PTC Therapeutics introduction

• PTC Therapeutics is a small biotech company whose founder, Stuart Peltz, remains the current CEO.

• Established in 1998; publicly traded since mid-2013.

• US Headquarters is in South Plainfield, NJ.

• Actively engaged in the discovery, development, and commercialization of drugs for:
  • Genetic disorders: Duchenne and Spinal Muscular Atrophy
  • Oncology
  • Gene Therapy

• PTC has grown to 500+ employees in 18 countries.

• Footprint in 47 countries, through local PTC teams and partnerships.
Everyone has a different definition of progress. For the last 20 years, we've measured our progress researching rare disease in moments. Smiling ones and crying ones. Moments spent with our boys' families and ones with their friends. We know that every step forward comes after several steps backward, because we've lived it—whether spending time with families in their homes or with our scientists researching in our labs.

It can be easy to lose yourself as you progress further. Although we've grown, our heart remains in the same place, because we've never measured ourselves like larger companies do. Our biggest accomplishment has always been the time we can give to all of our families. Whether it's hours, days, months, or years, every small moment is a big win.
PTC Therapeutics

A history of commitment to Duchenne muscular dystrophy patients

Translarna™ discovery
Phase 1
62 healthy volunteers
Phase 2a (004)
38 patients
Phase 2b (007)
174 patients
Phase 3 (020)
228 patients

1998 – 2003
2004 2005 2006 2007 2008
2013 2014 2015 2016 2017 2018

EMFLAZA® Launch
(May 8, 2017)
EMFLAZA® FDA Approval
(February 9, 2017)

Over 20 years of research and development

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PTC Therapeutics

Expanding pipeline through innovation¹

* Deflazacort is approved in the US.
† Ataluren is an investigational drug in the US.
‡ Marketing authorization has specific obligation to conduct additional nmDMD trial and requires annual renewal.

Improving patient outcomes by delivering best-in-class therapies earlier in disease progression

- Earlier diagnosis
- Increase disease awareness
- Genotyping
- Improving standards of care

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PTC is committed to Duchenne families through ongoing programs

**Duchenne and YOU**

- Duchenne and YOU
- Register to stay up to date on news about Duchenne

**Siblings Program**

- First-in-kind program for siblings of Duchenne clinical trials

**STRIVE**

- Annual Competitive Grant Program for Patient Advocacy Groups

**DECODE DUCHENNE**

- Removes the financial barrier of genetic testing

**Peer Navigator Program**

- For families considering corticosteroids

**PTC Cares**

- Patient support program
Role of Corticosteroids in Duchenne
Duchenne muscular dystrophy treatment guidelines support corticosteroid use as standard of care

2018 Centers for Disease Control and Prevention (CDC) Guidelines

Recommendations for using corticosteroids:
- Treatment with glucocorticoids remain the mainstay of DMD treatment and should continue after loss of ambulation
- If functional decline is observed, increase to target dose per weight on the basis of starting dose
- If side-effects are unmanageable or intolerable, reduce steroids by 25% to 33%
- Continue treatment beyond loss of ambulation
- Initiate treatment in steroid-naïve, non-ambulatory patients

2016 American Academy of Neurology (AAN) Guidelines

Recommendations for using corticosteroids:
- Treatment with glucocorticoids remains the mainstay of DMD treatment and should continue after loss of ambulation
- The benefits of long-term glucocorticoid therapy have been shown to include loss of ambulation at a later age, preserved upper limb and respiratory function, and avoidance of scoliosis surgery

Corticosteroid effects on the immune-mediated pathway in Duchenne

1. Dystrophin-deficient muscle cells are susceptible to contraction-induced injury, leading to muscle necrosis and release of proteins that may serve as neoantigens.

2. An innate response leads to MHC presentation of peptides derived from muscle antigens, which initiates an adaptive immune response via crosstalk between macrophages and T cells.
   - IL-4 released during muscle damage activates the regenerative actions of muscle resident fibro/adipocyte progenitors (FAPs). Activated FAPs promote proliferation of FAPs to support myogenesis, inhibit differentiation into adipocytes, and rapidly clears necrotic debris necessary for timely and complete regeneration of tissues.

3. Release of cytokines further drives the immune response; specific cytokines can result in activation of T cells or B cells and polarization of macrophages.
   - IFN-γ leads to M1 polarization
   - IL-10, IL-4, TGF-β can lead to M2 polarization
Deflazacort interrupts the inflammatory pathways early in the process.

Deflazacort inhibits IFN-gamma.

IFN-g

Immunomodulation

Inflammatory Pathways

IFN-γ

IFNγR

IKK-β

Jak1/2

RIP1

NF-κB

STAT1

Cytoplasm

Nucleus

Ripk1, pro-necrotic genes

Sod2, other pro-survival genes

ROS

https://mcb.asm.org/content/31/14/2934/F11
Deflazacort differs from prednisone in the way it works in Duchenne

• There are distinct differences in the T-cell expression, as measured by IFN-gamma, between prednisone and deflazacort

• The difference in the mean number of spot forming colonies (SFC) per 10 PBMCs between the two groups is both marked (Fig. 5) and statistically significant, raising the possibility that deflazacort is more efficacious in modulating T-cell pathways

PTC Cares™
Accessing PTC Commercial Therapies
Patient Support and Assistance

- Education and personalized case management
- Benefits investigation
- Prior authorization assistance
- Appeals support
- Co-pay Assistance program
- Patient assistance program
- Patient Foundation Support
- Bridge program

*to eligible participants

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Translarna®
(ataluren)
Investigational drug in the US
Translarna® (ataluren)*  
Conditionally approved in Europe

- In Europe, Translarna® is indicated to treat nonsense mutation patients aged two years and older with Duchenne muscular dystrophy who are able to walk
- Orally administered; available as granules that are mixed with liquids or semi-solid food
- Studies underway to prepare for FDA resubmission

*Investigational drug in the US
How ataluren works on a nonsense mutation

• Errors in genetic code are called mutations which cause changes to cell DNA sequence

• A nonsense mutation introduces a **premature stop codon** into the part of the gene that translates into a protein – like a period at the end of a sentence - only part of the protein will be made
**STUDY 041**  
A clinical study to determine the long-term effect of ataluren

**DYSTROPHIN STUDIES**  
Clinical studies to determine the ability of ataluren to increase dystrophin levels

<table>
<thead>
<tr>
<th>STUDY 041</th>
<th>DYSTROPHIN STUDIES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PLACEBO CONTROLLED</strong></td>
<td><strong>OPEN LABEL</strong></td>
</tr>
<tr>
<td><strong>ELIGIBILITY</strong></td>
<td><strong>ELIGIBILITY</strong></td>
</tr>
<tr>
<td>Males • Age ≥5 years</td>
<td>Males • Age 2–7 years</td>
</tr>
</tbody>
</table>
| Nonsense mutation Duchenne muscular dystrophy  
Use of corticosteroids for at least 12 months, stable for at least 3 months | Nonsense mutation Duchenne muscular dystrophy  
Ataluren naive |
| **LENGTH** | **LENGTH** |
| 72 weeks study followed by 72 week open label extension | 40 weeks |
| **PARTICIPATION REQUIREMENTS** | **PARTICIPATION REQUIREMENTS** |
| Clinic visit every 12 weeks through first 72 weeks of study, every 24 weeks in following 72 weeks of study  
Muscle function tests  
Blood tests | Needle biopsies taken from 2 muscles at 2 different time points:  
1. Study Start  
2. After 40 weeks of treatment  
4 Clinic visits  
Muscle function tests  
Blood tests |

**INTERNATIONAL STUDY SITES, INCLUDING MULTIPLE SITES IN US**  
Travel expenses for participants in the trial will be reimbursed.  
For information about contacting participation sites, please visit ClinicalTrials.gov

**MULTIPLE US STUDY SITES**  
Travel expenses for participants in the trial will be reimbursed.  
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**1 US STUDY SITE**  
Travel expenses for participants in the trial will be reimbursed.  
For information about contacting participation sites, please visit ClinicalTrials.gov

**BOYS THAT HAVE NOT BEEN PREVIOUSLY EXPOSED TO ATALUREN**  
- Nonsense mutation Duchenne muscular dystrophy  
- Ataluren naive  
- Currently taking ataluren for ≥9 months  
- Ambulatory as assessed by 10m run walk test (<30s) and Brooke upper extremity scale of 1 or 2

**BOYS THAT HAVE BEEN ON ATALUREN FOR AT LEAST 9 MONTHS**  
- Nonsense mutation Duchenne muscular dystrophy  
- Currently taking ataluren for ≥9 months  
- Ambulatory as assessed by 10m run walk test (<30s) and Brooke upper extremity scale of 1 or 2
Thank you!

Questions and information please contact:

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(732) 675-2474
BACK UP
**Patient Assistance Support**

<table>
<thead>
<tr>
<th>Program</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td><strong>Bridge Supply Program</strong></td>
<td>• PTC provides a temporary supply of drug to eligible patients in the event the insurance coverage determination is delayed for patients actively taking Emflaza.</td>
</tr>
<tr>
<td><em><em>Copay Assistance Program</em> †</em>*</td>
<td>• For patients with commercial insurance who qualify and have out-of-pocket costs when the prescription is filled ($0 copay).</td>
</tr>
<tr>
<td><strong>Alternative Funding</strong></td>
<td>• PTC Cares™ provides referrals to independent charitable patient assistance foundations that may help patients with their out-of-pocket costs, if they qualify as determined solely by the charitable foundation (NORD and TAF).</td>
</tr>
<tr>
<td><strong>Patient Assistance Program ‡</strong></td>
<td>• Program that may provide free drug to qualifying uninsured or underinsured patients.</td>
</tr>
</tbody>
</table>

*Low to no out-of-pocket costs for most patients who qualify.
†Not valid for prescriptions eligible to be reimbursed, in whole or in part, by Medicaid or Medicare (including Medicare Part D).
‡For most patients who qualify per eligibility requirements.