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"From Regulator to Roadblock: How FDA Bureaucracy Stifles Innovation"
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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 troriluzole 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 troriluzole 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 troriluzole, 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 troriluzole 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 troriluzole 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 troriluzole 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 troriluzole 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 troriluzole 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 troriluzole 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 troriluzole 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 troriluzole, 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 troriluzole 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

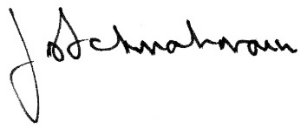
to whether they were being taken off treatment and then seeing if they worsen to further prove the effect of the drug. My colleagues and I find either approach to be unethical. It violates the principle of beneficence in human studies research, to act with charity, mercy, and kindness to promote the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



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