Parent Project Muscular Dystrophy

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Submitted to the Cellular, Tissue, and Gene Therapies Advisory Committee
May 5, 2023

RE: NEW PATIENT & CAREGIVER GENE THERAPY PREFERENCE STUDY SUMMARY FOR SRP-9001 ADVISORY COMMITTEE

Thank you for the opportunity to provide written comments to the Advisory Committee. We are grateful for being able to share the voice of the Duchenne patient community with the agency during such pivotal moments.

Parent Project Muscular Dystrophy's mission is to end Duchenne. We accelerate research, raise our voices to impact policy, demand optimal care for every single family, and strive to ensure access to approved therapies. We pursue those goals through the development of data-driven evidence – our guiding principle. This intent guides how we select the research which our community-raised funds support, how we help our clinicians shape standards of care for all people with Duchenne, and importantly, how we amplify the singular patient voice to a clarion call to action for those they love.

At PPMD, we believe it is crucial the patient voice is captured and reflected in regulatory decisions. While the voices of individual members of our community provide necessary context of the lived experience of Duchenne, informing regulators on the values of this community, we recognize that anecdotal evidence is not sufficient, on its own, for representing such a diverse community. We are an organization strongly driven by science and believe the FDA must continue to make their decisions supported by the data they have available to them, including patient preference data.

Understanding Duchenne Patients' and Caregivers' Attitudes Towards Gene Therapy

To that end, PPMD partnered with Duchenne UK, a UK-based patient advocacy group, and social scientists at RTI International to conduct a scientific, rigorous study capturing the Duchenne community's views on risk tolerance to gene therapy. This work is a follow-up to a previously conducted study by PPMD and RTI in 2018 to ascertain similar information about gene therapy risk tolerance.[1] While we published the results of that study in 2021, the risk tolerance data collected at that time was prior to the first systemic delivery of a gene therapy product in a Duchenne population. We recognize that as new information emerges and a population is exposed to real world outcomes in clinical trials — whether perceived benefits or witnessed adverse events — the perceptions of a community may shift. In 2023, after five years of exposure to a multitude of gene therapy clinical trials from various sponsors, we invited the patient community to participate in this new survey to capture their current risk tolerance in this area of research.

Preference Study Construct

The primary aim of this study is to assess the maximum acceptable mortality risk (MAMR) that caregivers (parents and guardians) of individuals with Duchenne would accept for gene therapy to treat Duchenne. Respondents were asked to consider being offered an approved gene therapy

[1] (Peay HL, Fischer R, Mange B, Paquin RS, Smith EC, Sadosky A, Russo L, Ricotti V, Rensch C, Morris C, Martin AS, Ganot A, Beaverson K, Mansfield C. Patients' and caregivers' maximum acceptable risk of death for non-curative gene therapy to treat Duchenne muscular dystrophy. Mol Genet Genomic Med. 2021 May;9(5):e1664. doi: 10.1002/mgg3.1664. Epub 2021 Mar 23. PMID: 33755338; PMCID: PMC8172191.)

product that would slow progression (non-curative), that may only be able to be used once in a person's life, and with an uncertain duration of benefit which was estimated at about 10 years for the purposes of the study. We used a threshold technique (TT) to assess the maximum acceptable risk of gene therapy-caused death for a non-curative treatment of limited duration given at four time points: (1) when their child was a newborn; (2) "right now;" (3) when their child is in the last year of walking well; and (4) when their child is in last year of being able to raise hands to mouth. We used interval regression to estimate the mean MAMR for each scenario.

Results

In a soon-to-be submitted manuscript, **we report high tolerance for risk of death for a gene therapy that would slow disease progression across all four time points**. United States respondents (n=136) were willing to accept a mean MAMR of 2.6% (95% CI 1.8-3.4) when the child was a newborn; 3.4% (95% CI 2.5-4.3) for their child "right now"; 4.5% (95% CI 3.5-5.6) in the last year of walking well; and 5.2% (95% CI 4.0-6.3) in the last year that the child could raise hands to mouth (Figure 1). These results show that **parents are willing to accept high risk of gene-therapy associated mortality for a time-limited slowing of disease progression**. Of particular relevance, caregivers are, on average, **willing to accept a risk of death of more than 4 in 100 in their child's last year of walking well**.

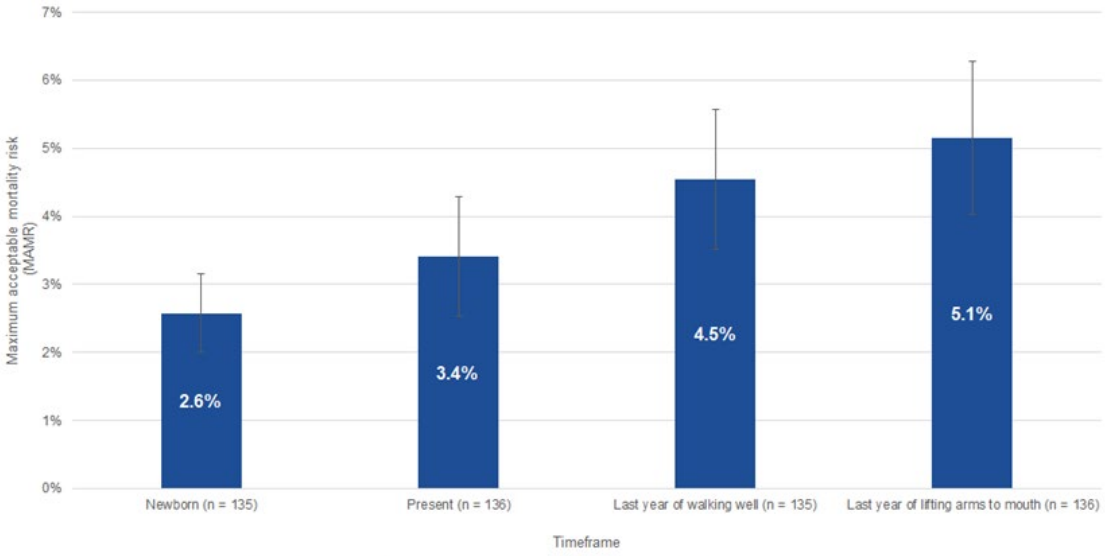

Figure 1 – Maximum acceptable risk of mortality among U.S. caregivers at various timeframes

These findings are very similar to the MAMRs generated in our previous study published in 2021, which also revealed a high risk tolerance in the Duchenne community for gene therapies. **We trust that this quantifiable data will be used by agency officials in the evaluation of SRP-9001 as they consider what is an appropriate risk-benefit ratio given the high risk tolerance of the families who would decide whether or not a gene therapy is appropriate for their families.**

Moving Forward

The realities of Duchenne are inescapable; patients face a relentlessly progressive loss of function, they lose ambulation, they decline in pulmonary and cardiac function, and, sadly, most lose their lives by the third or fourth decade. Families fully understand what lies ahead and while they are grateful for the time they do have with their child, that doesn't detract from their desire

and preference for therapies to prolong their functional abilities and independence. Parents and caregivers want more time for their child to keep up with their peers on the playground, more time before they must rely solely on the use of a wheelchair, more time before they need to consider nighttime ventilation, and more time with their child to be present in their family's lives.

While a cure is the great hope that we all strive for, therapies aimed at slowing disease progression, thus giving patients and their families more moments together, are profoundly meaningful.

The voice of the patient matters and should resonate with all stakeholders. It is the patients, parents, caregivers, and family members who have to face Duchenne daily. When it comes to accepting risks from a therapy in return for a potential benefit, it is the patient and family that ultimately must make the treatment choices; not the company who developed it, the clinician who prescribed it, or the regulator who approved it.

Caregiver and patient preferences must be taken into consideration and weighed when regulators decide whether to approve new therapies, as the final decision to accept risk in exchange for benefit will inevitably fall to the patients and caregivers of Duchenne. It is paramount that the agency officials acknowledge that this community is willing to accept significant risk in exchange for the slowing of disease progression as they evaluate potential therapies for Duchenne.

Disclosure Statement: PPMD was an early funder of Dr. Jerry Mendell's research at Nationwide Children's Hospital leading to SRP-9001. We have recovered some of that investment from Sarepta Therapeutics and will receive an additional payment from the company if SRP-9001 is approved. We also have received milestone-based payments from Nationwide Children's Hospital based on its licensing of the therapy; and expect additional payments if the therapy is approved. Any returns will be reinvested in programs supporting PPMD's mission. PPMD has a comprehensive approach to identify opportunities to accelerate development of all therapies in Duchenne, including regulatory, research, and patient-recruitment counsel to help expedite the progress of SRP-9001.

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