Patient Focused Drug Development 2.0

September 15, 2015

Pat Furlong, PPMD
Understanding the Duchenne Muscular Dystrophy Environment
About Duchenne muscular dystrophy

- X-linked, pediatric neuromuscular disease, with onset in early childhood
- Incidence rate: 1:4600 boys (30% spontaneous)
- Diagnosis: 3-5 years of age
- Predictable course
- Progressive loss of function
- 100% lethal
Why are we here?

A drug development ecosystem is a community of stakeholders (universities, companies, patient organizations, patients, government organizations) living in conjunction with the nonliving components of their environment (regulations, economic factors, reimbursement potential), interacting as a system. These components are linked together through clinical research cycles and funding flows.
• Basic Steps:
• Characterize disease
• Capture patient data (Duchenne Connect)
• Community Engagement
• Regulatory Engagement
• Stating your Case
• Patient (Caregiver Preferences)
• Consider Developing Draft Guidance
Community Engagement to Determine Acceptable Benefits/ Risks of Emerging Therapies

Pat Furlong
Holly L Peay, PhD (lead on program)
Case Study: Parent Project
Muscular Dystrophy

- Anticipated FDA legislation introducing Patient-Focused Drug Development
- Needed to inform the FDA about our community preferences and priorities for therapeutic dev’t
- Developed pilot research study on benefit/risk as part of a comprehensive engagement effort with the FDA
- Study data jump-started FDA engagement
- Comprehensive effort led to community-engaged development of draft guidance for DMD
- Subsequent therapeutic-specific study
- Subsequent preference study focused on meaningful benefit and uncertainty
Importance of Measuring Preferences

- The FDA:
  - Wants to improve their benefit-risk framework
  - Is mandated to better understand the patient experience and preferences
  - Is interested in your testimony but... deals in data
“I understand the need for caution and care, but I also know that our children are dying. Parents should be able to decide the risk/benefit of a drug that has gone through and passed preliminary testing. I would rather my son die trying and fighting than waiting and wondering and wishing....I am one parent willing to take an educated risk!” [PPMD Share Your Story]
Demands and Benefits to a Disorder Community

- Highly collaborative process
- Outcomes inform advocacy
- A large number of people can participate, even those who cannot/do not want to testify
- Resource and time intensive
- You may not get the results you “want”
- Requires larger sample sizes; more generalizable than testimony
Your Community’s Role…

Collaborating with experts in stated preference research to:

• Set the research agenda
• Develop a meaningful study
• Weigh in on interpreting the results
• Disseminate to sponsors and regulators (and your community)
CASE STUDY: THERAPEUTIC PRIORITIES AND PREFERENCES

This study is being conducted by PPMD in collaboration with Johns Hopkins. It is sponsored by Santhera Pharmaceuticals.
Goals

• To what extent do parents and patients assess the pulmonary outcomes associated with the clinical trial as meaningful benefits?

• What are the maximal acceptable risks, harms, and/or burden that patients and parents will be willing to accept?

• Is there significant heterogeneity in the estimates of meaningful benefit or maximal acceptable risk among parents and patients?
Community Engagement

• Leadership Committee
  – Charge: guide survey development, inform policy implications and later dissemination of results

• Stakeholder Committee
  – Charge: refine pool of potential treatment attributes/associated levels and inform survey language

• Review Committee
  – Charge: participate in cognitive interviewing to help finalize instrument
## Example Survey Item

**Treatment profile:**

<table>
<thead>
<tr>
<th></th>
<th>Best</th>
<th>Worst</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cough strength:</strong></td>
<td>Maintained for 10 years</td>
<td></td>
</tr>
<tr>
<td><strong>Lung infections during your life:</strong></td>
<td>No benefit</td>
<td></td>
</tr>
<tr>
<td><strong>Your chance for diarrhea:</strong></td>
<td>1 in 5 (20%)</td>
<td></td>
</tr>
<tr>
<td><strong>How often you need a blood test:</strong></td>
<td>4 times a year</td>
<td></td>
</tr>
</tbody>
</table>

**Would you choose to use this treatment?**

- Yes
- No
Preliminary: Priority Order for Non-Skeletal Muscle Treatment Targets

1. Weaker heart pumping
2. Lung infections
3. Weaker ability to cough
4. Bone fractures
5. Non-healthy weight
6. Depression
7. Headaches
8. Constipation
9. Feeling tired
10. Frequent waking at night
11. Poor attention span
Preliminary findings: Treatment Preferences

- Cough weakening
- Lung infections
- Diarrhea
- Blood draws
Next Steps

• Complete analysis
• Develop a report on the findings for the FDA
• Provide a lay summary for the patient and caregiver community
• Publish the study
• Use the results to inform an ongoing advocacy, education and outreach agenda
Importance of Patient Voice
Why Develop a Draft Guidance for the FDA?
Why the Duchenne community?

**Existing understanding:** Development of natural history, biomarkers and appropriate clinical endpoints as each evolves alongside drug development process.

**Identified gaps:** Inconsistent regulatory goals and standards posed little incentive for pharmaceutical companies to stay in field.

**Community interest:** Community felt FDA wasn’t taking its experiences and preferences into consideration.

**Need:** Rare childhood neurologic diseases cannot be held to same standards as conventional regulatory policy and procedure.
To fully realize the potential to speed responsible access to new therapies for Duchenne, the FDA should:

**Expand the use of accelerated approval for therapies intended to treat rare diseases**, including Duchenne muscular dystrophy.

**Issue clear guidance outlining the level of evidence required for the use of surrogate endpoints in order to expand the scope of acceptable endpoints**, including novel surrogate and intermediate clinical endpoints, used to approve drugs for serious or life-threatening diseases with unmet medical need.

**Pilot the use of adaptive approval** for serious and life-threatening disorders with significant unmet medical need, using existing authority under current law.

**Give greater weight to the demonstrated benefit/risk preferences of patients, as well as caregivers in the case of pediatric illness**, when making risk benefit determinations. Subpart D considerations must be evaluated here, yet benefit/risk should also be addressed within the context of patients living with Duchenne.
FDA Safety and Innovation Act (FDASIA)

Opportunities (FDA)

- PDUFA (FDASIA) Food and Drug Administration Safety and Innovation Act
- PPMD, Genetic Alliance, EveryLife Foundation and advocates like YOU collaborated to ensure strongest language included in final law

Results

- Accelerated Approval provision
- “Breakthrough Therapy” provision
- Patient-Focused Drug Development initiative/Benefit Risk
**European activities set the stage**

European Medicines Agency (EMA) develops draft guidance for Duchenne & Becker MD

| Important first step; however guidance drafted without community consultation | European community held scientific meetings, inviting academic and industry experts, regulators, parents and patients to discuss ways to improve guidance | Based on feedback provided to EMA, draft guidance is under review |
# FDA engagement

| PPMD met regularly with FDA, requesting draft guidance for Duchenne community | FDA declined but instead invited community to develop draft guidance | PPMD convened national Duchenne Policy Forum engaging 19 FDA officials and 200 researchers, clinicians, patients, advocates, industry | FDA agreed to consider draft guidance created by Duchenne community |
Understanding the Process
January 2014
Steering committee established to oversee draft guidance development

April – June 2014
Working group teleconferences up to three times a month

August 13, 2014
Internal FDA meeting to review guidance

December 12, 2013
Policy forum convened in Washington, D.C.

February 2014
Working groups established

June 25, 2014
PPMD submitted first-ever patient group-initiated draft guidance to FDA

October 6, 2014
Open docket closed for public comments on the draft guidance

April 2013
“Putting Patients First” white paper released
Organizational structure

- Steering Committee
- Community Advisory Board
- Working Groups
- Project Management
- Professional Writer
Support team

Professional Medical Writer
Theo Smart
HIV/TB treatment activist and journalist

Project Management
Yena Chung, Associate
Mark Krueger, MPH, President
Pritha Kuchaculla, MPH, Senior Associate
Mark Krueger & Associates, Inc.

Regulatory Consultant
Tim Franson, MD,
Chief Medical Officer
YourEncore
Community involved throughout

**Community Advisory Board**
22 patient group representatives and 20 parents and patients reviewed and provided comments on the guidance as it was written.

**Duchenne Drug Develop Panel**
PPMD’s panel of industry, patient group and government agencies provided input on the guidance.
<table>
<thead>
<tr>
<th>Working group topic</th>
<th>Working group chair</th>
<th>Title</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1: Benefit/risk analysis</td>
<td>John Bridges, PhD</td>
<td>Associate Professor</td>
<td>John Hopkins University</td>
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<tr>
<td>#2: Diagnosis</td>
<td>Kevin Flanigan, MD</td>
<td>Neurologist</td>
<td>Nationwide Children’s</td>
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<tr>
<td>#3: Natural history</td>
<td>Craig McDonald, MD</td>
<td>Director, Neuromuscular Disease Clinics</td>
<td>UC Davis Health System</td>
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<tr>
<td>#4: Biomarkers I:</td>
<td>Justin Fallon, PhD</td>
<td>Professor of Neuroscience</td>
<td>Brown University</td>
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<td>Molecular genetics and muscle biopsy</td>
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<td>#5: Biomarkers II:</td>
<td>Lee Sweeney, PhD</td>
<td>Director, Center for Orphan Disease Research and Therapy</td>
<td>University of Pennsylvania</td>
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<td>MRI, serum and urine</td>
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<td>#6: Clinical trial designs &amp;</td>
<td>Lawrence Charnas, MD, PhD</td>
<td>Medical Director</td>
<td>Shire</td>
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<td>outcome measures</td>
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<tr>
<td>#7: Imperatives</td>
<td>Pat Furlong</td>
<td>Founding President, CEO</td>
<td>PPMD</td>
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What does this mean to you?

An organized patient voice is necessary and important for regulatory change.