Margaret Plews-Ogan, MD
Brodie Professor of Medicine
University of Virginia
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Chairman Casey, Ranking Member Braun, members of the committee,

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

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

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

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

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

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

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

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

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

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

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