August 23, 2022

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

Re: FDA-2022-N-1436: Peripheral and Central Nervous System Drugs Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments

Dear Members of the Peripheral and Central Nervous System Drugs Advisory Committee,

In service of the neuromuscular disease patient community, including individuals with amyotrophic lateral sclerosis (ALS), the Muscular Dystrophy Association (MDA) thanks you for the opportunity to submit comments on the September 7th, 2022 proceedings of the Peripheral and Central Nervous System Drugs Advisory Committee (the "Committee") as it discusses sodium phenylbutyrate/taurursodiol (AMX0035) powder for oral suspension intended for use by those with ALS.

MDA is the nation's leading nonprofit organization dedicated to transforming the lives of individuals living with neuromuscular diseases through innovations in science and innovations in care. Since inception, MDA has invested more than $1 billion in research grants to accelerate treatments and cures for neuromuscular disorders, making MDA the largest source of neuromuscular disease research funding in the U.S. outside of the federal government. We serve all individuals with neuromuscular diseases, including ALS, in a variety of ways including advocating for the accelerated development of more and better therapies for the neuromuscular disease patient population.

MDA does not participate in product-specific advocacy, and thus will not make a specific recommendation on this drug. With several therapies approved by the Food and Drug Administration (FDA or "Agency") each year for neuromuscular diseases, plus hundreds more in the therapeutic pipeline, MDA simply cannot evaluate the incredibly complex justifications for any specific regulatory action, including approval, for each of these therapies to make comprehensive endorsements on regulatory action.

Instead, MDA channels the neuromuscular disease community's desire for more and better therapies into recommendations for systemic cross-therapeutic approaches the Agency should employ when regulating the development and potential approval of neuromuscular disease therapies. The following outlines flexible regulatory approach we expect the FDA and this Advisory Committee to utilize when considering this and all rare neuromuscular disease therapies.

First, we are grateful that the FDA is flexibly evaluating this therapy by considering additional methods of analyses not already considered or discussed by this Committee. We are similarly grateful for the Agency's continued emphasis on considering the uniquely cruel experience of living with ALS with few available treatment options as it considers this and other new therapies.

We believe the Agency can exercise this recognized need for flexibility in the following ways. First, we encourage FDA and the Advisory Committee to consider all the ways of demonstrating substantial evidence of effectiveness, including through the use of one adequate and well controlled clinical investigation plus confirmatory evidence. As outlined in its December 2019 guidance, FDA states that the Agency, "will consider a number of factors when determining whether reliance on a single adequate and well-controlled clinical investigation plus confirmatory evidence is appropriate, including the seriousness of the disease, particularly where there is an unmet medical need; the size of the patient population; and whether it is ethical and practicable to conduct more than one adequate and well-controlled clinical investigation."

Second, we remind the FDA and the Advisory Committee of flexibilities outlined in the ALS Developing Drugs for Treatment Guidance, including that the "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", and, "FDA has long stressed the appropriateness of exercising regulatory flexibility in applying the statutory standards to drugs for serious diseases with unmet medical needs, while preserving appropriate assurance of safety and effectiveness."

Finally, the FDA has a well-established record of approving treatments for serious and life-threatening rare diseases without the standard level of proof of effectiveness required in more common or less serious diseases. Analyses have shown that at least two-thirds of rare disease drug approvals are done so by the Agency flexibly considering whether the effectiveness evidence is adequate. These flexibilities have been reiterated by the Food and Drug Administration Safety and Innovation Act (FDASIA), the Food and Drug Administration Reauthorization Act (FDARA), and consistently supported by patients, their loved ones, the organizations that serve them, their clinicians, and their elected officials.

Developing treatments for rare neuromuscular diseases presents unique challenges that must be addressed with the aforementioned flexibilities. Once again, we are asking the FDA reviewers and this Advisory Committee to remember these flexible approaches already put forward by the Agency when evaluating this and all new potential treatments for ALS and rare neuromuscular diseases.

We are grateful for the opportunity to comment on the Committee's September 7th, 2022 proceedings. For questions regarding MDA or the above comments, please contact me at 202-253-2980 or pmelmeyer@mdausa.org.

Sincerely,

Paul Melmeyer, MPP
Vice President, Public Policy and Advocacy
Muscular Dystrophy Association