VIA ELECTRONIC SUBMISSION

March 16, 2022

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: FDA-2018-N-0410 for "Peripheral and Central Nervous System Drugs Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments."

Dear Sir or Madam,

The ALS Association is pleased to provide comments in response to the meeting of the Peripheral and Central Nervous System Drugs Advisory Committee for new drug application (NDA) 216660, for sodium phenylbutyrate/taurursodiol (AMX0035) powder for oral suspension, submitted by Amylyx Pharmaceuticals, Inc., for the treatment of amyotrophic lateral sclerosis (ALS). This is a critical step in bringing new treatments and hope to people living with ALS today.

ALS is a progressive neurodegenerative disease that affects nerve cells in the brain and the spinal cord. Ultimately, people with ALS become prisoners within their own bodies, unable to eat, breathe, or move on their own. Their mind, however, often remains sharp so they are aware of what's happening to them. There is no cure for ALS, and most people with the disease die within 2-5 years of diagnosis. For unknown reasons, veterans are twice as likely to develop ALS as the general population. Until we can cure ALS, our goal is to make ALS a livable disease for all.

In the more than 100 years since the creation of the Food and Drug Administration (FDA), only a few treatments have been approved for ALS and there still is tremendous unmet need. The ALS Association is strongly in favor of all therapies that are safe and reasonably likely to provide any clinical benefit to be approved as quickly as possible by the FDA. As the Peripheral and Central Nervous System Drugs Advisory Committee and FDA evaluate AMX0035, we would emphasize that AMX0035 met its primary endpoint in clinical trials— slowed decline of function — and also extended life.

People with ALS have stated their willingness to accept significant risk both of safety and uncertainty of benefit over and over again.[1,2,3] The risk-benefit calculation should be influenced heavily by the progressive, often rapid, and invariably fatal

[1] https://www.als.org/advocacy/we-cant-wait
[2] Docket ID: FDA-2017-D-6503, See sections on Benefit Risk and Addendum C
[3] https://www.als.org/sites/default/files/2020-07/The-FDA-Report_09132018_FINAL.pdf

course of the disease. In the case of AMX0035, the formulation contains two already-approved compounds with established safety profiles, and the trials conducted to-date have shown the treatment to be both safe and effective at slowing down disease progression.

Additionally, a follow-up open label extension study showed a statistically significant and clinically meaningful 6.5 month increase in survivability compared to the control group. Both of these benefits were observed in a sample already receiving standard of care, which includes two other ALS drugs, riluzole and edaravone.

People with ALS do not have time to spare and the potential for additional months of life would have a profound impact. In the words of people with ALS[1]:

> *"I need to slow or stop my progression NOW to give me more time as we await a definitive cure and give me time to make more memories with my family. What you might think of as a modest benefit, may be of critical importance to me in maintaining my quality of life."*
>
> *"Given the chance, we are very strong people and just want a little more time."*
>
> *"I am anxious to have a chance to try any therapy that shows even a modest benefit such as slowing of disease progression or additional survival time, even if it showed such benefit in just a subset of patients."*
>
> *"I am willing to risk any side effect in order to have more days."*

While we recognize FDA typically relies on two adequate and well-controlled trials, we implore the Agency to exercise the flexibility described in the FDA's 2019 guidance on Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products. This guidance specifically allows for the approval of therapies with just one adequate and well-controlled trial in the case of severely debilitating and deadly rare diseases with substantial unmet medical need. Given the important findings and the enormous unmet medical need for people with ALS, we believe the AMX0035 studies conducted to date are sufficient to support approval.[4]

In other words, there is no ethical or scientific justification to delay access to AMX0035 for people living with ALS. AMX0035 complements, and does not duplicate, all other ALS treatments available. It offers unique benefit to people living with ALS today and more than 50,000 people have signed a petition calling for FDA to approve AMX0035. Every year of delay in approval will result in thousands of life-years lost.

We urge the Advisory Committee to take into consideration the effects of this severely debilitating and deadly rare disease, along with the willingness of people living with ALS to accept risks of uncertainty, and to make a favorable

[4] FDA should lead the way on new ALS treatments - STAT (statnews.com)

recommendation given the strong clinical benefits of AMX0035. The FDA, in turn, should move swiftly to approve this therapy to treat ALS. Our community cannot wait.

Sincerely,

Calaneet Balas
CEO and President
The ALS Association

ALS ASSOCIATION