

## VIA ELECTRONIC SUBMISSION

August 23, 2022

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

**Re: FDA-2022-N-1436 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 second meeting of the Peripheral and Central Nervous System Drugs (PCNS) 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).

We strongly support the convening of a second Advisory Committee meeting on this potential therapy considering additional data evidence supporting the effectiveness of AMX0035 and urge the Advisory Committee to consider this information again carefully in responding to any questions posed by the Food and Drug Administration (FDA). As this letter describes, The ALS Association has consulted extensively with our community and independent experts to conclude:

- a. the safety and efficacy evidence are sufficient within the context of this disease for the FDA to use its regulatory authority to approve AMX0035 for marketing at this time; and
- b. people living with ALS and their health care providers should have full access as soon as possible to this promising treatment.

Therefore, we urge the FDA to ask the Advisory Committee the following question: “Do we know sufficient evidence about the safety and effectiveness of AMX0035 to make it a treatment option for people living with ALS today?”

ALS is a progressive neurodegenerative disease that affects nerve cells in the brain and the spinal cord. 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 is 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.



OUR VISION: Create a world without ALS.

OUR MISSION: To discover treatments and a cure for ALS, and to serve, advocate for, and empower people affected by ALS to live their lives to the fullest.

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## **AMX0035 is Safe and Effective**

AMX0035 [met its primary endpoint](#) in clinical trials, slowed decline of function, and [extended life](#). Since the first Advisory Committee meeting, newly published analyses of long-term data show a potential [survival benefit](#) of more than 10 months and that AMX0035 [reduced complications](#) associated with ALS, such as hospitalizations and tracheostomy, by half.

People with ALS have consistently emphasized their willingness to accept significant risk both of safety and uncertainty of benefit (see 1, 2, 3) associated with therapies under development. The risk-benefit calculation for regulatory approval should be influenced heavily by the progressive, often rapid, and invariably fatal 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.

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.”*

## **The FDA has the Flexibility to Approve AMX0035**

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. AMX0035 recently received approval in Canada, making it the first new treatment for ALS since 2017. People living with ALS in the US *CAN’T WAIT* two to three years for results from the ongoing phase 3 clinical trial of AMX0035 to provide certainty. Canadian health experts have already concluded that AMX0035 is safe and effective for people with ALS, and the FDA should move swiftly to join them in approving it.



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## **Safety and Equity Considerations Require Approval**

We also have significant concerns over safety and equity issues around off label access to AMX0035. Anecdotal reports of doctors prescribing the pre-cursor ingredients for AMX0035 is leading to shortages of these drugs and extremely high out of pocket costs for patients. People with ALS are purchasing ingredients from unregulated sources (such as Amazon) and compounding it themselves, raising significant safety concerns. Now that AMX0035 is approved in Canada, we expect the situation to get far worse, where only those with financial means will be able to access the treatment through “medical tourism”.

There is no ethical or scientific justification to delay approval and access to AMX0035 for people living with ALS; especially if the committee answers the underlying question of whether we know enough about the safety and effectiveness of AMX0035 to make it a treatment option for people living with ALS today. AMX0035 complements, and does not duplicate, all other ALS treatments available. It offers unique benefits to people living with ALS today. Prominent ALS clinicians have signed a [letter](#) and called on the FDA to approve AMX0035 so that they can work with their patients to determine if AMX0035 is right for them and ethically prescribed for treatment. Every year of delay in approval will result in thousands of life-years lost to ALS.

We urge the Advisory Committee to take into consideration the effects of this severely debilitating and deadly rare disease and the willingness of people living with ALS and clinicians who care for them to accept the risks of uncertainty and make a favorable recommendation for AMX0035 given the potential clinical benefits and underlying safety. The FDA, in turn, should move swiftly to approve this therapy to treat ALS. Our community cannot wait.

Sincerely,



**Calaneet Balas**

President & CEO



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