Pathway Development Consortium

Duchenne Muscular Dystrophy (Duchenne) Roundtable Agenda

April 6, 2021

12:30 – 12:35 PM Welcome & Introductions by Rachel Sherman, MD, MPH

12:35 – 12:40 PM Peter Marks, MD, PhD, CBER, FDA, Opening Remarks

12:40 – 1:00 PM Ken Mills, REGENXBIO and Ilan Ganot, Solid Biosciences

"AAV Gene Therapy Development for Duchenne: Challenges and Opportunities"

1:00 – 1:10 PM Overview of Roundtable Agenda by Cole Werble (Moderator)

1:10 PM – 2:00 PM Benefit/Risk of AAV Gene Therapy and Risk Mitigations

10 minutes current landscape and gap analysis
40 minutes full discussion

Discussion questions:

1. How do perspectives about risks change when the clinical outcome changes? For example, survivorship versus prevention of disease progression. What are views on current safety/monitoring strategies implemented in clinical trials?
2. How does the known or expected length of the therapeutic benefit factor into the assessment of benefit/risk?
3. What matters most to patients when assessing benefit/risk in Duchenne?
    - Placebo control arm
    - Receiving a lower than optimally effective dose in clinical trial
    - Inability for repeat treatment
    - Washout periods of current therapies
    - Inability to participate in other clinical studies

2:00 – 2:15 PM Break

2:15 – 3:05 PM Perspectives and Priorities in Clinical Trial Design

10 minutes current landscape and gap analysis
40 minutes full discussion

Discussion questions:

1. What elements of a clinical trial make it more or less likely that patients/family will enroll? For example, randomization, placebo-control vs natural history control, number of patients in safety-focused phases (I/II).
2. What is the role of patient reported outcomes, surrogate endpoints, and more in gene therapy clinical trials?
3. Absent a survival benefit, what is the evidence threshold needed to support therapeutic benefit?
4. What is the role for standardized central lab testing to allow for patients to gain information about antibody titers for decision making?

3:05 – 3:55 PM Pathway Forward: Endpoints, Assessing Clinical Benefit and the Role of Quality of Life Metrics

10 minutes current landscape and gap analysis
40 minutes full discussion

Discussion questions:

1. What are the endpoints most meaningful to those living with Duchenne and those caring for someone with this condition? And what the metrics and methods to measure these endpoints? And how do they relate to clinically meaningful function?
2. Strengths and weaknesses of current primary functional outcome assessments (NSAA and 6MWT) and ways to expedite regulatory validation/use of more novel measures.
3. Define patient reported outcomes of great interest and discuss opportunities and challenges for incorporating them into clinical trial design.

3:55 – 4:20 PM Wrap Up and Next Steps, Cole Werble

4:20 – 4:30 PM Peter Marks, Closing Remarks