Paul Melmeyer's testimony at the FDA Peripheral and Central Nervous System Drugs Advisory Committee (PCNS) Meeting:

March 22nd, 2023 – "Thank you for the opportunity to speak to you today. I am Paul Melmeyer, Vice President of Public Policy and Advocacy at the Muscular Dystrophy Association, and 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. I have no financial relationships to mention.

The Muscular Dystrophy Association does not participate in product specific advocacy, and thus will not make a specific recommendation on this drug. Instead, I will outline the flexible regulatory approach we expect the FDA and this Advisory Committee to utilize when considering this and all rare neuromuscular disease therapies.

We are grateful the FDA has emphasized exercising appropriate regulatory flexibility, including in the published briefing document and in Dr. Burrachio's opening statement, and we encourage this Committee to remember the following three key points when evaluating this and all other neuromuscular therapies.

First, we urge the FDA to flexibly and consistently use the accelerated approval pathway for approving rare neuromuscular disease treatments when proving clinical effectiveness in heterogeneous, often slowly progressing, neuromuscular diseases is not possible. We understand some have called for more infrequent use of the accelerated approval pathway, but to do so may essentially halt all possibility of safe and effective treatments reaching some neuromuscular diseases, an absolutely unacceptable result. We urge the Agency to continue to flexibly apply the accelerated approval pathway in rare neuromuscular diseases while utilizing the authorizations pertaining to post-market confirmatory trials enacted by Congress last year.

Second, we are grateful for FDA's reiteration of the various ways substantial evidence of effectiveness can be demonstrated within its briefing document, stating "our regulations allow for regulatory flexibility to expedite the development, evaluation, and marketing of new therapies intended to treat persons with life-threatening and severely debilitating illnesses, especially where no satisfactory alternative therapy exists". The briefing document further quotes its 2019 guidance, stating "a second trial may be infeasible in certain rare disease settings where the limited patient populations preclude the conduct of a second trial. In these cases, the substantial evidence of effectiveness would typically be provided by a single trial plus confirmatory evidence". FDA has demonstrated several recent examples of using confirmatory evidence to support approval of neuromuscular disease treatments, and we encourage the Agency to continue to do so.

Finally, 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."

Thank you for the opportunity to testify today."