Neil Thakur, Ph.D.
Chief Mission Officer, The ALS Association
Written Testimony
United States House of Representatives
Energy and Commerce Subcommittee on Health
The Path Forward: Advancing Treatments and Cures for Neurodegenerative Diseases
July 29, 2021

On behalf of the more than 20,000 Americans living with amyotrophic lateral sclerosis (ALS) and their loved ones whom we serve each year, The ALS Association appreciates the opportunity to share our views on ALS therapy development and research. By leading the way in global research, providing assistance for people with ALS through a nationwide network of chapters, coordinating multidisciplinary care through certified clinical care centers, and fostering government partnerships, The ALS Association builds hope and enhances quality of life. We seek to make ALS a livable disease for all by finding new treatments and cures, reducing the impact of ALS, and preventing it and optimizing care for people living with ALS.

ALS is a progressive neurodegenerative disease that affects nerve cells in the brain and the spinal cord. About 90 percent of ALS cases occur without family history. The remaining 10 percent of ALS cases are inherited through gene mutations. Research indicates ALS is up to twice as prevalent in people who have served in the U.S. military.

As ALS progresses, people lose the ability to move, eat, and breathe on their own. Most people who develop ALS are between the ages of 40 and 70, but ALS can strike anyone. Because it is a complex disease, it takes on average twelve months to receive a final diagnosis. Most people with the disease die within 2-5 years of diagnosis of respiratory failure. ALS impacts the whole family as spouses, children, siblings, and friends seek to provide the critical support needed. Approval and access to new treatments is an urgent priority for the ALS community because there is no alternative. Given the choice between

death and a modest hope to prevent loss of function, people with ALS are willing to accept higher risks for less certain benefit. (For more information, see the We Can't Wait Action Meeting.)

ALS Therapy Development: Challenges and Opportunities

There are many challenges to ALS therapy development and research, but these challenges are also the biggest opportunities for progress. Accelerating development, approval, and access to effective new ALS treatments requires more funding to increase the number of clinical trials, but also innovative trial design. ALS clinical trials must be designed to be efficient, impactful, and respectful. Most importantly, FDA must use its regulatory authority to be fast and effective and speed ALS trials and drug approvals.

The ALS Association's Principles for Urgent, Patient-Centered ALS Clinical Trials provide specific approaches and recommendations for clinical trial sponsors and regulatory bodies worldwide to achieve these goals. For example, experimental treatments need testing to determine their effectiveness and safety using the fewest possible participants, shortest length of follow-up, and least burden on participants. ALS clinical trials should also be designed to provide as much information and certainty as possible. Lastly, clinical trial sponsors and regulators should honor the wishes and perspectives of people with ALS and their caregivers.

Making approval decisions about promising treatments is never easy, especially when it comes to fatal diseases. The agency is right to be judicious and consider all perspectives. But when a new treatment has been shown to be effective and safe, the FDA has an obligation to act.

There are promising ALS treatments in the pipeline. Among them include AMX0035, in which the Phase 2 clinical trial met its primary endpoint — slowed decline of function -- and extended life. The strong safety data for this drug make it clear that the risks of pursuing an approach like accelerated approval are low. The trial sponsor is moving forward in both Canada and the European Union to secure

expedited approval for AMX0035. Although approval is not guaranteed, Canadians and Europeans living with ALS could get this drug long before Americans. (For more information, see this editorial by ALS Association President and CEO Calaneet Balas.)

Approving a new drug for ALS can have a bigger impact than just providing people with a single new treatment. New approvals can spur innovation and investment by industry in a disease space with few available treatments. In cases of fatal neurological diseases without cures, when a promising drug comes along that has the potential to retain function and extend life, patients' needs are paramount. The FDA must use its regulatory flexibility, as it has for other drugs, for promising treatments for ALS.

Congress Must Act

While it is incumbent on FDA to use its authority to expedite treatments for ALS, Congress is also critical to ensuring the federal research and regulatory enterprise is focused on getting effective treatments to people with ALS as soon as possible. We urge Congress to take the following actions:

- Pass the *Accelerating Access to Critical Therapies (ACT) for ALS Act* (H.R. 3537/S. 1813). The bill builds new pathways to fund early access to ALS investigational therapies, accelerates ALS and rare neurodegenerative disease therapeutic development and increases research on, and development of, interventions for rare neurodegenerative diseases through a new FDA research grants program.
- Pass legislation to create a new FDA conditional approval pathway modeled on the successful experience of the European Union with its conditional marketing authority.
- Strengthen the proposed *Advanced Research Projects Agency for Health (ARPA-H*) initiative so that it is impactful, does not create additional bureaucracy, and is provided distinct funding that

supplements rather than supplants current dollars for NIH, DOD or other federal research efforts that are critical to advancing basic science and new treatments.

- Consider creating a *Center of Excellence for Neuroscience* at FDA that is explicitly charged with the mission of accelerating development, approval, and access to effective new treatments. At the same time, it must not create additional bureaucracy that focuses on processes over impact.

Investments Urgently Needed in ALS Research

Making ALS a livable disease also requires increased investments in ALS research. This means more ALS scientists, more ALS clinical trials, and more ALS research that can lead to effective treatments and prevent new cases of ALS. This year, The ALS Association announced its aggressive fiscal year 2022 appropriations priorities, and we urge Congress to provide the following funding for ALS research:

- $130 million for ALS research at NIH to attract the next generation of neuroscientists, accelerate discovery and development of new treatments and increase the number of ALS clinical trials;
- $60 million for the DOD ALS Research Program to fund clinical trials to pull through promising preclinical research and human studies into ALS drug development;
- $50 million for ALS research at the Orphan Products Grants Program at FDA to expedite product development, foster innovative trial designs, and enable natural history studies to better understand disease progression and pathology;
- $10 million for the CDC National ALS Registry to help researchers identify candidates for clinical trials, identify risk factors for ALS, and collect biological samples that will aid the search for treatments and a cure;

- $1 million to commission a National Academies of Science, Engineering and Medicine study to develop a plan and policy recommendations for what can be done by the government and all stakeholders to make ALS livable.

Together, these investments would increase the number of ALS clinical trials to find treatments and cures as well as identify risk factors. These investments must also be integrated with increased collaboration across agencies so that discoveries are translated into application. The National Academies study would provide a blueprint to achieve these goals.

Conclusion

We appreciate your consideration of our recommendations for accelerating development, approval, and access to effective new treatments for ALS. By passing the ACT for ALS Act (H.R. 3537), creating a new FDA pathway to conditionally approve therapies for diseases with unmet needs, and increasing funding for ALS research, we can make ALS a livable disease by 2030 and ultimately end it. We stand ready to work with Congress to achieve these goals.