Bringing Differentiated Therapies
to Duchenne Patients
Stuart Peltz, PhD

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Main Objectives

- Translarna™ (ataluren) Update
  - FDA pathway forward for NDA
  - Ongoing clinical trials
- EMFLAZA® (deflazacort) Update
  - Standard of care
  - Clinical data
  - Clinical trial
20-year history marked by commitment to Duchenne

Translarna™ discovery

98 – 2003

Phase 1

62 healthy volunteers

2004

Phase 2a (004)

38 patients

2005

Phase 2b (007)

174 patients

2006

Phase 2b (007)

174 patients

2007

Initial Natural History Publications

2008

Phase 3 (020)

228 patients

2009

EMA DMD Draft Guidelines

2010

FDA DMD Draft Guidelines

2011

EU Initial Approval for Translarna™

2012

FDA Translarna™ path after CRL

2013

98 – 2003

18 years of research and development

1,000+ healthy volunteers / patients exposed / treated

Safety profile: generally well tolerated
Translarna™ (ataluren) approvals

- Translarna is available in 47 countries outside the US; Continuing to add new countries
- Greater than 90% of identified boys in EU-5 are on commercial therapy
- The Translarna approval in Europe has been renewed
- CHMP to expand use to include younger Duchenne nonsense patients (down to 2 years)
Bringing Translarna™ (ataluren) to the US

- FDA has recommended a pathway to potential accelerated approval

- Dystrophin Study
  - New methodologies discussed with FDA
  - Expectations:
    - Start by end of year
    - Complete in one year
    - Expedited review by FDA
Study 041: ataluren in boys 5 years and older with nonsense mutation Duchenne is underway

- Placebo Controlled for 72 weeks
- Open-Label arm for 72 weeks; All receive ataluren
- Walk at least 150 meters
- Multiple US Sites
- Perform certain timed function tests
- On a stable dose of corticosteroids for at least 12 months

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Care Considerations for Duchenne recommend corticosteroids

Published January 2018
Based on data from published clinical and natural history studies, deflazacort results in a number of benefits compared to placebo.

**Benefits of deflazacort**

| Preserve functional parameters (demonstrated through reduced change in 6MWD and TFTs)
|---|
| Reduce the risk of developing scoliosis and delay the need for spinal surgery
| Preserve pulmonary function and delay the need for nocturnal ventilation
| Result in significantly less weight gain compared to prednisone
| Prolong survival in the second decade of life

6MWD = 6-minute walk distance; TFT = timed function test.

2. Data on File. PTC Therapeutics, Inc.; 2017; Permission to use was granted by Trajectory Analysis Project Collaboration (cTAP).
Pharmacologic differences between Emflaza® (deflazacort) and other corticosteroids

- Emflaza is a synthetic corticosteroid, structurally different from prednisone:
  - Higher anti-inflammatory properties
  - Lower mineral corticoid impact
  - Longer duration of action
Small structural variances can have big impacts

(-)(S)-thalidomide

(++)(R)-thalidomide

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Small structural variances can have big impacts

Thalidomide underscores the concept that even seemingly small structural differences can have major therapeutic impacts

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Small structural variances can have big impacts

Teratogen

Effective sedative

Thalidomide underscores the concept that even seemingly small structural differences can have major therapeutic impacts.
Pharmacologic differences between Emflaza® (deflazacort) and other corticosteroids

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Data from peer reviewed publications show significant treatment differences between EMFLAZA® and prednisone.

Placebo-Controlled Clinical Trial

McDonald, et al (Lancet) 10-Year Natural History Study (CINRG)

ACT DMD SOC (Accepted for Publication)
Placebo arm of ataluren trial

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Deflazacort significantly improved muscle strength at Week 12 vs placebo and from Week 12-52 vs prednisone\(^1\)


<table>
<thead>
<tr>
<th>Treatment</th>
<th>LS Mean Change (ITT Population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deflazacort 0.9 mg/kg/d</td>
<td>0.15</td>
</tr>
<tr>
<td>Prednisone 0.75 mg/kg/d</td>
<td>0.27</td>
</tr>
<tr>
<td>Placebo</td>
<td>-0.10</td>
</tr>
</tbody>
</table>

Change in average muscle strength (modified MRC scale) from baseline to Week 12

- **P<0.05** vs placebo
- **P<0.01** vs placebo

Change in average muscle strength (modified MRC scale) from Week 12 to Week 52*

- **P<0.01** vs prednisone
- -0.12

*Secondary endpoint.

ITT = intent-to-treat; LS = least squares; MRC = Medical Research Council.

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Deflazacort resulted in significantly less weight gain at Week 52 vs prednisone¹

**Mean weight change from baseline to week 52**

- **Deflazacort**
  - 0.9 mg/kg/d (n=41)
  - 5.05 kg

- **Prednisone**
  - 0.75 mg/kg/d (n=37)
  - 8.45 kg

*P* < 0.0001

There were fewer discontinuations due to weight gain with deflazacort compared to prednisone¹

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ITT = intent-to-treat; LS = least squares.

Deflazacort had a lower incidence of most TEAEs compared to prednisone at Week 52¹

<table>
<thead>
<tr>
<th>TEAEs occurring in ≥10% of patients in any treatment group (safety population)</th>
<th>Deflazacort 0.9 mg/kg/d (N=68) n (%)</th>
<th>Prednisone 0.75 mg/kg/d (N=63) n (%)</th>
<th>Placebo (N=50) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients with ≥1 TEAE</td>
<td>58 (85.3)</td>
<td>58 (92.1)</td>
<td>38 (76.0)</td>
</tr>
<tr>
<td>Cushingoid</td>
<td>41 (60.3)</td>
<td>49 (77.8)</td>
<td>6 (12.0)</td>
</tr>
<tr>
<td>Hirsutism</td>
<td>24 (35.3)</td>
<td>28 (44.4)</td>
<td>1 (2.0)</td>
</tr>
<tr>
<td>Erythema</td>
<td>19 (27.9)</td>
<td>33 (52.4)</td>
<td>3 (6.0)</td>
</tr>
<tr>
<td>Weight gain</td>
<td>19 (27.9)</td>
<td>22 (34.9)</td>
<td>3 (6.0)</td>
</tr>
<tr>
<td>Central obesity</td>
<td>17 (25.0)</td>
<td>27 (42.9)</td>
<td>2 (4.0)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>16 (23.5)</td>
<td>10 (15.9)</td>
<td>3 (6.0)</td>
</tr>
<tr>
<td>Headache</td>
<td>15 (22.1)</td>
<td>17 (27.0)</td>
<td>11 (22.0)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>10 (14.7)</td>
<td>7 (11.1)</td>
<td>5 (10.0)</td>
</tr>
<tr>
<td>Pollakiuria</td>
<td>10 (14.7)</td>
<td>3 (4.8)</td>
<td>1 (2.0)</td>
</tr>
<tr>
<td>Increased appetite</td>
<td>8 (11.8)</td>
<td>12 (19.0)</td>
<td>1 (2.0)</td>
</tr>
<tr>
<td>Cough</td>
<td>7 (10.3)</td>
<td>8 (12.7)</td>
<td>3 (6.0)</td>
</tr>
<tr>
<td>Constipation</td>
<td>7 (10.3)</td>
<td>4 (6.3)</td>
<td>3 (6.0)</td>
</tr>
<tr>
<td>Abdominal pain upper</td>
<td>6 (8.8)</td>
<td>10 (15.9)</td>
<td>4 (8.0)</td>
</tr>
<tr>
<td>Abnormal behavior</td>
<td>6 (8.8)</td>
<td>9 (14.3)</td>
<td>3 (6.0)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>6 (8.8)</td>
<td>6 (9.5)</td>
<td>4 (8.0)</td>
</tr>
<tr>
<td>Influenza</td>
<td>4 (5.9)</td>
<td>10 (15.9)</td>
<td>2 (4.0)</td>
</tr>
</tbody>
</table>

Data from peer reviewed publications show significant treatment differences between EMFLAZA® and prednisone.

Placebo-Controlled Clinical Trial

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10-Year Natural History Study (CINRG)

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Overview: Cooperative International Neuromuscular Research Group (CINRG) study

- The CINRG is the largest prospective multicenter DMD natural history study
- The results of a 10-year analysis of a large prospective cohort study were just published in the Lancet
- Over 400 DMD patients have enrolled since 2006 in top centers of excellence across the world.

Grants from the Department of Education (DOE), National Institutes of Health (NIH), Department of Defense (DOD), and Parent Project Muscular Dystrophy (PPMD) have enabled the collection of data and study visits from these 400+ participants for up to 10 years.
### CINRG: Results demonstrate that deflazacort significantly delays the loss of multiple functional milestones

<table>
<thead>
<tr>
<th>Milestone Lost</th>
<th>Difference between deflazacort and prednisone (in years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supine to stand &gt;5 s</td>
<td>1.76</td>
</tr>
<tr>
<td>Supine to stand &gt;10 s</td>
<td>1.22</td>
</tr>
<tr>
<td>Supine to stand ability</td>
<td>2.06</td>
</tr>
<tr>
<td>4-stair climb ability</td>
<td>2.11</td>
</tr>
<tr>
<td>Ambulation (ability to walk)</td>
<td>2.70</td>
</tr>
<tr>
<td>Full overhead reach (Brooke ≥2)</td>
<td>2.83</td>
</tr>
<tr>
<td>Hand-to-mouth function (retained hand function) (Brooke ≥5)</td>
<td>2.71</td>
</tr>
</tbody>
</table>

“In patients with Duchenne muscular dystrophy, glucocorticoid treatment is associated with reduced risk of losing clinically meaningful mobility and upper limb disease progression milestones across the lifespan as well as reduced risk of death.”

Data from peer reviewed publications show significant treatment differences between EMFLAZA® and prednisone.

**Placebo-Controlled Clinical Trial**

**McDonald, et al (Lancet)**
10-Year Natural History Study (CINRG)

**ACT DMD SOC (Accepted for Publication)**
Placebo arm of ataluren trial

*Not approved for promotional use*
Analysis from ACT-DMD placebo arm provides data on deflazacort and prednisone

Retrospective analysis of the placebo arm of ACT-DMD

<table>
<thead>
<tr>
<th>Test</th>
<th>Deflazacort (n)</th>
<th>Prednisone/ Prednisolone (n)</th>
<th>In favor of deflazacort</th>
<th>LS Mean Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6MWD</td>
<td>53</td>
<td>61</td>
<td></td>
<td>31.6 (0.2, 62.9)</td>
</tr>
<tr>
<td>10-m Run/Walk</td>
<td>53</td>
<td>61</td>
<td></td>
<td>0.1 (-1.9, 2.1)</td>
</tr>
<tr>
<td>4-Stair Climb</td>
<td>53</td>
<td>61</td>
<td></td>
<td>2.9 (0.5, 5.23)</td>
</tr>
<tr>
<td>4-Stair Descend</td>
<td>53</td>
<td>61</td>
<td></td>
<td>1.8 (-1.0, 4.5)</td>
</tr>
<tr>
<td>Rise from Supine</td>
<td>53</td>
<td>61</td>
<td></td>
<td>2.6 (0.0, 5.2)</td>
</tr>
<tr>
<td>NSAA (Total)</td>
<td>53</td>
<td>61</td>
<td></td>
<td>1.1 (-0.4, 2.6)</td>
</tr>
<tr>
<td>PODCI (Mobility)</td>
<td>53</td>
<td>61</td>
<td></td>
<td>1.7 (-3.9, 7.2)</td>
</tr>
<tr>
<td>PODCI (Sports)</td>
<td>53</td>
<td>61</td>
<td></td>
<td>6.0 (0.7, 11.3)</td>
</tr>
<tr>
<td>LOA</td>
<td>53</td>
<td>61</td>
<td></td>
<td>3.84 (-2.43, 10.11)</td>
</tr>
</tbody>
</table>

6MWD = 6-minute walk distance; CL = confidence limit; LS, least squares; NSAA = North Star Ambulatory Assessment; TFTs = Timed Function Tests; PODCI = Pediatric Outcomes Data Collection Instrument. Post-hoc analysis is retrospective and includes only patients from placebo arm of ACT-DMD.

Accepted for publication in a premier neuromuscular journal and will be published in the upcoming weeks.
Completion of trial provides the basis for seeking extension of US label to DMD patients ≥2 to <5 years of age

DMD Patients will be matched to appropriate natural history control

Period 1 – Safety & PK
26 Weeks

- Eligible DMD subjects ≥2 to <5 years
- 0.45 mg/kg DFZ
  - N=25
- 0.9 mg/kg DFZ
  - N=25

Primary Safety Evaluation & PK

Period 2 - Extension
78 Weeks

- 0.9 mg/kg DFZ
  - N=25

Study Complete

Plans to conduct study with Emflaza® (deflazacort) in DMD patients 2-5 years old
PTC Therapeutics is working to improve age of diagnosis and standard of care for DMD patients

- Importance of early diagnosis; confirm by genotyping
- Awareness and understanding of current DMD treatment guidelines
  - Importance of beginning treatments early as recommended by guidelines
- Continue to understand the benefits of corticosteroid treatment
  - Ask about EMFLAZA® (deflazacort)
  - First and only steroid specifically approved for DMD in patients 5 years and older
- Provide resources to patients to help access approved medications
PTC Cares will help navigate the process for access to Emflaza® (deflazacort)

- Education and personalized case management
- Benefits investigation
- Prior authorization assistance
- Appeals support
- Co-pay Assistance program
- Patient assistance program
- Bridging program
- Patient foundation support (e.g., The Assistance Fund, NORD)

*Patient financial assistance* to eligible participants

Stop by the display and meet members of the team! They can answer your questions.
Enhanced our websites to provide additional information

www.emflaza.com

www.ptcccares.com
Thank you for your continued partnership and commitment

• Together we will…
  – Increase awareness and diagnose earlier
  – Raise the standards of care
  – Discover and develop new therapies
  – Ensure access to medication

• We’re looking forward to another great 20 years together!