

Thank you for the invitation to speak today and for convening this important forum.

My name is Ryan Fischer and I serve as Chief Advocacy Officer for Parent Project MD or PPMD. The Duchenne landscape has changed dramatically and can be directly linked to research investments from the National Institutes of Health, 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. Today my comments will address unique tools and approaches related to how sponsors and the FDA can apply patient experience data in gene therapy studies.

I first want to highlight our community-led therapy development guidance. In 2014, PPMD led the creation of the first-ever patient group initiated Draft Guidance on Duchenne. Our goal was to provide a roadmap for companies developing therapies for our community. The completed draft guidance was submitted to FDA and posted to the docket; and FDA later released their own Guidance, which was finalized in 2018.

Since that time, much progress has been made, including 5 FDA approvals, and a growing therapeutic pipeline including several gene therapies, prompting our community to reconvene and update the Guidance document with new knowledge. The guidance includes 2 new sections - one on cardiac and the other on gene therapy. We formally submitted the update in September **and** are hopeful both CBER and CDER will utilize and disseminate the community-led document internally.

An example of impactful patient experience data I'd like to discuss is patient preference information. PPMD has been conducting preference studies since 2014. Our work is aimed at quantifying how patients and caregivers think and feel about emerging therapies and their priorities for new treatment targets. With such published data in hand, we can better advocate on behalf of the community.

Through testing various methodologies, we have demonstrated that preference research can be rigorously performed in our population and may be adapted for other rare disorders.

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

On the right you can see two examples using different methods from our studies. In both, participants chose tradeoffs based on treatment attributes included in the surveys, which provide quantifiable preference data on how patients and caregivers weigh the value of therapy options and which attributes of emerging therapy profiles are most meaningful and important for those making treatment decisions. Such depictions should be informative for regulator decision considerations.

We have continued to adapt and advance the use of different preference methods over time as PFDD guidance's emerge, and given today's topic, today I would like to highlight our work in gene therapy looking at Maximum acceptable risk that is tolerable to adults with Duchenne and caregivers for a non-curative, time-limited gene therapy

On the left side of this slide, you see the set up for this experiment. In the survey we proposed a hypothetical gene therapy treatment benefit of up to 10 years of slowing disease progression.

We then asked participants to imagine their doctor proposes gene therapy as a treatment option but there is a risk of death following therapy administration. They are then presented with a series of risks starting with the lowest risk of death presented as 1/2000 and increasing up to 200/2000 risk, 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 levels increase if they indicate they would be willing to accept the risk presented.

On the right you see the results, the darker the blue, the higher the tolerance for risk chosen. The results clearly highlight that risk tolerance increases with disease progression with the **highest tolerance in the last year of being able to feed themselves**. Though some heterogeneity is seen, the overall results demonstrate a clear willingness by most participants to accept some level of risk of death in exchange for the potential benefit.

It is our hope that regulators will incorporate such PFDD data into decision-making and **IMPORTANTLY** as well in labeling of future gene therapy products, so that practitioners will consider individual and aggregate preference data in care decisions.

We are currently working on a second study with our partner Duchenne UK to account for the current state of science in gene therapy because preferences change over time as new knowledge comes to light.

We urge FDA to incorporate robust patient experience data – such as the two examples presented – into gene therapy study designs and regulatory decision-making within the PFDD construct that is stimulating pipelines across conditions. Thank you.