



Ataluren: An Investigational Dystrophin Restoration Drug for Nonsense Mutation Duchenne Muscular Dystrophy

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Parent Project Muscular Dystrophy **JOIN THE FIGHT. END DUCHENNE.**

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Saturday, June 29th 11:20–11:40 a.m.

Topics for Discussion

- Who is PTC?
- What is ataluren?
 - Ataluren mechanism of action
 - Definition of nonsense mutation
- Ataluren clinical development program
- Ongoing clinical studies
 - Studies 041, 045, and 046
- STRIDE observational real world evidence



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Forward-looking statement

- This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. All statements contained in this release, other than statements of historic fact, are forward-looking statements, including statements regarding: the future expectations, plans and prospects for PTC; expansion of commercialization of Translarna and Emflaza and related regulatory submissions; PTC's strategy, future operations, future financial position, future revenues, projected costs; and the objectives of management. Other forward-looking statements may be identified by the words "guidance", "plan," "anticipate," "believe," "estimate," "expect," "intend," "may," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions.
- PTC's actual results, performance or achievements could differ materially from those expressed or implied by forward-looking statements it makes as a result of a variety of risks and uncertainties, including those related to: the outcome of pricing, coverage and reimbursement negotiations with third party payors for Emflaza and Translarna and any other product or product candidates that PTC may commercialize in the future; whether, and to what extent, third party payors impose additional requirements before approving Emflaza prescription reimbursement; PTC's ability to complete a dystrophin study necessary to support a re-submission of its Translarna NDA for the treatment of nonsense mutation Duchenne muscular dystrophy (nmDMD) to the FDA, and PTC's ability to perform any necessary additional clinical trials, non-clinical studies, and CMC assessments or analyses at significant cost; PTC's ability to maintain its marketing authorization of Translarna for the treatment of nmDMD in the European Economic Area (EEA), including whether the European Medicines Agency (EMA) determines in future annual renewal cycles that the benefit-risk balance of Translarna authorization supports renewal of such authorization; PTC's ability to enroll, fund, complete and timely submit to the EMA the results of Study 041, a randomized, 18-month, placebo-controlled clinical trial of Translarna for the treatment of nmDMD followed by an 18-month open-label extension, which is a specific obligation to continued marketing authorization in the EEA; the eligible patient base and commercial potential of Translarna, Emflaza, or any of PTC's other products or product candidates; PTC's scientific approach and general development progress; and the factors discussed in the "Risk Factors" section of PTC's most recent Quarterly Report on Form 10-Q and Annual Report on Form 10-K, as well as any updates to these risk factors filed from time to time in PTC's other filings with the SEC. You are urged to carefully consider all such factors.
- As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. There are no guarantees that any product will receive or maintain regulatory approval in any territory, or prove to be commercially successful, including Translarna and Emflaza.
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PTC Therapeutics, Inc.

Founded over 20 years ago

Science-led, global biopharmaceutical company focused on the discovery, development and commercialization of clinically-differentiated medicines that provide benefits to patients with rare disorders

Multiple programs across genetic disorders and oncology

www.ptcbio.com



Passionate about making a difference for the rare disease community



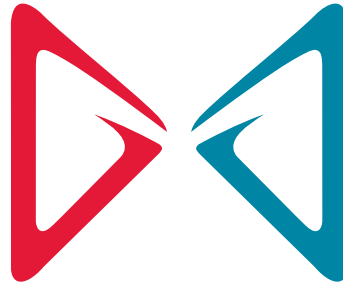
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PTC Therapeutics is the leader in Duchenne muscular dystrophy treatment with 2 of 3 approved products globally, and 1 of 2 in the US

- ✓ Ataluren is the first-ever targeted therapeutic approved for nonsense mutation Duchenne muscular dystrophy (DMD) anywhere in the world (EMA 2014; ANVISA 2019)^a
- ✓ Ataluren is now available in >40 countries worldwide ex-US and in trials for potential US approval in 2020
- ✓ Emflaza® (deflazacort) is a corticosteroid approved in the US specifically for DMD as tablet and suspension (US, 2017)
- ✓ Emflaza data demonstrate best-in-class corticosteroid for the treatment of DMD
- ✓ PTC Therapeutics is helping many thousands of families living with DMD around the world

Label expansion under
review for ataluren in
non-ambulatory patients
by the EMA



FDA approved Emflaza®
for 2-5 year old patients in
the US on June 7th 2019



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a. Ataluren is not approved by the FDA for use in the US. DMD, Duchenne muscular dystrophy; ANVISA, Brazilian National Health Surveillance Agency; EMA, European Medicines Agency; FDA, Food and Drug Administration; US, United States. https://www.ema.europa.eu/en/documents/product-information/translarna-epar-product-information_en.pdf Accessed June 2019. Bello L, et al. *Neurology*. 2015;85:1048-1055; McDonald CM, et al. *Lancet*. 2018;391:451-461; <http://ir.ptcbio.com/news-releases/news-release-details/ptc-therapeutics-receives-fda-approval-expansion-emflaza> Accessed June 2019.

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Ataluren overview

- Conditionally approved in Europe for ambulatory patients 2 years and older with DMD caused by a nonsense mutation
- Available to boys in over 40 countries through commercial and PTC-ACTs
- Active discussions with the FDA regarding approval in the US
 - A clear pathway forward has been provided
 - Additional clinical study required
 - Resubmission upon completion of clinical study
- Ataluren is considered an investigational product in the US



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DMD, Duchenne muscular dystrophy; FDA, Food and Drug Administration; US, United States.
https://www.ema.europa.eu/en/documents/product-information/translarna-epar-product-information_en.pdf
Accessed June 2019.

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Ataluren overview



Taken orally 3x a day; recommended dosage:

- 10 mg/kg in the morning
- 10 mg/kg at midday
- 20 mg/kg in the evening (total daily dose of 40 mg/kg)



- Slows progression of the disease
- Allows patients to walk longer and stay more physically able
- Fewer accidental falls
- Preserves lung function
- Improves quality of life scores
- Generally well tolerated
 - Adverse reactions were generally mild or moderate in severity, and no treatment-related serious adverse events were reported



The positive risk/benefit profile prompted EMA conditional approval in 2014 and ANVISA approval in Brazil in 2019

See table in Section 4.2 of the Translarna Summary of Product Characteristics for recommended dosing by body weight range. ANVISA, Brazilian National Health Surveillance Agency. EMA, European Medicines Agency.

https://www.ema.europa.eu/en/documents/product-information/translarna-epar-product-information_en.pdf Accessed June 2019. Bushby K, et al. Muscle Nerve. 2014;50:477–487. McDonald CM, et al. Lancet. 2017;390:1489–1498.



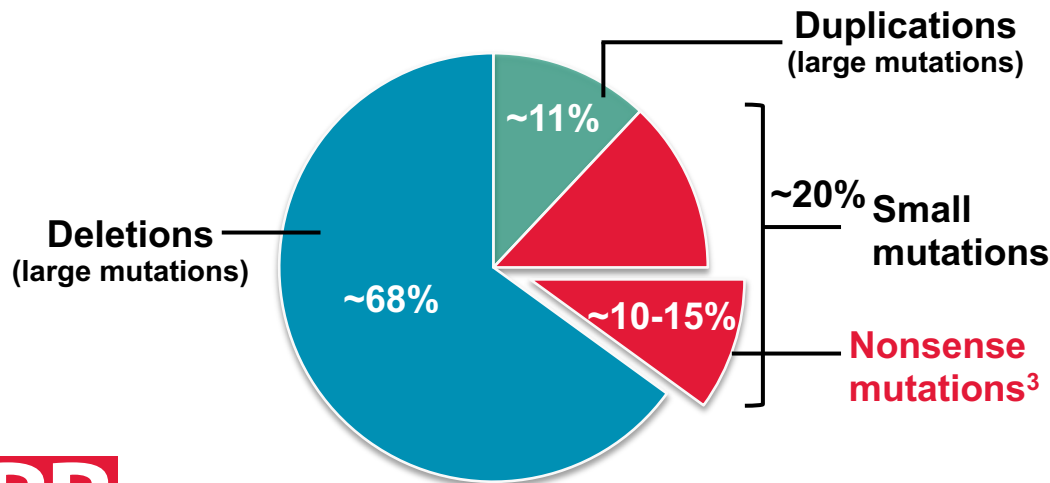
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Epidemiology and genetics of DMD

Incidence of DMD
1:3,600–6,000
Live male births

~20,000
Children are
diagnosed with
Duchenne globally
each year



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Bushby K, et al. *Lancet Neurol.* 2010;9:77-93; Aartsma-Rus A, et al. *J Med Genet.* 2016;53:145-151; McDonald CM, et al. *Muscle Nerve.* 2013;48:343-356; Bladen CL, et al. *Hum Mutat.* 2015;36:395-402; Pichavant C, et al. *Mol Ther.* 2011;19:830-840.

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How ataluren works

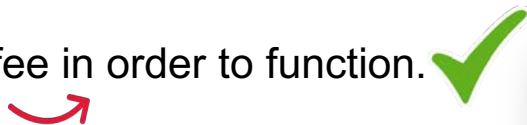
- A nonsense mutation in the dystrophin gene creates a premature termination that forms a shortened, non-functional dystrophin protein
- A nonsense mutation is like putting a period in the middle of a sentence:

I need coffee in. order to function.

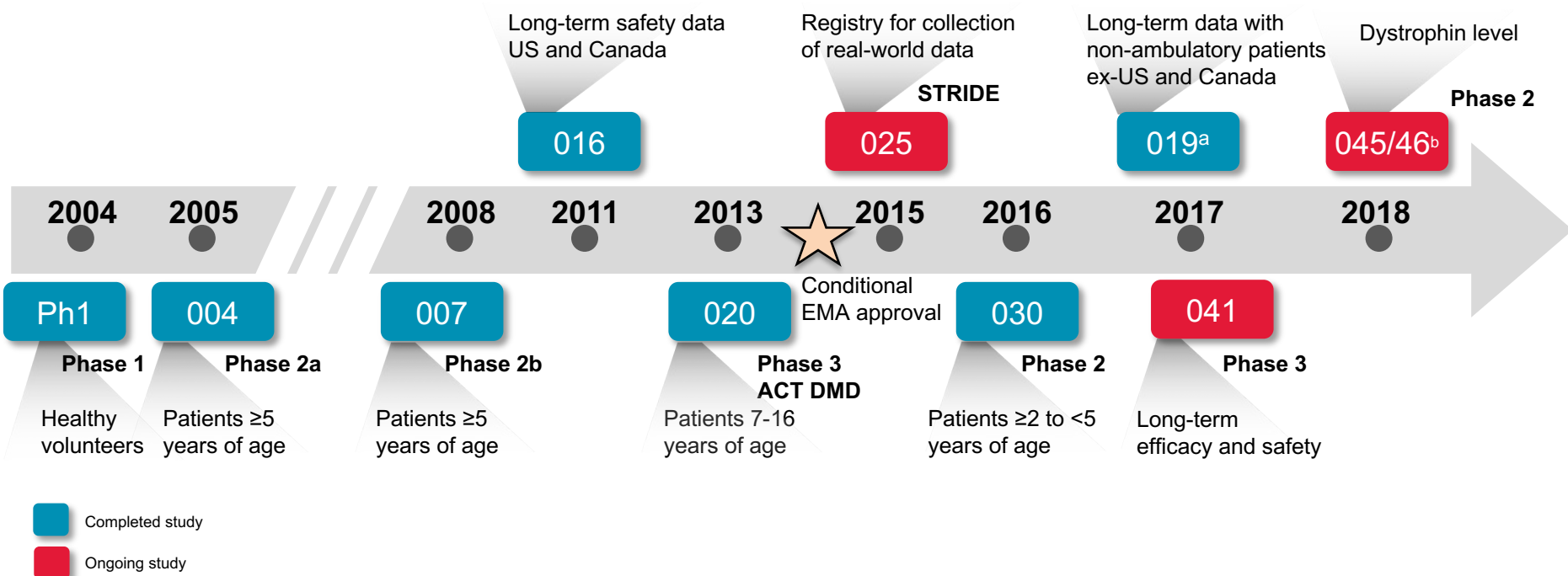


- Ataluren *bypasses* the nonsense mutation and allows for formation of a full-length, functional dystrophin protein

I need coffee in order to function.



Clinical trial program for ataluren approval



^aEndpoints updated in 2017. ^bStudy 045 is in an ataluren-naïve patient population; Study 046 includes patients who were previously treated with ataluren. ACT DMD=Ataluren Confirmatory Trial in Duchenne Muscular Dystrophy; EMA=European Medicines Agency; STRIDE=Strategic Targeting of Registries and International Database of Excellence.

https://www.ema.europa.eu/en/documents/product-information/translarna-epar-product-information_en.pdf Accessed June 2019.



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Ongoing ataluren clinical studies

STUDY 041

A clinical study to determine the long-term effect of ataluren

PLACEBO CONTROLLED

ELIGIBILITY

Males  Age ≥ 5 years

- Nonsense mutation Duchenne muscular dystrophy
- Use of corticosteroids for at least 12 months, stable for at least 3 months

LENGTH

72 weeks study followed by 72 week open label extension

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

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](https://clinicaltrials.gov)

DYSTROPHIN STUDIES

Clinical studies to determine the ability of ataluren to increase dystrophin levels

Boys that have not been previously exposed to ataluren

OPEN LABEL

ELIGIBILITY

Males  Age 2–7 years

- Nonsense mutation Duchenne muscular dystrophy
- Ataluren naive

STUDY 045

LENGTH

40 weeks

PARTICIPATION REQUIREMENTS

- 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

MULTIPLE US STUDY SITES

Travel expenses for participants in the trial will be reimbursed.

For information about contacting participation sites,
please visit [ClinicalTrials.gov](https://clinicaltrials.gov)

Boys that have been on ataluren for at least 9 months

OPEN LABEL

ELIGIBILITY

Males 

- Nonsense mutation Duchenne muscular dystrophy
- Currently taking ataluren for ≥ 9 months
- Ambulatory as assessed by 10m run walk test (<30 s) and Brooke upper extremity scale of 1 or 2

LENGTH

1 clinic visit followed by a phone call ~1 week after

PARTICIPATION REQUIREMENTS

- Needle biopsies taken from 2 muscles 1 time only
- 1 visit, followed by a phone call
- Muscle function tests
- Blood tests

STUDY 046

1 US STUDY SITE

Travel expenses for participants in the trial will be reimbursed.

For information about contacting participation sites,
please visit [ClinicalTrials.gov](https://clinicaltrials.gov)



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NCT03179631; NCT03648827; NCT03796637

https://www.ema.europa.eu/en/documents/product-information/translarna-epar-product-information_en.pdf Accessed June 2019.

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If you would like to participate

- Confirm that the dystrophin mutation is a nonsense mutation
- Review the inclusion and exclusion criteria with your physician
- If you feel your son is a candidate for one of the studies contact the following study sites:
 - Study 041: Contact details available on 2 websites: www.clinicaltrials.gov and www.dmdstudy041.com
 - Study 045: Dystrophin study for ataluren-naïve boys: Principal investigator sites listed on www.clinicaltrials.gov
 - **Study 046 recruitment completed:** Dystrophin study for those on ataluren for at least nine months
- Additional questions: Mary Frances Harmon mharmon@ptcbio.com

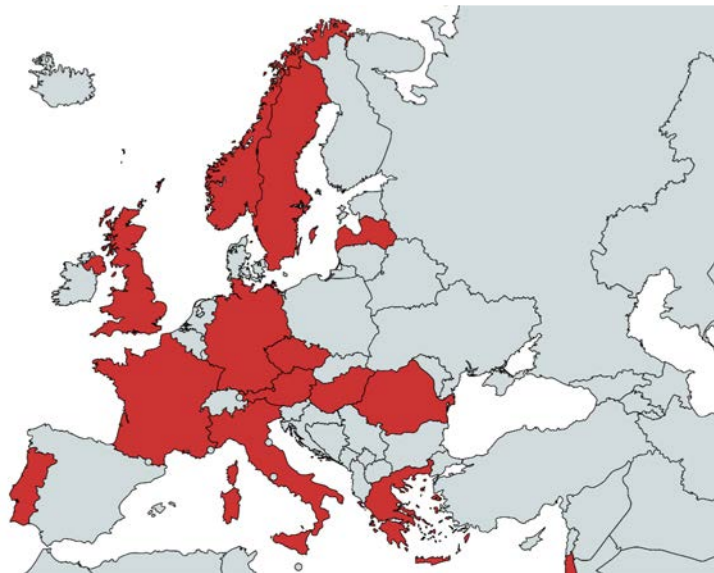


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STRIDE Registry



- Post-approval registry to obtain long-term real world evidence on the safety and effectiveness of ataluren
- Observational study of ataluren and the utilization patterns in routine clinical practice

Thank you

We thank the boys and their families for their participation in these studies; individuals who were instrumental in the conduct of the studies and the collection of data – in particular, principal investigators, supporting investigators, clinical coordinators, clinical evaluators, and study coordinators



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Questions?



Thank you!