith on that guidance, and was then told the guidance never

existed has been denied basic procedural fairness. Senior FDA officials have since briefed multiple journalists anonymously with scientific arguments that were never formally communicated to uniQure across five regulatory meetings over 15 months. A company learning the FDA's actual scientific objections through media briefings rather than formal regulatory communications is not a functioning regulatory process. This Committee should demand a full accounting of what was communicated in the November 2024 meeting and why it was never formally documented.

World-renowned experts including Professor Sarah Tabrizi of University College London (based in the United Kingdom where the government has now officially endorsed this therapy) have called the AMT-130 data the most convincing evidence in the field to date. Professor Edward Wild, whose research helped build the natural history infrastructure the FDA rejected, has published detailed analysis demonstrating the clinical meaningfulness of these results. The European Medicines Agency reached out to uniQure unsolicited after reviewing the three-year data. Anonymous FDA officials briefing journalists with arguments never formally communicated to the company is not a regulatory process. It is a public relations campaign to defend an indefensible decision.

Thousands of Americans living with Huntington's disease have no approved disease-modifying treatment. Every month of delay represents irreversible progression in a uniformly fatal disease. The FDA has a working therapy in front of it, supported by robust biomarker data with a 40-percentage point spread against natural history, validated by the world's leading HD researchers, endorsed by the British government, and confirmed by treating physicians in direct communication with the agency.

Finally, this Committee should address not only the substance of this decision but the manner in which it has been conducted. Senior FDA officials have chosen to wage a public relations campaign against a drug under active review through anonymous media briefings to Bloomberg, STAT, and Endpoints News making scientific claims that were never formally communicated to the company across five regulatory meetings over 15 months. One official told Bloomberg the drug is a 'failed product' and 'stone cold negative' on the same day the UK Government Office for Science called it a breakthrough. Another told a patient advocate that the FDA is 'protecting' HD patients from something that 'can only hurt them', a statement so disconnected from the clinical reality of four-year patient outcomes that it demands accountability. This is not the conduct of a rigorous scientific agency but is the conduct of an institution that has made a decision it cannot defend through proper channels and is attempting to win a political argument through journalists rather than through science. The HD community, the clinical researchers who built this field, and the American public deserve better from their federal regulators.

I ask the Committee to compel Commissioner Makary and Director Prasad to:

- Honor the clinical and biomarker evidence generated to date.
- Honor the November 2024 regulatory agreement regarding external controls.
- Grant AMT-130 the accelerated approval it has earned to prevent further loss of life.

Respectfully submitted,

Peter Mantas

David Mulhearn – March 5th, 2026

Written Testimony

Hello,

Like others, I am emailing about the FDA's puzzling decision-making regarding Uniqure's AMT-130 gene therapy. I am requesting that the Senate Aging Committee write a letter to the FDA requesting a public advisory committee meeting regarding Uniqure's AMT-130 gene therapy.

The FDA has backtracked on former agreements and turned a blind eye to promising clinical trial data for a therapy that could change the lives of Huntington's Disease patients throughout the United States.

I hope you will seriously consider my request.

Sincerely,

David Mulhearn

Monica Charles – March 6th, 2026

Written Testimony

Written Statement for the Record

U.S. Senate Special Committee on Aging
Hearing on Rare Diseases and Access to Treatments

Every year that a treatment for Spinocerebellar Ataxia is delayed means another year that patients like me lose abilities we may never regain.

My name is Monica Charles, and I am a resident of Brooklyn, New York. I am a mother of two children, ages 16 and 12, and I am living with Spinocerebellar Ataxia Type 3 (SCA3), a progressive and currently incurable rare neurological disease. I was diagnosed about five years ago.

SCA3 affects coordination, balance, and motor function. Over time, the disease gradually takes away abilities that most people take for granted—walking steadily, using our hands with precision, speaking clearly, and maintaining independence. One of the hardest realities of living with SCA is that there are currently no FDA-approved disease-modifying treatments. As the disease progresses, skills that are lost cannot be recovered.

For patients with SCA, delays in treatment development and approval have real and irreversible consequences. Each year that passes without access to therapies can mean further physical decline. These delays create emotional distress, anxiety, and uncertainty for patients and families who are watching time move forward while their abilities slowly decline. For rare disease patients, time lost to progression is something we cannot regain.

I have personally experienced both the challenges of this disease and the hope that research can bring. Discovering Dr. Kuo and his team at Columbia University has made a tremendous difference in my life. Through Columbia's clinical study, I have been able to take troriluzole, an experimental medication that has been investigated as a potential treatment for Spinocerebellar Ataxia. Since participating in the study, I have experienced improvements in my motor function and believe it has helped slow the progression of my disease. Access to this research opportunity has given me hope and allowed me to maintain more independence in my daily life.

So far, SCA has already taken things I love from me. I can no longer ride a bike or roller skate—two activities that once brought me joy and freedom. I do not want to keep adding to that list.

I have two children who are 16 and 12 years old. Like any parent, my greatest wish is simply to be present in their lives—to watch them grow, graduate, and build their futures. Access to treatments that slow disease progression could mean the difference between remaining active in my children's lives or losing that ability too soon.

I respectfully urge policymakers and regulators to recognize the urgency faced by rare disease patients, including those living with Spinocerebellar Ataxia. Greater regulatory flexibility and timely review of promising therapies—such as accepting the New Drug Application for troriluzole for a full review—could make a meaningful difference for patients who do not have time to wait.

For the SCA community, waiting is not a neutral pause. It carries a real cost measured in lost mobility, lost independence, and lost time with our families.

Thank you for the opportunity to share my experience and for considering the voices of patients as you shape policies that affect the future of rare disease treatments.

Monica Charles

February 24, 2026

The Honorable Rick Scott
Chairman
Special Committee on Aging
U.S. Senate
Washington D.C. 20515

The Honorable Kirsten Gillibrand
Ranking Member
Special Committee on Aging
U.S. Senate
Washington D.C. 20515

Chair Scott, Ranking Member Gillibrand, and Members of the Committee:

We, the undersigned organizations, representing millions of taxpayers and consumers across the country, urge you to safeguard the vital role medications play in the American healthcare ecosystem. Recent hearings and statements from the committee have expressed deep concern over internationally sourced active pharmaceutical ingredients (APIs). However, there are ways this committee can support domestic production of APIs without sweeping mandates or burdensome regulations on the drugs—which result in fewer cures coming to market and high costs for taxpayers and consumers.

According to a 2022 report sponsored by the Department of Health and Human Services (HHS), there are significant regulatory barriers preventing the efficient production of APIs domestically. That report showed—with permitting issues and inspections by the Food and Drug Administration (FDA)—setting up a new plant in the U.S. takes 5-7 years, while adding another line to that plant would take an additional 3-5 years.¹ Congress in tandem with the agency can take steps to foster expedited permitting to incentivize domestic production.

Further, FDA approval of medications takes entirely too long, leaving needed savings on the table. An in-depth analysis by the oncology news and information platform OncoDaily concludes, “Developing a new drug typically takes an average of 10 to 15 years, depending on various factors such as the type of drug and regulatory processes.”² These unnecessarily-long wait times and high development and regulatory costs result in patients not getting the care they need and taxpayers footing the bill for sprawling bureaucracy.

Manufacturers have tried to keep these costs under control by looking for more efficient, affordable alternatives overseas. However, mandatory discounts for the 340B Drug Pricing program exacerbate existing problems with drug affordability and availability. Many of the groups on this letter have also raised alarms about broader waste, fraud, and abuse within the 340B program.

¹ https://www.armiusa.org/wp-content/uploads/2022/07/ARMI_Essential-Medicines_Supply-Chain-Report_508.pdf.

² https://oncodaily.com/drugs/ema-vs-fda-drug-development?utm_.

Drug manufacturers should be able to source their APIs from abroad while being able to pass those savings along to consumers without poorly targeted government policies getting in the way. Other countries are able to produce high-quality APIs at scale in a way that would simply not make economic sense in the U.S. Rather than shrink from global markets, lawmakers should reduce regulatory barriers here at home and support efforts by manufacturers to strengthen the nation's drug supply. Restrictions, at this stage, would mean fewer therapies available to patients at a higher price.

With many Americans rightfully frustrated about the high cost of medications, this committee has an opportunity to promote commonsense reforms that increase the supply of critical medications. Reducing red tape would be a significant win for taxpayers and patients.

Sincerely,

David Williams
President
Taxpayers Protection Alliance

Justin Leventhal
Senior Policy Analyst
American Consumer Institute

Ryan Ellis
President
Center for a Free Economy

Jeremy Nighohossian
Senior Fellow/Economist
Competitive Enterprise Institute

Pete Sepp
President
National Taxpayers Union