ACCELERATING THE SEARCH FOR THERAPIES: WHAT’S HAPPENING, WHAT’S NEXT

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To enhance the quality of life of people living with myotonic dystrophy (DM) and advance research focused on treatments and a cure.
BASIC RESEARCH

TRANSLATIONAL RESEARCH

CLINICAL RESEARCH and TRIALS

REGULATORY

PAYORS & ACCESS & ADVOCACY

4
BASIC RESEARCH
Laboratory experiments to understand basic biology

TRANSLATIONAL RESEARCH
Use information from basic research to create tools or techniques to support and inform drug development

CLINICAL RESEARCH and TRIALS
Research on normal healthy volunteers or patients

REGULATORY
Government bodies that regulate drug development

PAYORS & ACCESS & ADVOCACY
Government agencies funding DM research; insurance and reimbursement stake-holders
Our Goal is to Accelerate the Development of Treatments and a Cure for Myotonic Dystrophy

- Continue to eliminate or lower barriers to therapy development
- Support researchers and companies already committed to DM
- Increase number of companies working on myotonic dystrophy
Three Year Cure Research Plan
Launched in 2015 ($5M)

CURE Budget by Category

- Basic Research: 51%
- Translational Research: 19%
- Clinical Research: 21%
- Regulatory Engagement: 5%
- Access & Advocacy: 4%
MDF Research Programs Target All Aspects of the Drug Development Pathway

**BASIC RESEARCH**
- 19 Post-doctoral and Pre-doctoral Fellows Funded
- Population-based prevalence study

**TRANSLATIONAL RESEARCH**
- Development of muscle MRI as a potential biomarker
- Development of RNA slicing in urine as potential biomarker
- iPS cell-lines for DM1 and DM2
- New Tg BAC Mouse model

**CLINICAL RESEARCH**
- DMCRN 500 Patient Natural History Study (US)
- PHENO-DM1 Natural History Study (UK)
- International Muscle Endpoint SOP consensus developed
- *Myotonic Dystrophy Family Registry*

**REGULATORY**
- CNS Patient voice workshop
- MDF FDA Workshop focused on DM
- PFDD Workshop; Voice of the Patient Report
- FDA Educational meetings

**PAYORS & ACCESS & ADVOCACY**
- Burden of disease analysis
- MDF active participant on Muscular Dystrophy Coordinating Committee
- DM added to DoD Funded Diseases (PRMRP)
- CDM added to SSA list for reimbursement
Patient Registries are Important!

Type of Information Collected

What It Is Used For

Demographics

Symptoms

Impact of the Disease from Patient’s Perspective

Disease Progression

Interest in Clinical Trials

Educate Researchers on Disease Burden / Impact on QoL

Help Identify Right Endpoints

Help Design Clinical Trials

Help Communicate About Trial Opportunities
Myotonic Dystrophy Family Registry

Data cut July 22, 2018

(*) Includes subjects that selected “Other” or “I don’t know” or left the question blank

Total
N=1,768

DM1
N=1,173
66.3%

DM2
N=291
16.5%

Other*
N=304
17.2%
DM Family Registry
n=1768

DM1
n=1173
- Congenital DM1
  n=236
- Juvenile DM1
  n=126
- Adult Onset DM1
  with symptoms
  n=745
  without symptoms
  n=66

Other
n=304

DM2
n=291
- DM2 with symptoms
  n=273
- DM2 without symptoms
  n=18
Demographics of Patients in MDF Registry

- **Average Age**: 44 yr
- **Identify as White**: ~90%
- **Male to Female Ratio**: ~1:1
- **First Person in Family with Diagnosis**: ~45%
- **Born in US; Over 60 other Countries Represented**: ~76%
MDF Registry Collects Prevalence of Multiple Disease Symptoms

**Eye**
- Vision trouble due to cataracts
- Cataract surgery

**Cardiovascular System**
- Heart condition diagnosis
- Pacemaker or ICD

**Skeletal Muscle**
- Walking difficulty
- Use of orthopedic aids
- Myotonia (negative impact)

**Central Nervous System**
- Daytime sleepiness
- Other sleep issues
- Fatigue (negative impact)
- Pain (negative impact)
- Psychiatric / emotional disorders

**Respiratory System**
- Breathing difficulty
- Use of ventilation device

**Gastrointestinal Tract**
- Swallowing difficulty
- Use of gastric/nasal feeding tube
Prevalence of Symptoms (Adult DM1 vs DM2)

- Myotonia (some impact)
- Fatigue (some impact)
- Daytime Sleepiness
- Walking Difficulty
- Other Sleep Issues
- Pain (some impact)
- Swallowing Difficulty
- Breathing Trouble
- Heart Condition Due to Cataracts
- Depression (diagnosis)
- ADD or ADHD (diagnosis)
- Anxiety Disorder (diagnosis)
- Emotional / Behavioral^ (diagnosis)

Diagram showing the prevalence of symptoms in Adult DM1 and DM2.
Prevalence of Symptoms (DM1 Subtypes)

- Myotonia (some impact)
- Fatigue (some impact)
- Daytime Sleepiness
- Walking Difficultly
- Swallowing Difficultly
- Breathing Trouble
- Heart Condition Due to Cataracts
- Depression Disorder Due to Diagnosis
- ADD or ADHD Disorder Due to Diagnosis
- Emotional / Behavioral Disorder Due to Diagnosis

Adult DM1
Juvenile DM1
Congenital DM1
Significant Use of Orthopedic Devices or Physical Therapy Observed in All Groups

<table>
<thead>
<tr>
<th></th>
<th>Congenital DM1 (n=211)</th>
<th>Juvenile DM1 (n=119)</th>
<th>Adult Onset DM1 (n=689)</th>
<th>DM2 (n=250)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use at Least One Orthopedic Device or Physical Therapy</td>
<td>68%</td>
<td>38%</td>
<td>48%</td>
<td>50%</td>
</tr>
<tr>
<td>Physical Therapy</td>
<td>36%</td>
<td>10%</td>
<td>12%</td>
<td>17%</td>
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<tr>
<td>Orthotics</td>
<td>22%</td>
<td>11%</td>
<td>7%</td>
<td>6%</td>
</tr>
<tr>
<td>Ankle/Leg Braces</td>
<td>38%</td>
<td>13%</td>
<td>12%</td>
<td>8%</td>
</tr>
<tr>
<td>Cane</td>
<td>7%</td>
<td>8%</td>
<td>21%</td>
<td>26%</td>
</tr>
<tr>
<td>Walker</td>
<td>9%</td>
<td>3%</td>
<td>8%</td>
<td>15%</td>
</tr>
<tr>
<td>Wheelchair</td>
<td>23%</td>
<td>11%</td>
<td>13%</td>
<td>17%</td>
</tr>
</tbody>
</table>
Education Status and Use of IEP Program

Highest Level of Education Completed

- **Graduate School**
  - Adult Onset DM1: 21.6%
  - DM2: 21.0%
- **College or Technical School**
  - Adult Onset DM1: 45.1%
  - DM2: 48.4%
- **High School**
  - Adult Onset DM1: 23.3%
  - DM2: 23.0%
- **Grade School**
  - Adult Onset DM1: 1.3%
  - DM2: 1.6%
- **Other**
  - Adult Onset DM1: 8.6%
  - DM2: 6.0%

Other Includes the following answers: I don’t have any formal education, Not applicable-Participant is an infant or child, I don’t know, Other-open text

Used An Individualized Education Program (IEP) in School

- **Congenital DM1**: 55%
- **Juvenile DM1**: 67%
- **Adult DM1**: 6%
- **DM2**: 5%
What’s Next?
Plans for the Next 3-Year Initiative

- BASIC RESEARCH
  - Post- & Pre-doctoral Fellows
  - Genome Editing Program

- TRANSLATIONAL RESEARCH
  - Mouse Drug Testing Facility
  - Biomarker Development
  - iPS Cell-Line Characterization
  - Tg Mouse Model SOPs

- CLINICAL RESEARCH
  - Expansion of Patient Registry
  - CNS Natural History Study

- REGULATORY
  - Continue FDA and EMA Interactions and Educational Meetings

- PAYORS & ACCESS & ADVOCACY
  - Continue to lobby for PRMRP Funding each year
  - MDF Active Participant on Muscular Dystrophy Coordinating Committee

VENTURE PHILANTHROPY PROGRAM
What is Genome Editing?

- Way to precisely make changes to the DNA of a cell or organism
  - Cut out pieces of DNA
  - Add pieces of DNA
  - Change sequence of DNA
- Genome editing can potentially be used to treat myotonic dystrophy
  - Cut out the repeat sequence
  - Delete the gene
- Much work is still needed to evolve the technology before it is transformed into an effective therapy for DM
MDF’s Genome Editing Initiative to Accelerate Development for DM

- Workshop held on April 17th, 2017 with 14 experts from universities, NIH, FDA, MDF and donors
- Request for Applications was released July 27th 2018
- Fund 2 awards of up to $250,000 to evaluate genome editing strategies for DM1 that target the DMPK gene
Venture Philanthropy Helps Promising New Therapies Cross the Valley of Death

- Basic Research
- Clinical Trials & Product Development

10,000 Compounds

1 Drug
Venture Philanthropy Helps Promising New Therapies Cross the Valley of Death

Make Strategic Investments in
For-Profit Companies
(Small Biotech, Early Stage Drug Development)

- Prioritize Myotonic Dystrophy
- Bring new companies into DM drug development
- Transition promising drugs across the ‘valley of death’