Paul Melmeyer's Rare Disease Framework Testimony at the October 28th Public Meeting:

"Thank you for the opportunity to speak to you today. I am Paul Melmeyer, with the Muscular Dystrophy Association, and we serve the neuromuscular disease community in a variety of ways including advocating for the accelerated development of more and better therapies.

Neuromuscular diseases are complex, heterogeneously and irreversibly progressive, are sometimes severe and other times slowly progressive over many years, and most are considered ultra-rare. Each of these features makes developing new treatments for neuromuscular diseases incredibly challenging, and evaluating safety and effectiveness all the more difficult. This is why a new paradigm, a rare disease framework, could be critically important for our community.

I will briefly touch on several topics for the framework to consider and we will expound further in written comments. Neuromuscular diseases progress unevenly and sometimes slowly making traditional clinical trials unlikely to capture a prospective therapy's true effectiveness. The Framework should invest in paradigm-shifting clinical, statistical, and regulatory approaches to evaluating effectiveness in slowly and/or heterogeneously progressive rare diseases

The use of biomarker surrogate endpoints are critical for these same reasons but few are truly validated or FDA-qualified. This framework should include FDA investments to generate, validate, and qualify surrogate endpoints in progressive rare diseases with a re-evaluation of the often un-obtainably high bar for FDA's qualification program. FDA cannot simply be an arbiter – it must be a partner, and ideally a leader.

The framework should invest in "fit-for-disease" approaches that could feature tailored regulatory pathways, evidentiary requirements, clinical trial structures, statistical approaches, and more that fit the disease in question rather than the disease needing to fit arbitrary and unrealistically strict standards. This includes more robust and progressive use of patient-generated data to inform benefit/risk evaluations tailored to the disease.

This framework should include a dramatic expansion of the use of platform technologies, particularly in ultra-rare and n-of-few diseases and allow for multiple NDA/BLA approvals across genetic subtypes of a rare disease without recreating the wheel each time. Flexibilities on non-clinical, clinical, and CMC requirements for n-of-few diseases developed by non-profit and academic developers must be considered to unlock development pathways in n-of-few treatments.

We urge the FDA to move forward as quickly as possible. We'll say it once more – time is muscle. Thank you again for the opportunity to comment on this very exciting initiative."