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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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