

Approval of Eteplirsen: ~~Patient Advocate~~ Perspective participant

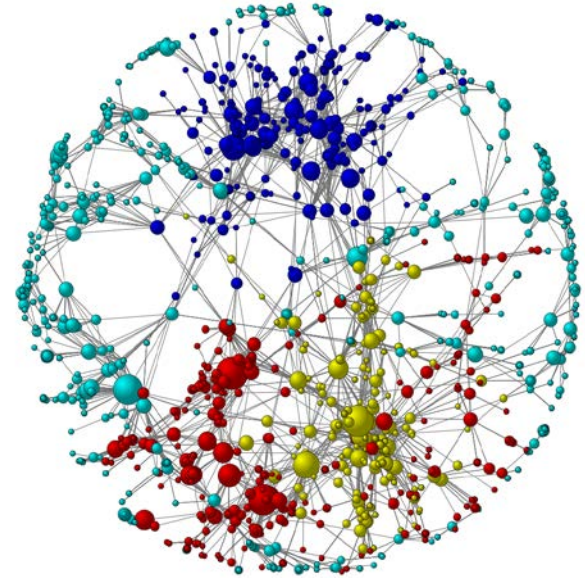


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Genetic Alliance engages individuals, families, and communities to transform health.

- In the beginning: a network of rare genetic (Mendelian) disease advocacy organizations
- 30 years later: network of 10,000+ stakeholders across advocacy, research, and care





Think of people as participants... not patients

Case Study: Duchenne Muscular Dystrophy and Eteplirsen

Duchenne Muscular Dystrophy

- Rare disease occurring as a result of mutations in the dystrophin gene
- Mutations lead to an absence of or defect in the protein, which is key to muscle function
- Individuals slowly lose the ability to perform activities independently and often require use of a wheelchair by their early teens
- As the disease progresses life-threatening heart and respiratory conditions can occur
- Individuals typically die in their 20s or 30s

Parent Project Muscular Dystrophy

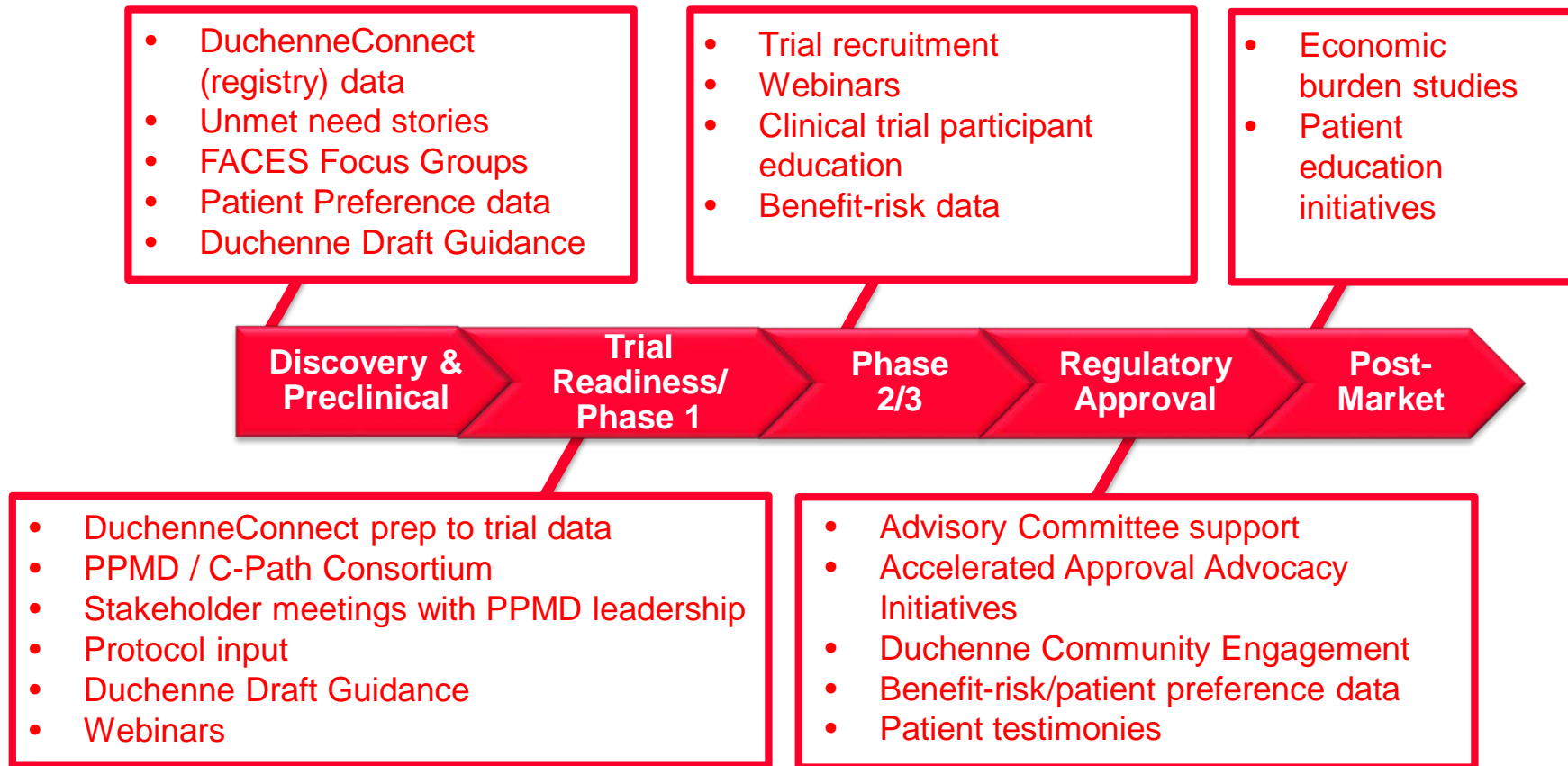
LEADING THE FIGHT TO END DUCHENNE

Parent Project Muscular Dystrophy's mission is to end Duchenne.

We accelerate research, raise our voices in Washington, demand optimal care for all diagnosed, and educate the global community.

We focus on the RACE against time: a comprehensive approach to end Duchenne through **R**esearch, **A**dvocacy, **C**are, and **E**ducation

Patient Engagement From Discovery to Delivery



Benefit Risk Study

Peay HL, et al. Watching time tick by...: Decision making for Duchenne muscular dystrophy trials. *Contemp Clin Trials*. 2016 Jan;46:1-6.

- Pilot study of 11 clinicians and 15 parents
 - Most parents describe undertaking B/R assessment
 - Parents
 - Most expected direct benefit; few considered trial failure
 - Most had decided to participate before consenting
 - Clinicians
 - Felt responsible to balance consent with hope
 - Felt that they had more influence on parental decisions than parents felt they did
- Participants prioritized protection of muscle function over any other attribute, including longer lifespan
- Participants' most significant worries were related to the child's illness progression and care
- Parents have great concerns about DMD's effect on their child's strength, and are willing to accept risk and uncertainty for a treatment that would slow or stop muscle weakness.

"PATIENTS ARE WAITING..."

Messages from Duchenne

To collect meaningful information from a group of people and caregivers managing muscular dystrophy (Duchenne) and the development of new treatments, Muscular Dystrophy (PPMD) launched the **Risk in Duchenne Therapies** program. The goal is to inform the FDA and other agencies, as well as biopharmaceuticals, about the priorities and risk tolerance of the Duchenne community.

Duchenne families often feel as if they are an untouchable and unreachable group, tasked with making critical decisions about drugs. In order to bridge that gap, the Risk Program includes:

1. A rigorous first-of-its-kind benefit-risk analysis using patient preference data on treatment preference and tolerance using stated-preference methods.
2. "Share Your Story," an open-ended survey that allowed parents and patients to speak their minds to the FDA.

Objectives and Methods

The program objective is to share stories with the FDA and other agencies to help them better understand the needs of Duchenne families. Using an online survey implemented on the Parent & Caregiver website, we asked families, "If you had a chance to talk to the FDA, what would you want them to know?" No further prompts were given to participants. The responses were publicly available, so participants could read previous entries before posting their own comments.

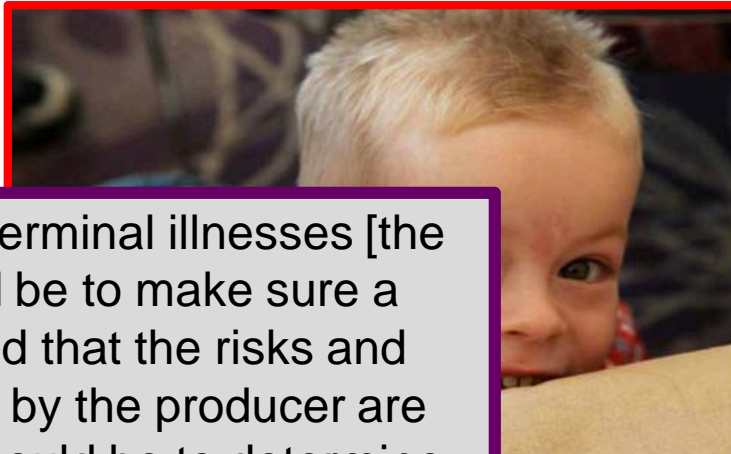
The most common theme reflected on the **burden of managing Duchenne**, on patients, caregivers, the family, and the broader community. Specific burdens include **progressive loss of function and ability to participate** for the patients; **anticipating further disease progression and a short lifespan**; **impact on caregivers, siblings, and other relatives**; and

Duchenne pipeline. Time is something our boys do not have."

"Because DMD shortens the life span of those afflicted, I would encourage the FDA to consider being more aggressive with the approval of certain drugs where the benefits

to meet the urgent need for new treatment options; more than half of the participants urged the FDA, sponsors, and other stakeholders to come together and **facilitate a faster, more flexible drug development and approval process**. This major theme includes requests to **harmonize efforts between U.S. and other regulatory bodies** to allow

"When it comes to terminal illnesses [the FDA's] job should be to make sure a product is safe and that the risks and benefits presented by the producer are accurate. Our job should be to determine, given all that information, whether to give it to our children. It is an intensely personal decision that involves the parents and the child with Duchenne."



and life span. Some risks that may come from doing something like this are waiting for their child to

of the clock very loudly in that science will take too long to get that treatment that will slow/stop progression. Our bigger worry is to develop it and the FDA will approve it."

REGULATORY FLEXIBILITY
% of participants

CLINICAL BENEFIT

vs

MEANINGFUL BENEFIT

6 MWT

Slow/Halt Progression

Walk/Stand

4 STAIR CLIMB

Self-Feed

Touch Head

Life Span

Turn Over in Bed

Wrist and Finger Function

Breathing

The Decision (first approval in Duchenne)

September 19 2016: Eteplirsen Approved (Exondys 51)



Clinical Trial, NDA, Advisory Committee

- Flawed study
 - Outcomes, dystrophin, open label, small number
- Scientific community support
- 1,000 people participated in the Advisory Committee
- 52 speakers, only 1 negative
- Advisory Committee split vote
- PDUFA date ignored



The Fallout

- 162 page FDA document describes agency turmoil
- NORD meeting: Dr. Jenkins states 'eteplirsen should not be approved'

[Sarepta Therapeutics Announces Third Quarter 2016 Financial Results and...](#)

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[Humana spells out its conditional Exondys 51 coverage policy... endpts.com](#)1d

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[cnafinance.com](#)1d

[After 'Female Viagra,' Muscular Dystrophy Drug, Will FDA Stand...](#)

[Forbes](#)1d

[The FDA's Controversial Duchenne Drug Approval And The Moral...](#)

[Health Affairs](#)2d

[FDA expert lashes out at 'worrisome' Sarepta approval in JAMA Fierce Biotech](#)2d

Learnings

- Rare disease is hard
- Deserves the greatest degree of flexibility when making decisions
- Once a drug is approved, utilizing the established process – ALL STAKEHOLDERS MUST MAKE PEACE WITH THE DECISION.
- No one wants their child to receive weekly infusions, injections or for that matter oral drugs if they have no efficacy
- Given the trajectory of the illness, the limited life span, once safety is established and a trend toward benefit, consider adaptive licensing
- Without this conversation, patients will wait and wait and wait....
- Eteplirsen is approved – the community is interested in a real-world experience to fully understand both benefit and risk

Researchers, regulators, and families MUST find a way to balance the concerns of people against regulatory and clinical trial requirements

Tools to capture the voices of individuals, families, and communities in a meaningful way...

Protocols that recognize the real-world experience of participants...

...And regulatory and post-market pathways to match