Brian Wallach & Sandra Abrevaya
Co-Founders, I AM ALS
Hearing Testimony
House Energy & Commerce Subcommittee on Health
July 29, 2021

Chairman Pallone, Chairwoman Eshoo and Ranking Members McMorris Rodgers and Guthrie, thank you for the opportunity to testify before you today. My name is Brian Wallach. I am 40 years old and have been fighting ALS for 4 years. I am Sandra Abrevaya. I am a caregiver and Brian's wife. We have two young daughters - who just turned 6 and 4 this month.

We are all here today to talk about how to advance treatments and cures for neurodegenerative diseases. The aspirational goal of cures is what we all aim for. But the more pressing question today is how do we keep patients suffering from these fatal illnesses alive long enough so that they can be here for when the cures are found. The answer for ALS is both within your power and shockingly simple: make FDA uphold its 2019 promises to the ALS community to act urgently and with regulatory flexibility in approving therapies. Starting right now with two therapies, AMX0035 and NurOwn.

ALS is a 100% fatal neurodegenerative disease that affects every race, gender, age, political persuasion and congressional district, whose stories we have submitted for the record along with this testimony. As it progresses, ALS robs people of most of what makes us human - the ability to talk, walk, eat and eventually breathe.

For the first time since it was discovered 160 years ago, we actually have the chance to turn ALS from terminal to chronic. In the last 10 years, researchers have discovered hundreds of new ALS-linked genes, pathways and biomarkers. These discoveries have transformed the ALS therapy pipeline. Biotechs and pharmaceutical companies have now launched nearly 100 ALS

therapy programs. And these programs are producing therapies that are actually slowing or stopping ALS in people right now.

So what is blocking the advancement of treatments and cures for ALS patients living today? FDA's refusal to approve and provide access to safe and effective therapies.

In 2019, FDA promised ALS patients urgency and regulatory flexibility. Instead, it has blocked any type of approval for two therapies for rapidly dying ALS patients while leaning in to approve therapies for slower progressing diseases. This must change immediately.

In September 2019, FDA released an updated guidance for ALS clinical trials entitled "Amyotrophic Lateral Sclerosis: Developing Drugs for Treatment Guidance for Industry." It took the FDA six years to develop that Guidance during which we lost 35,000 to 42,000 Americans to ALS.

When the Guidance was finally released, the ALS community was filled with hope as it stressed the need for "regulatory flexibility in applying the statutory standards to drugs for serious diseases with unmet medical needs." Moreover, it explicitly stated that "[w]hen making regulatory decisions about drugs to treat ALS, FDA will consider patient tolerance for risk and the serious and life-threatening nature of the condition in the context of statutory requirements for safety and efficacy."

The first two tests of CDER's and CBER's - two divisions of the FDA - promise of flexibility and urgency for ALS came in the form of AMX0035, an oral medication, and NurOwn, a stem cell therapy. FDA failed both tests.

The first ALS therapy, AMX0035, is a combination of two drugs, one approved by FDA for other diseases and one you can buy on Amazon. The Phase II/III trial and subsequent open label extension for AMX0035 showed that this combination is very safe. The trial also met its

primary endpoint - showing that AMX0035 slowed the progression of ALS. In fact, compared to placebo, patients taking AMX0035 lived on average 6.5 months longer. These “patients” have names, families and lives: like Olin Thompson, a father of 3 sons, whose progression slowed due to AMX0035, allowing him to be at his oldest son’s high graduation this year. Others will similarly tell you they are alive or able to speak, eat or move their fingers today because they had access to AMX0035. Approving this therapy should be a “no brainer,” which is exactly why AMX0035 appears headed toward approvals in Canada and Europe based on the same data presented to CDER over a year ago, begging the question of why didn’t FDA approve this a year ago?

The second, NurOwn, involves the extraction, enrichment and injection of a patient’s own stem cells. The Phase III trial for NurOwn did not meet its overall primary endpoint. Going into the trial the drug company identified a score of 35 on the ALSFRS, the clinical assessment of a patient’s disease progression, as the mean expected score of patients when they first enrolled. In the end, more patients with lower ALSFRS scores enrolled in the trial than was expected. Thus, the actual mean ALSFRS was below 35. Of the patients who started the trial with a score of more than 35, they not only had a significantly higher response rate than those on placebo, but also their ALSFRS was two points higher than those on the placebo at the end of the trial. Given these results, why didn't the FDA approve NurOwn for at least those patients with ALSFRS scores above 35 and at the same time require the company to complete a confirmatory trial on the larger group? That is an approach that gives people living with ALS today a chance while giving FDA more data. With a disease as complex and heterogeneous as ALS we need this type of flexibility and urgency from the FDA.

Outside the trial, several patients have been able to access NurOwn through Right To Try and a small expanded access program. Of these patients, a number have seen NurOwn halt their progression or improve function. For example, Matt Belina, a US Navy veteran, was able to stand up from his wheelchair and saw his breathing ability improve. Eric Stevens, a former NFL player, was progressing rapidly until receiving NurOwn and has now stabilized. Sandy Morris, a mother of 3, regained the use of her hands and the ability to eat solid foods like pizza. And Phil Green, a father of 4, saw his progression stop both during the trial and when he was on the therapy during the expanded access program. Indeed, just a few days ago, Phil posted a video of him buckling his seatbelt, a function he had lost until receiving NurOwn. These are real people. These are real ALS patients. Showing real benefits from this therapy.

Despite the promises in the guidance, FDA denied any type of approval for AMX0035 and NurOwn. It exercised no regulatory flexibility, gave no consideration to the fatal nature of ALS, the utter lack of approved effective therapies for ALS or the hundreds of thousands who signed petitions to the FDA pleading for access to both.

Instead, CDER and CBER asked each drug company to run another large, long placebo-controlled trial. In addition, CBER took the highly unusual step of putting out a press release announcing the full denial of NurOwn, but did not mention anything about the significant slowing of progression in the over 35 ALSFRS pre-specified subgroup of patients.

The decisions by FDA through CDER and CBER, if allowed to stand, mean that at best AMX0035 and NurOwn won't be approved for 4 years. By then, nearly every ALS patient in the US alive today - 30,000 Americans - will have died without access to either. So desperate ALS patients in the US are forced to try to replicate the formula for AMX0035 on their own and to travel abroad for risky stem cell procedures.

I've been told that the FDA has claimed to members of Congress and their staff that it is doing everything it can and that there was nothing else it could do with respect to these two therapies. This is simply not true or, if FDA actually believes this, it has provided Congress a clarion call to reform how the FDA regulates treatments for rapidly progressing fatal diseases like ALS. This is why bipartisan bills like the Promising Pathways Act, that would allow for conditional approval of promising therapies after Phase II for life-threatening diseases like ALS, have been introduced.

We are both former federal government employees. We truly believe the FDA is filled with honorable, dedicated public servants. However, its actions here do not square with its own Guidance. Like HIV and cancer advocates before us, we have tried every way imaginable to explain this to the FDA. To explain that we are dying and that access to these therapies could help save our lives. That we understand ALS is extremely heterogeneous, which means it's possible that a given therapy may not work for all of us. That knowing this, we want the chance to try it if it is safe and effective for some, as without it ALS will for sure kill us. That six or 12 more months from AMX0035 or NurOwn means we get to see another birthday, graduation or wedding. That while we ultimately seek cures, right now we are just trying to find a way to slow progression so we are alive when cures are found.

Nothing has worked. So we are here asking you to hold the FDA accountable for failing to live up to its own guidance. The science and the therapies are ready to make ALS a treatable disease. All that we need is the FDA to make good on its promises in the 2019 guidance.

We also believe an approach that takes the FDA best practices and applies them aggressively to neurodegenerative diseases is essential. So, we ask that you hold a separate hearing on the Accelerating Access to Critical Therapies for ALS (ACT for ALS) bill. ACT uses

an existing, successful pathway that FDA utilizes in other diseases by leveraging public private partnerships for small biotech companies to fund expanded access to ALS investigational therapies for patients who do not qualify for clinical trials and so they have no other options for access. As it has in Oncology, expanded access will give FDA and drug sponsors critical data on patients excluded from clinical trials for whom we have little to no research and which will be tremendously impactful in developing new therapies. This legislation also will accelerate ALS and neurodegenerative disease therapy development through, and increase research on and development of interventions for rare neurodegenerative diseases through a new Food and Drug Administration (FDA) research grants program.

We want to leave you with this thought: ALS is currently called a "rare disease" but it is not rare. ALS and Multiple Sclerosis are diagnosed at the same rate in the United States: 1 out of every 300 Americans. The difference between ALS and MS is that people diagnosed with MS often live decades. ALS, on the other hand, kills quickly, with the average patient living 2-5 years post diagnosis. Throughout the history of ALS most people were diagnosed, disappeared with their families, and went home to die. In fact, four out of five - 80% - of the patients diagnosed with me in 2017 are dead. This generation of patients and our families demand better from ourselves, the medical community and policymakers. You have the power to help make ALS like MS, to change ALS from a "rare disease" to a disease that more than 1 million Americans are living with. Moreover, ALS is linked to Alzheimer's, Parkinson's and Frontotemporal Dementia, among others. Meaning if we cure ALS, we can help unlock cures for all. That is a future worth fighting for.