

**Parent Project Muscular Dystrophy**

JOIN THE FIGHT.  
END DUCHENNE.

VIA ELECTRONIC DELIVERY

December 15, 2022

Division of Dockets Management (HFA-305)  
Food and Drug Administration  
Docket No: FDA-2022-N-2394 5630  
Fishers Lane Room 1061 Rockville, MD 20852

To Whom It May Concern,

On behalf of the Duchenne patient community, Parent Project Muscular Dystrophy (PPMD) is pleased to submit written comments following our participations in the November 15<sup>th</sup> FDA CBER OTAT *Patient-Focused Drug Development Listening Meeting: Patient Perspectives on Gene Therapy Products*.

PPMD's mission is to end Duchenne. Duchenne muscular dystrophy is the most common muscular dystrophy in children. It is a relentlessly progressive disease that causes muscles to become weaker over time until it affects the whole body, ultimately leading to premature death by the third decade of life. About one out of every 5,000 live male births are diagnosed with Duchenne. Parent Project Muscular Dystrophy (PPMD) estimates that there are about 15,000 people living with Duchenne today in the United States.

There are currently five FDA approved treatments for Duchenne, all aimed at slowing disease progression. Much of this progress can be directly linked to research investments from the National Institutes of Health which led to private investment, quality care guidelines from the Centers for Disease Control and Prevention, and regulatory innovation from the Food & Drug Administration under the Patient-Focused Drug Development paradigm

The Duchenne pipeline of potential therapies in development continues to grow, including several gene therapy studies currently underway. With that in mind, the following comments are recommendations to advance patient focused drug development for cell and gene therapies in Duchenne.

**i. The Evolution of Patient Focused Drug Development (PFDD) and Patient Experience Data**

Starting with passage of PDUFA V, and through passage of PDUFA VI and VII, PFDD has truly evolved ensuring patients and caregivers are provided greater opportunity for their views to be considered and integrated into the drug development and review process. The passage of 21<sup>st</sup> Century Cures codified patient focused drug development further, including the creation of the Statement of Patient Experience Table, providing transparency between the review division and the public regarding whether patient experience data (PED) was included in the data package at the time of regulatory review. CDER has issued a series of guidance documents that have been extremely informative to patient groups and companies for providing direction on the collection of patient experience data through the drug development continuum.

**More clarity is needed regarding how CBER will incorporate patient views into regulatory decision-making. We are hopeful that efforts made to generate community-based patient experience data (data related to unmet needs, benefit/risk preferences, or PED that informs the analysis of a condition) currently being considered by CDER will also be considered by those at CBER. Furthermore, we ask that CBER indicate clearly how any PED is weighed at the time of regulatory review.**

**It is also important that patient focused drug development is taken through into the access environment. We urge CBER to consider the incorporation of appropriate PED into product labeling. This will better inform both payers and prescribers regarding how patient experience data were considered in (and informed) product approvals.**

#### **ii. Duchenne Community-Led Guidance**

The Duchenne community has spent over a decade advancing patient focused drug development through direct engagement with regulators, including submitting the first-ever patient advocacy initiated draft guidance on Duchenne in 2014. The Duchenne community recently reconvened over one hundred stakeholders to update the 2014 guidance, submitting the [finalized document](#) to FDA in September 2022. The update included new sections on cardiac and gene therapy.

**We ask that CBER review the newly updated community-led guidance document including specific community imperatives related to gene therapies. We are hopeful CBER will consider producing draft guidance related to developing gene therapies in Duchenne so that sponsors and the patient community can better understand FDA's current thinking on conducting gene and cell therapy trials in Duchenne, including the use of expedited pathways. We would also invite collective advice from CDER and CBER as to how PED will be considered in matters such as consideration for accelerated approval status (such as with qualifying intermediate clinical outcome measures), as well as labeling implications.**

#### **iii. Duchenne Patient Experience Data Related to Patient Preferences**

The Duchenne community has led efforts to advance patient preference research in rare disease using a variety of stated preference and other survey methods through a community engaged approach.

Over the course of 8 years, preference data elicited directly from patients and caregivers have generally demonstrated a considerable tolerance for risk and uncertainty in exchange for a therapy that could stop or slow disease progression.<sup>1</sup> Additional studies have explored parental worries<sup>2</sup>, symptom prioritization for treatments<sup>3</sup>, meaningful benefit in pulmonary outcomes<sup>4</sup>, caregiver vs. patient preferences<sup>5</sup>, clinical trial decision-making and preferences for emerging gene therapies.<sup>5,6,7</sup>

In terms of the learnings from these studies, results have consistently shown that Duchenne patients and caregivers have generally demonstrated a tolerance for even serious risks and uncertainty in exchange for a therapy that could stop or slow disease progression.

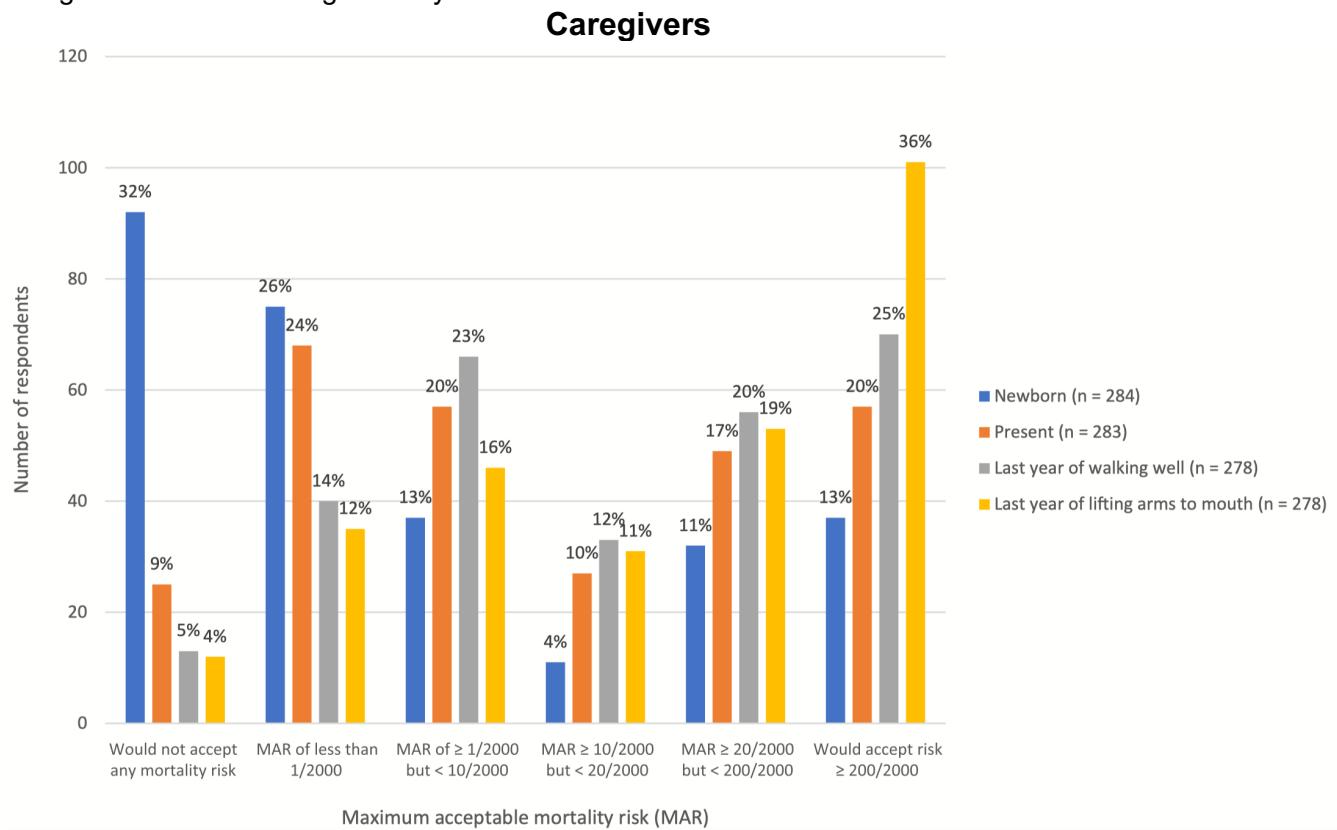
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As gene therapy clinical trials began to enroll patients, PPMD led a pre-competitive effort to measure treatment preferences of patients and caregivers as they relate to emerging gene therapies. The study included measuring maximum acceptable risk for death.<sup>7</sup>

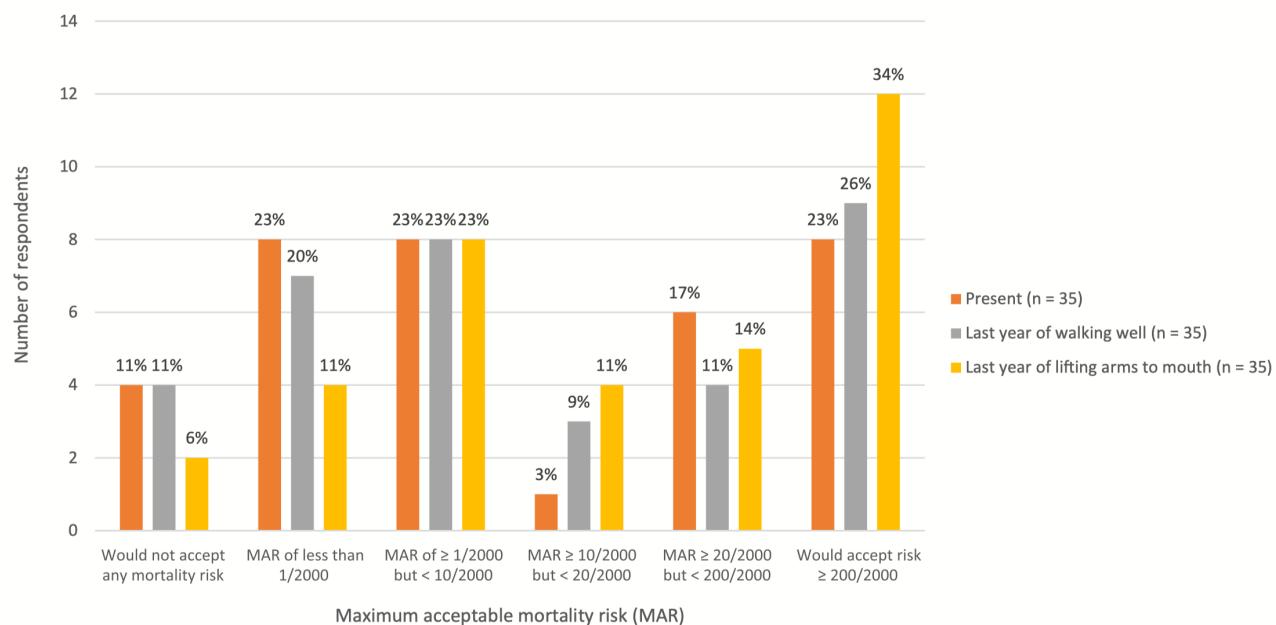
In the study we proposed a hypothetical gene therapy treatment benefit of up to 10 years of slowing disease progression. We then sought to quantify maximum acceptable risk (MAR) for death using a stated preference method called threshold technique. Participants were asked to imagine their doctor proposes gene therapy as a treatment option but that there is a risk of death following therapy administration. They are then presented with a series of risks starting with the lowest risk presented as 1/2000 and increasing up to 1/10 - risk of death. They are asked to choose if they would take gene therapy across different stages of disease, which also consider linkage to time points in disease progression. The risks get higher if they choose the therapy at any stage.

In this first quantitative study to assess MAR associated with first-generation Duchenne gene therapy, we found relatively high tolerance for mortality risk in response to a non-curative treatment scenario. Results also showed risk tolerance increased with disease progression. Patients and caregivers did not have significantly different MAR.



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**Adults with Duchenne**



The majority of caregivers and adults with Duchenne indicated the willingness to accept a treatment-related risk of death equal to or greater than 1 in 2,000, even given a non-curative treatment with time-limited benefit.

**These depictions should be informative for regulator decision considerations.**

**We urge FDA to incorporate robust patient experience data into gene therapy study designs and regulatory decision-making within the PFDD construct that is stimulating pipelines across conditions.**

**It is also our hope that regulators will incorporate such patient experience data into decision making including labeling of future gene therapy products, so that practitioners will consider individual and aggregate preference data in care decisions.**

PPMD believes in advancing the science of patient input and that to ensure we have the views and preferences of a greater number of patients and caregivers; we need to provide them with opportunities to engage. Rigorous preference research provides such opportunities and is a valid data driven process to obtain information on patient perspectives, after all, it is they who will ultimately have to make the treatment choices and bare any potential risks.

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In conclusion, the preceding advances in PFDD in terms of expedited development and approval of candidate therapies have the potential to have a life-altering positive impact on the lives of Duchenne patients, which can be further amplified through broader application of regulatory flexibility and creativity across all therapeutics under both CDER and CBER oversight. With proper collaboration of regulator and development communities, hope becomes reality.

PPMD would greatly appreciate the opportunity to build on our years of engagement with CBER. We believe that as gene and cell therapies advance there is more work we can do together.

Thank you for all you do on behalf of the patient community.

Sincerely,



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## References

1. Peay HL, Hollin I, Fischer R, Bridges JF. A community-engaged approach to quantifying caregiver preferences for the benefits and risks of emerging therapies for Duchenne muscular dystrophy. *Clin Ther*. May 2014;36(5):624-37. doi:10.1016/j.clinthera.2014.04.011
2. Peay HL, Hollin IL, Bridges JF. Prioritizing Parental Worry Associated with Duchenne Muscular Dystrophy Using Best-Worst Scaling. *J Genet Couns*. Apr 2016;25(2):305-13. doi:10.1007/s10897-015-9872-2
3. Hollin IL, Peay H, Fischer R, Janssen EM, Bridges JFP. Engaging patients and caregivers in prioritizing symptoms impacting quality of life for Duchenne and Becker muscular dystrophy. *Qual Life Res*. Sep 2018;27(9):2261-2273. doi:10.1007/s11136-018-1891-7
4. Hollin IL, Peay HL, Apkon SD, Bridges JFP. Patient-centered benefit-risk assessment in duchenne muscular dystrophy. *Muscle Nerve*. May 2017;55(5):626-634. doi:10.1002/mus.25411
5. Landrum Peay H, Fischer R, Tzeng JP, et al. Gene therapy as a potential therapeutic option for Duchenne muscular dystrophy: A qualitative preference study of patients and parents. *PLoS One*. 2019;14(5):e0213649. doi:10.1371/journal.pone.0213649



6. Paquin RS, Fischer R, Mansfield C, et al. Priorities when deciding on participation in early-phase gene therapy trials for Duchenne muscular dystrophy: a best-worst scaling experiment in caregivers and adult patients. *Orphanet J Rare Dis*. May 9 2019;14(1):102. doi:10.1186/s13023-019-1069-6
7. Peay HL, Fischer R, Mange B, et al. Patients' and caregivers' maximum acceptable risk of death for non-curative gene therapy to treat Duchenne muscular dystrophy. *Mol Genet Genomic Med*. May 2021;9(5):e1664. doi:10.1002/mgg3.1664