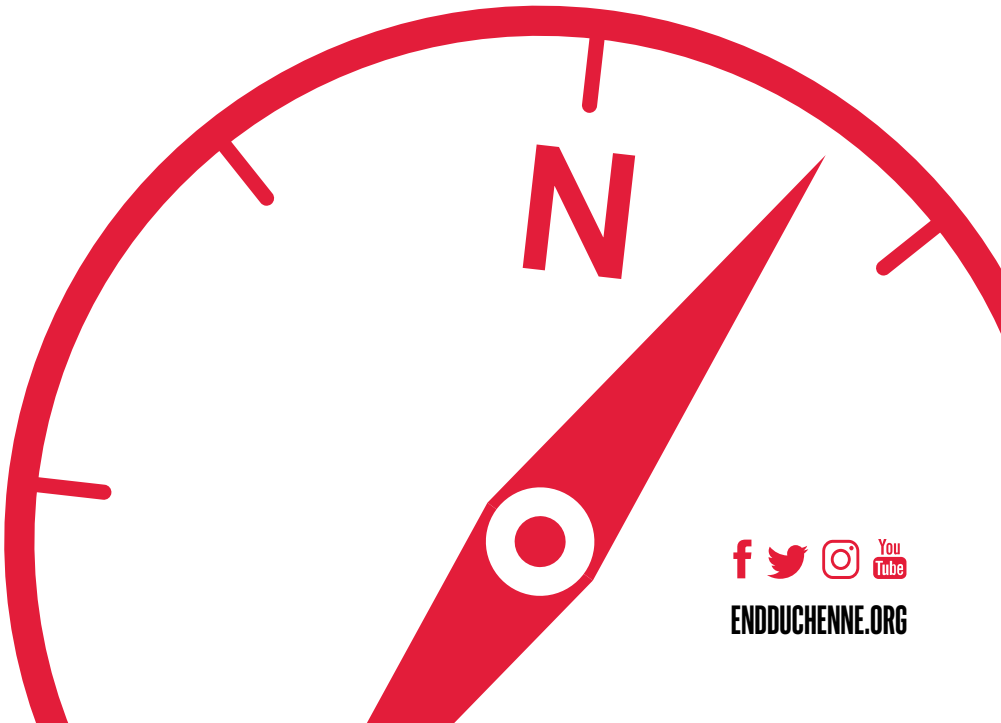
THE DUCHENNE PATIENT-FOCUSED COMPASS MEETING

A NAVIGATIONAL GUIDE & DIRECTIONAL ELEMENTS



Parent Project Muscular Dystrophy

JOIN THE FIGHT. END DUCHENNE.

ENDDUCHENNE.ORG

EXECUTIVE SUMMARY

The following white paper is intended to set the stage for the Duchenne Patient Focused Compass Meeting on March 5, 2018, and to provide background on the current treatment and care landscape in Duchenne to help inform discussions at the meeting.

In seeking the Duchenne Community's review and input regarding community plans for 2018 and beyond, PPMD has assembled:

1. A summary snap shot of progress to date in Duchenne policy and drug development as the foundation upon which new initiatives may be anchored, and
2. An overview of pending gaps and opportunities with respect to policy and development as the basis for a discussion of identifying, prioritizing, and pursuing navigational targets for the community.

As a community, we must ensure that we now bring our community's diverse patient voice, perspective, and current experience of Duchenne into the center of this conversation. That is the purpose of the Duchenne Patient-Focused Compass meeting.

About Duchenne

Duchenne muscular dystrophy is the most common fatal genetic disorder diagnosed in childhood, with 20,000 children diagnosed around the world each year. Although there are medical treatments that may help slow its progression, there is currently no cure for Duchenne. Duchenne results in skeletal, cardiac, and pulmonary muscle weakness, with disease symptoms progressing throughout the lifespan. Most people with Duchenne live into their late twenties.

Duchenne is among a spectrum of muscle diseases known as 'dystrophinopathies' that result from the absence of the muscle protein 'dystrophin'. The dystrophinopathy spectrum ranges from the more severe (Duchenne muscular dystrophy) to the milder yet variable (Becker muscular dystrophy). Because Duchenne is X-linked, it is found primarily in males, while effected females will be carriers. Some females can have symptoms of Duchenne and are therefore called "manifesting carriers." PPMD's mission – as well as, this meeting and related efforts – pertain to the full dystrophinopathy patient community, and for simplicity we will primarily refer to Duchenne.

The Duchenne Community – Innovators within Patient Focused Drug Development

To date, the Duchenne community has worked tirelessly to build a robust therapeutic pipeline and regulatory infrastructure. The FDA Safety & Innovation Act (FDASIA, 2012) and the Prescription Drug User Fee Act V (PDUFA V, 2012) aligned perfectly with the dawning of a new day for our Duchenne community – one in which basic laboratory breakthroughs had progressed into clinical trials, enabling the Duchenne pipeline of experimental therapies to become more robust than ever. We immediately embraced the opportunities presented to us through PDUFA V and have worked collaboratively to inform the science of patient input and advance the field of Patient-Focused Drug Development (PFDD).

We published a series of white papers analyzing PDUFA V through the lens of the Duchenne community, including *PPMD's Putting Patient's First* and *Patients Are Waiting*. These publications highlight our Duchenne community's policy priorities around the use of adaptive approval, limiting exposure to placebo, and the regulatory importance of a benefit-risk framework specific to each product. They also include narratives on the urgency and unmet need within our patient community.

We led a comprehensive and multi-stakeholder effort to prepare the first ever, patient- initiated draft guidance to industry developing Duchenne therapies. The guidance, *"Guidance for Industry Duchenne Muscular Dystrophy Developing Drugs for Treatment over the Spectrum of Disease"* was submitted to FDA in June 2014. Our guidance – along with a Duchenne Community Policy Forum convened in

December of 2013 – was the foundation used by the agency to develop its own draft guidance on the same topic issued in June of 2015 entitled, *"Duchenne Muscular Dystrophy and Related Dystrophinopathies: Developing Drugs for Treatment."*

In 2013, PPMD conducted the first-ever scientifically rigorous survey of parents of Duchenne patients to obtain quantitative evidence as to their views on benefit and risk. Results revealed a willingness of caregivers to accept considerable risk and uncertainty for a therapy that stops or even slows the progression of Duchenne. These findings have been useful in the therapeutic access based on community interest in accessing the first two approved drugs. A second preference study on both caregiver and patients' preferences for non-skeletal muscle benefits elicited the high value placed on cardiac and pulmonary benefits, including an acceptance for risk and uncertainty in order to achieve meaningful pulmonary outcomes such as a stronger cough and fewer lung infections. These findings provide insight into caregiver and patient priorities and preferences for treatments, and have value within both a regulatory and treatment access context.

In 2018, we are expanding our patient-preferences studies, including a global study of benefit-risk preferences and a study focused on risk tolerance in gene therapy interventions. Each of these studies represents collaborations with the patient community, social scientists, research experts, FDA, and industry.

The Duchenne community also has worked to ensure that patient-experience data being generated has a secure and transparent regulatory pathway aligned with the spirit of the PFDD provisions within PDUFA. Through the enacted Patient Focused Impact Assessment Act (PFIA, S. 1597; Sections 3001, 3002, 3004 of P.L. 114-255) and the pending Better Empowerment Now to Enhance Framework and Improve Treatments Act (BENEFIT, S. 1092), the Duchenne community and our partners ensured that patient experience is considered within a product's regulatory review (PFIA) and will be incorporated into the FDA's Benefit-Risk Framework (BENEFIT).

In 2017, the Duchenne Drug Development Roundtable (DDDR) partners together worked to evaluate our research and 'regulatory learnings' throughout 2015 and 2016. The Duchenne Drug Development Roundtable (DDDR) is group of industry and relevant stakeholders convened by PPMD that has the goals of accelerating the development of meaningful treatments for Duchenne through open discussion to minimize duplication and to pool resources in the precompetitive space. Through a series of targeted meetings, the DDDR together explored: 1) clinical trial harmonization from the patient perspective; 2) clinical trial optimization; and 3) clinical trial harmonization from the clinical site perspective, with each meeting resulting in a summary report. In 2017, PPMD also convened meetings to explore the role of inflammation, cardiac outcome measures in Duchenne, and the burden of clinical trial participation.

Developing & Implementing Duchenne Care Standards

Following the publication of the Centers for Disease Control and Prevention's (CDC's) Duchenne/Becker Care Considerations in *The Lancet Neurology* in 2010, PPMD wanted to ensure that the Duchenne community would have access to optimal, evidence-based standardized care and services. Our response was to establish a rigorous PPMD Certified Duchenne Care Center Program. Centers that qualify for certification must meet and maintain the highest standards – complying with CDC care guidelines and applying new, evidence-based knowledge and care as it emerges. Eligibility for certification is assessed by a committee comprised of Duchenne clinical experts and patient community members.

In addition, as a result of our community's efforts around the Paul D. Wellstone Muscular Dystrophy Community Assistance Research and Education (MD-CARE) Act Amendments of 2014 and a strong collaboration between the CDC and the Duchenne community, the Care Considerations were updated to reflect changing care standards. The updated Duchenne/Becker Care Considerations were published in three separate publications in *The Lancet Neurology* in January of 2018. Pediatrics supplements are pending publication in the Spring of 2018.

MD STARnet

MD STARnet is a multi-state surveillance network effort funded by the CDC and congressional authorization through the MD-CARE Act (amended) with sites in Arizona, Colorado, Georgia, Iowa, and Western New York.

The goals of MD STARnet include identifying everyone born after 1981 who has Duchenne and Becker within those states in order to estimate the number of people with Duchenne, to track changes over time, and collect relevant information about these diseases. The information collected through MD STARnet allows researchers to gain a better understanding of the health and service needs of people with Duchenne and their families, and is of interest to physicians, public health officials, therapists, educators, patients, their families, and the support organizations that serve them.

The Duchenne Landscape: Critical needs covered

An Engaged Patient Community	✔	Published Standards of Care	✔
Well-Characterized Disease	✔	Critical Path	✔
Natural History Studies	✔	Community-Specific Benefit-Risk Data	✔
Biomarkers	✔	Guidance for Industry	✔
Validated Screening Test	✔	Patient Reported Outcome Measures	✔
Developed Outcome Measures	✔	Collaborative Pharmaceutical Industry (DDR)	✔
International Patient Registry	✔	Federal Agency Engagement	✔
National Surveillance Program (Epidemiology)	✔	Clinical Care Center Network	✔

Separately, these infrastructure and actions constitute significant work in each of the thematic areas covered.

Together, these efforts represent a holistic approach to advancing — or contributing to — development, approval, access, and policy frontiers, each of which still demand additional work going forward, underlined by an unwavering sense of urgency.

Bringing the Patient Community Voice Back into the Center of the Conversation

As part of FDA's commitments under the PDUFA V reauthorization of 2012, FDA has taken several steps to inform assessment of benefit-risk in its regulatory decisions concerning new drugs. As noted previously, the PFDD initiative is part of FDA commitments under PDUFA V and FDASIA. The PFDD initiative's stated aim is to more systematically obtain the patient perspective on specific diseases and their treatments. The patient perspective is critical in helping FDA understand the context in which regulatory decisions regarding benefits and risks are made for new drugs. The "PFDD meetings" authorized in FDASIA and expanded more recently, give FDA an important opportunity to hear directly from patients, patient advocates, and caretakers about the symptoms that matter most to them, the impact the disease has on patients' daily lives, and patients' experiences with currently available treatments. This input can inform and enrich FDA's decisions, advice, and oversight both during drug development and during their review of a marketing application.

There are complexities and challenges in translating individual patient views, which may be subjective, into more structured information derived from many inputs across the patient population. Harmonizing the collective voices of individuals diagnosed with a specific disease results in an orchestrated symphony of symptoms, as well as, a collective view of meaningful benefit. This is an important aspect of advancing the impact, as well as the utility of PFDD.

We now want to ensure that we bring our patient community's voice, perspective, and current experience of Duchenne into the center of this conversation.

That is the purpose of the Duchenne Patient-Focused Compass meeting.

PPMD and the Duchenne community will build on the foundational format of the initial PFDD meetings by adding additional stakeholders to this day-long discussion, allowing for an in-depth analysis and assessment of barriers, needs, and opportunities for the Duchenne community in 2018. Our goal is the creation of a Navigational Action Guide for the Duchenne community, including the voice and experience of all relevant stakeholders involved in Duchenne research, drug development, and care going forward.

Through this day of structured dialogue, we will elicit patient perspectives on disease symptoms and the daily impacts that matter most across the lifespan of disease, as well as, patient perspectives on current approaches to trials, treatment, and access to approved treatments.

Topics considered will include:

- overall quality of life and what is considered to be meaningful benefit
- care standards implementation and access (physical therapy, occupational therapy, durable medical equipment, primary care, cardiopulmonary, endocrine, counseling and behavioral therapy)
- clinical trial opportunities and current clinical trial endpoints within that age group
- steroid use
- availability of approved therapies
- care burden
- access to appropriate and adequate personal care
- psychological and behavioral impacts
- family burden
- new opportunities and barriers encountered by adults with Duchenne

As we continue to listen to the experiences of our patient community, we realize there is so much more to learn, to understand. We believe the answer to navigating the Duchenne journey effectively is in our community's lived experience.

GIVEN THE LANDSCAPE WE'VE SHAPED, WHAT IS THE LIVED EXPERIENCE OF DUCHENNE IN 2018?

With the overarching intent to ensure that patient voices are influential in all areas of policy which impact Duchenne patients and families, there are five (5) areas of evolving concerns, which now demand our community's attention:

1. Improving patient and caregiver experiences in clinical trials;
2. Expanding patient community impact in regulatory decisions;
3. Facilitating patient access to approved treatments;
4. Assuring patient access to quality clinical care; access to both prescribed therapies and supports (to include DME and paid caregivers); and
5. Improving understanding and depiction of patient and caregiver disease burden.

ACKNOWLEDGEMENTS

Community Advisory Board

In preparing for this meeting we have invited all of our Duchenne community foundation partners to join the Community Advisory Board (CAB). PPMD is grateful to all foundations participating in this effort.

CAB members include:

BEST DAY EVER FOUNDATION

COALITION DUCHENNE

Foundation for a Future

Foundation to Eradicate Duchenne

HOPE for GUS
Finding Research for Duchenne Muscular Dystrophy

HOPE FOR JAVIER

JB's Keys to DMD
JB

Jett FOUNDATION

LITTLE HERCULES FOUNDATION

POWERS PROMISE
FINDING AN END TO DUCHENNE MD

Ryan's Quest
To Fight Duchenne Muscular Dystrophy

TEAM JOSEPH
Defeating Duchenne

WALKING STRONG

Zack Heger Foundation
for Duchenne Muscular Dystrophy

Faegre Baker Daniels

Tim Franson, MD, YourEncore
Allison Martin
Nick Manetto
David Zook