Approval of Eteplirsen: Patient Advocate Perspective

participant

Genetic Alliance

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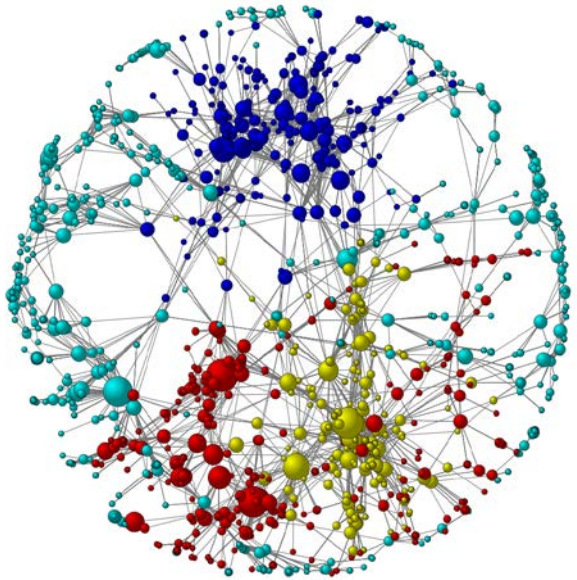
Genetic Alliance engages individuals, families, and communities to transform health.

- 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

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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

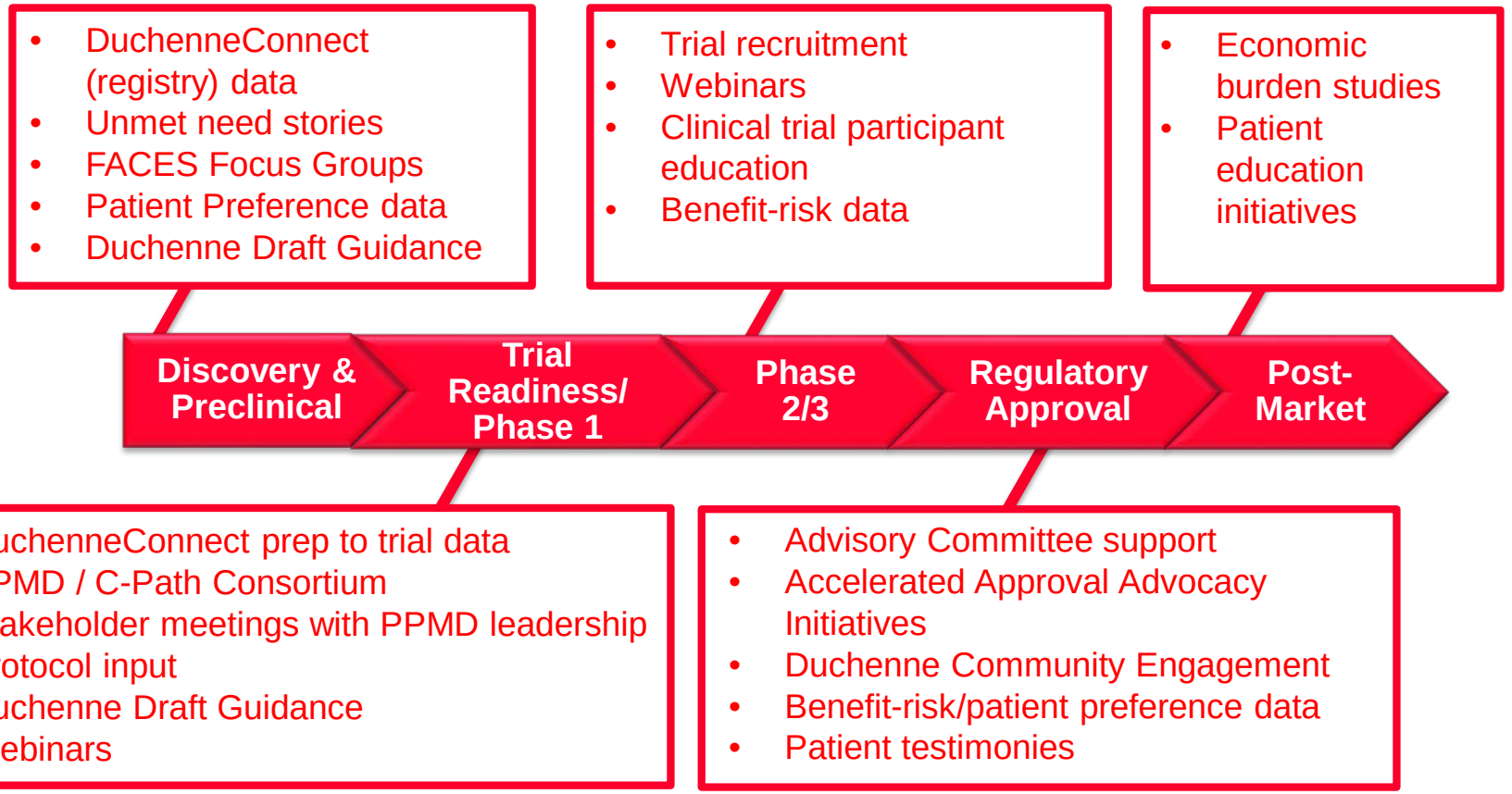
LEADING THE FIGHT TO END DUCHENNE

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

Adapted from slides provided courtesy of Pat Furlong, PPMD

Patient Engagement From Discovery to Delivery



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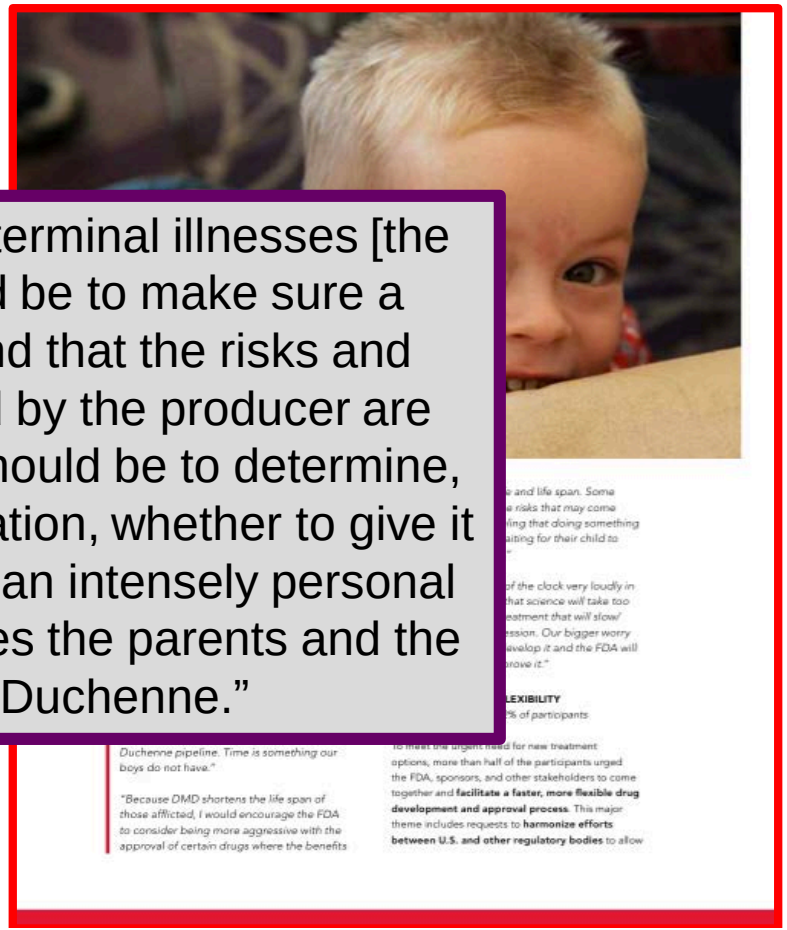
Benefit Risk Study

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.



"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."

Adapted from slides provided courtesy of Pat Furlong, PPMD

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

Adapted from slides provided courtesy of Pat Furlong, PPMD

The Decision (first approval in Duchenne)

September 19 2016: Eteplirsen Approved (Exondys 51)

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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

Adapted from slides provided courtesy of Pat Furlong, PPMD

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…
Business Wire15h
Humana spells out its conditional Exondys 51 coverage policy…
endpts.com1d
Sarepta Therapeutics (SRPT) Stock: They Can Shake And Rattle, But Will …
cnafinance.com1d
After 'Female Viagra,' Muscular Dystrophy Drug, Will **FDA** Stand…
Forbes1d
The **FDA**’s Controversial Duchenne Drug Approval And The Moral…
Health Affairs2d
FDA expert lashes out at 'worrisome' **Sarepta** approval in JAMA
Fierce Biotech2d

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

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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