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Translarna Deep Dive

December 15, 2020

Forward Looking Statements

This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. All statements contained in this presentation, other than statements of historic fact, are forward-looking statements, including statements regarding: the future expectations, plans and prospects for PTC, including with respect to the expected timing of clinical trials and studies, availability of data, regulatory submissions and responses and other matters; PTC's expectations with respect to the licensing, regulatory submissions and commercialization of its products and product candidates; 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 PTC's products or product candidates that PTC commercializes or may commercialize in the future; 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; significant business effects, including the effects of industry, market, economic, political or regulatory conditions; changes in tax and other laws, regulations, rates and policies; the eligible patient base and commercial potential of PTC's products and 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.

The forward-looking statements contained herein represent PTC's views only as of the date of this presentation and PTC does not undertake or plan to update or revise any such forward-looking statements to reflect actual results or changes in plans, prospects, assumptions, estimates or projections, or other circumstances occurring after the date of this call except as required by law.

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20 years of pioneering and leadership in Duchenne muscular dystrophy

- PTC has pioneered the understanding of DMD progression and natural history
- Established commercial infrastructure bringing Translarna™ and Emflaza® to DMD patients globally
- Enduring relationships with patient advocacy groups and treating physicians
- Translarna – the first and only approved dystrophin restoration therapy addressing the underlying cause of nonsense mutation DMD

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DMD is a relentlessly progressive, fatal, genetic disorder

- Debilitating X-linked genetic disorder leading to death in early adulthood
- 1 in every 3,500-5,000 live male births with ~13% caused by nonsense mutations
- Caused predominantly by the lack of dystrophin protein due to mutations that prevent its production

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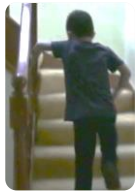
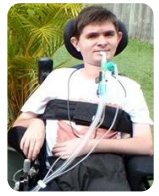
Average age of diagnosis for DMD boys is ~5 years of age with rapid decline in motor and pulmonary function

Birth | Age 5 | Age 10 | Age 15 | Age 20 | Age 25 | Age 30

EARLY physical manifestations

- Impaired ability to hop, run, jump, rise
- Loss of stair climb
- Loss of stair descend

LATE physical manifestations

- Loss of ambulation
- Loss of upper limb function
- Ventilation
- Death

Loss of ambulation is predictive of late physical manifestations

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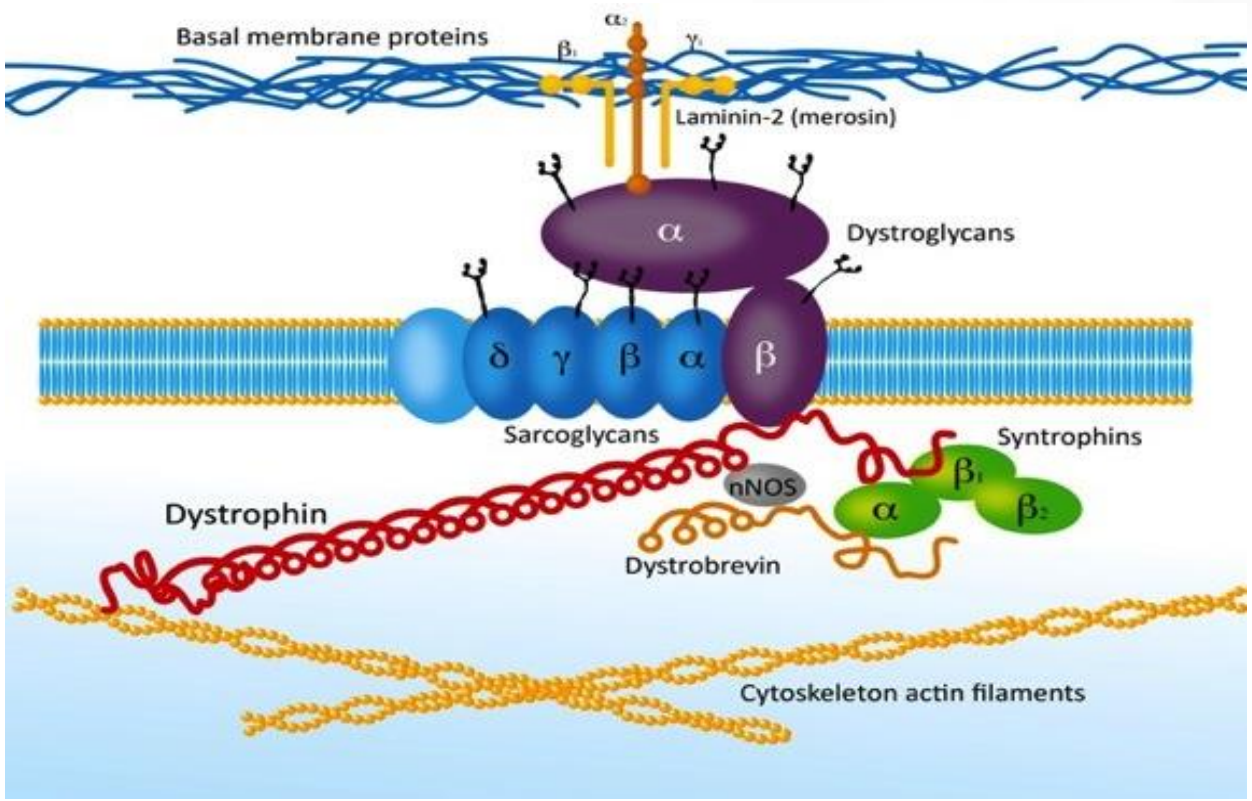
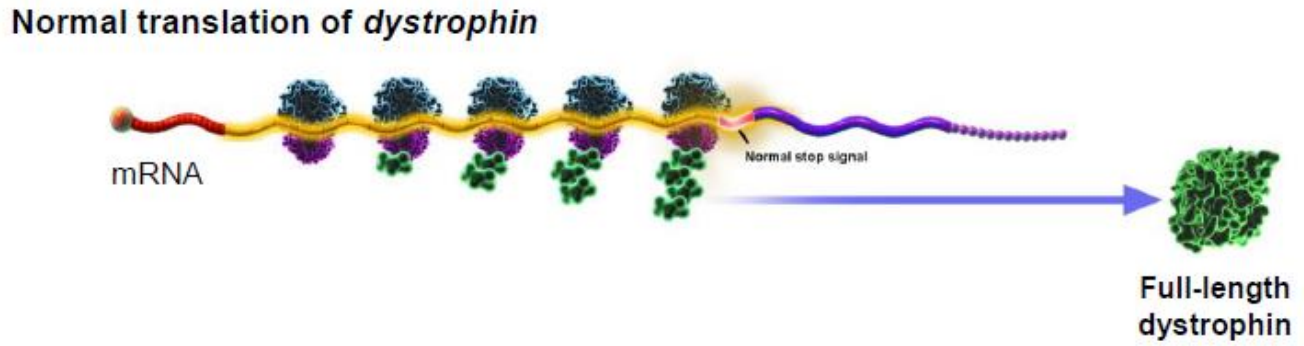
Dystrophin acts as a shock absorber in muscle cells

- Dystrophin connects the cytoskeleton to extracellular matrix and is critical during muscle contractions
- Muscles lacking dystrophin are more susceptible to damage
- Damaged dystrophin is replaced by fatty and connective tissue
- Once muscle is lost it cannot be regained
- Dystrophin restoration is expected to prevent muscle damage



Adapted from Geomans N, *et al.* 2014[4]

Translarna enables the production of full-length, functional dystrophin



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mRNA, messenger ribonucleic acid.
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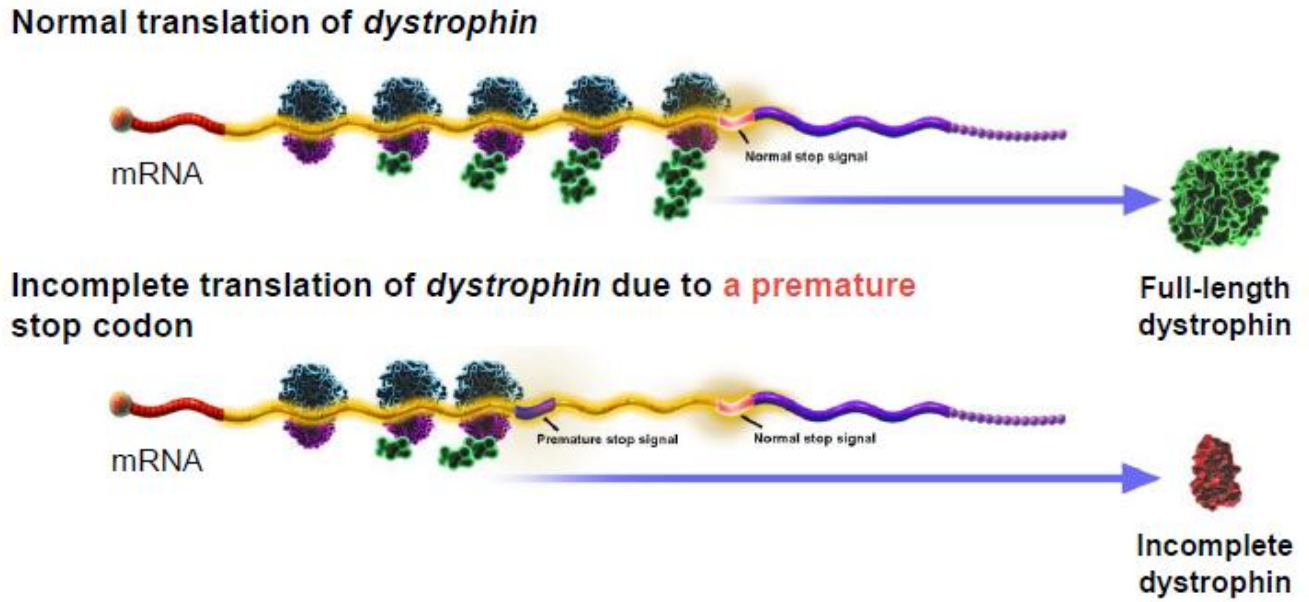

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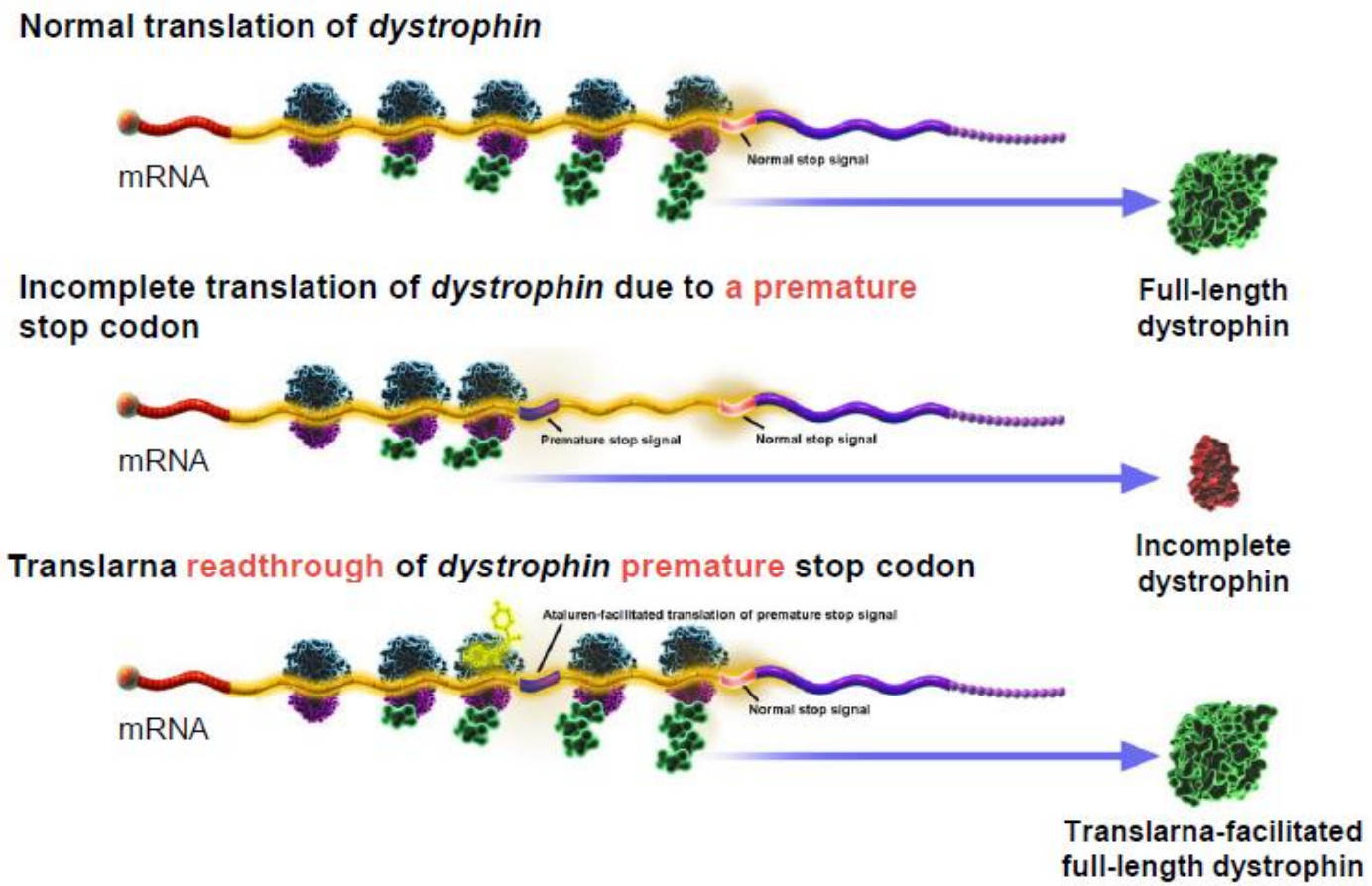

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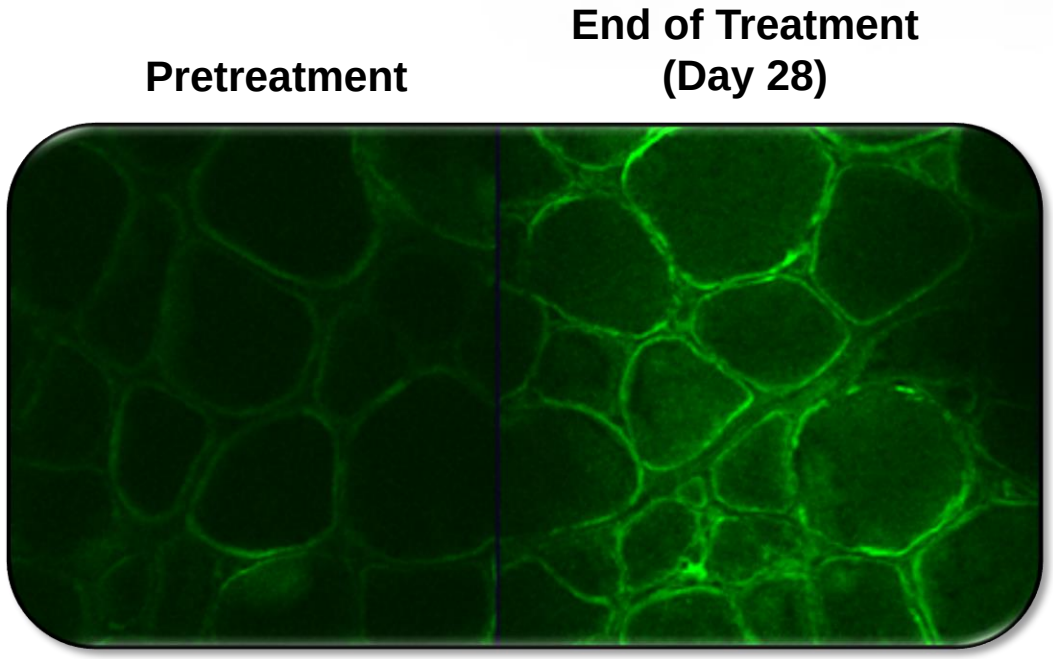
Proof of concept study supported larger trials with clinical endpoints

Phase 2a study

- Key finding: 61% of patients showed an increase in dystrophin staining after 28 days of treatment; the mean increase in dystrophin was 11%



Immunofluorescence assay

P = 0.008

Finkel 2013

Multiple Studies Provide Evidence of Translarna Benefit

2005-2007

Study 004 (Dystrophin Study) 28 days N=38

Production of full length dystrophin

2008-2009

Study 007 (RCT) 48 weeks N=174

Identified dose

Consistent results across multiple endpoints

2013-2015

Study 020 (RCT) 48 weeks N=228

Consistent results across multiple endpoints

Benefits in light of natural history

2012 - 2017

Study 019 (Long-term Study) ~3.5 years* N=94

Preservation of pulmonary function

*Median exposure

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Multiple Studies Provide Evidence of Translarna Benefit

Trials and registries

Study	Design
Phase 2b[2] (Study 007)	48-week, randomised, controlled study assessing the efficacy and safety of Translarna in patients aged ≥5 years
Phase 3[3] (Study 020)	48-week, randomised, controlled study assessing the efficacy and safety of Translarna in patients aged ≥7 to ≤16 years
Study 030[4]	Phase 2, 52-week, open-label study to evaluate the safety, pharmacokinetics and exploratory efficacy of Translarna in patients ≥2 to <5 years
Study 019[1]	Phase 3, 268-week, open-label study to evaluate the long-term safety of Translarna
STRIDE Registry[5]	Ongoing registry to evaluate long-term safety and effectiveness of Translarna in routine clinical practice

Meta-analyses

Study	Design
Pre-specified meta-analysis[3]	Included patients from the Phase 3 study and the patients from the Phase 2b study who met Phase 3 inclusion criteria (including baseline 6MWD ≥150 m and ≤80% of predicted, aged ≥7 to ≤16 years and receiving corticosteroids)
Post hoc meta-analysis[1]	Included all patients with baseline 6MWD ≥300 to <400 m from the Phase 3 and Phase 2b studies

† As of 31 July, 2020.

* Some patients included in this total will previously have been enrolled in a Translarna clinical trial. Phase 2b and 3 studies did not meet their primary endpoints. Patients in the treatment arm of Phase 2b received Translarna 10/10/20 mg/kg/day or 20/20/40 mg/kg (not approved dose). 6MWD, 6-minute walk distance; STRIDE, Strategic Targeting of Registries and International Database of Excellence.

1. PTC, Data on File. 2. Bushby K, *et al. Muscle Nerve*. 2014;50:477–487. 3. McDonald CM, *et al. Lancet*. 2017;390:1489–1498. 4. Tian C, *et al.* Presented at the 15th International Congress on Neuromuscular Diseases, 6–10 July 2018, Vienna, Austria. 5. Delage A, et al. Long-term efficacy of ataluren for the treatment of nonsense mutation Duchenne muscular dystrophy: observational data from the STRIDE Registry. Poster presented at the 23rd International Annual Congress of the World Muscle Society, October 2–6, 2018, Mendoza, Argentina.

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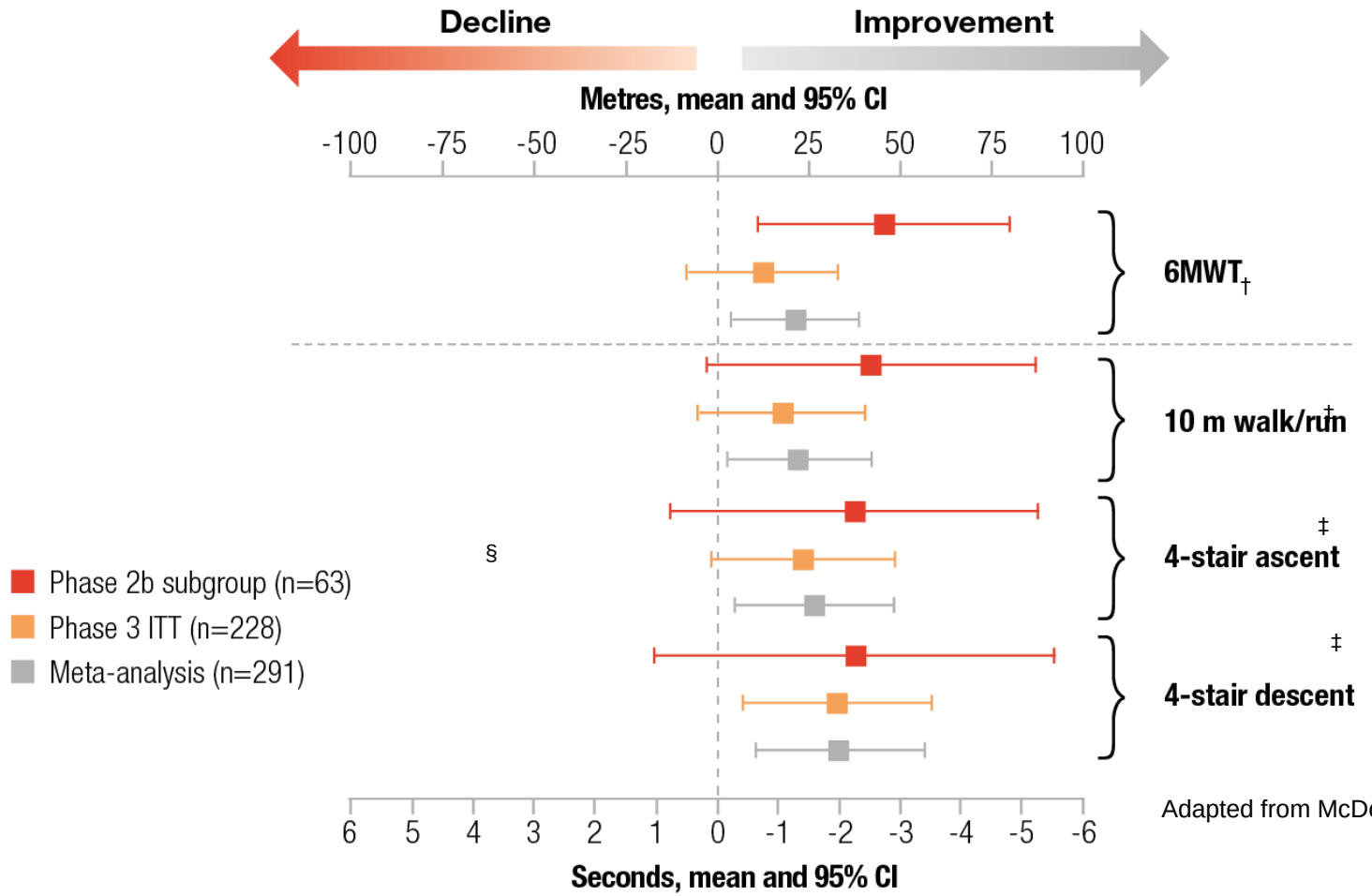
Totality of data shows a consistent treatment effect for Translarna across multiple endpoints*[1]



Meta-analysis LS mean difference (SEM)
21.1 (9.0) m
–1.4 (0.6) s
–1.6 (0.7) s
–2.0 (0.7) s

Adapted from McDonald CM, *et al*. 2017[1]

Phase 2b and 3 studies did not meet their primary endpoints. *In children aged ≥7 to ≤16 years old. † Primary endpoint. ‡ Secondary endpoint. § Patients from the Phase 2b study that met ACT DMD inclusion criteria. The meta-analysis included patients from the Phase 2b subgroup matching the entry criteria for the Phase 3 trial. 6MWD, 6-minute walk distance; CI, confidence interval; LS, least-squares; SEM, standard error of the mean. 1. McDonald CM, *et al. Lancet.* 2017;390:1489–1498.

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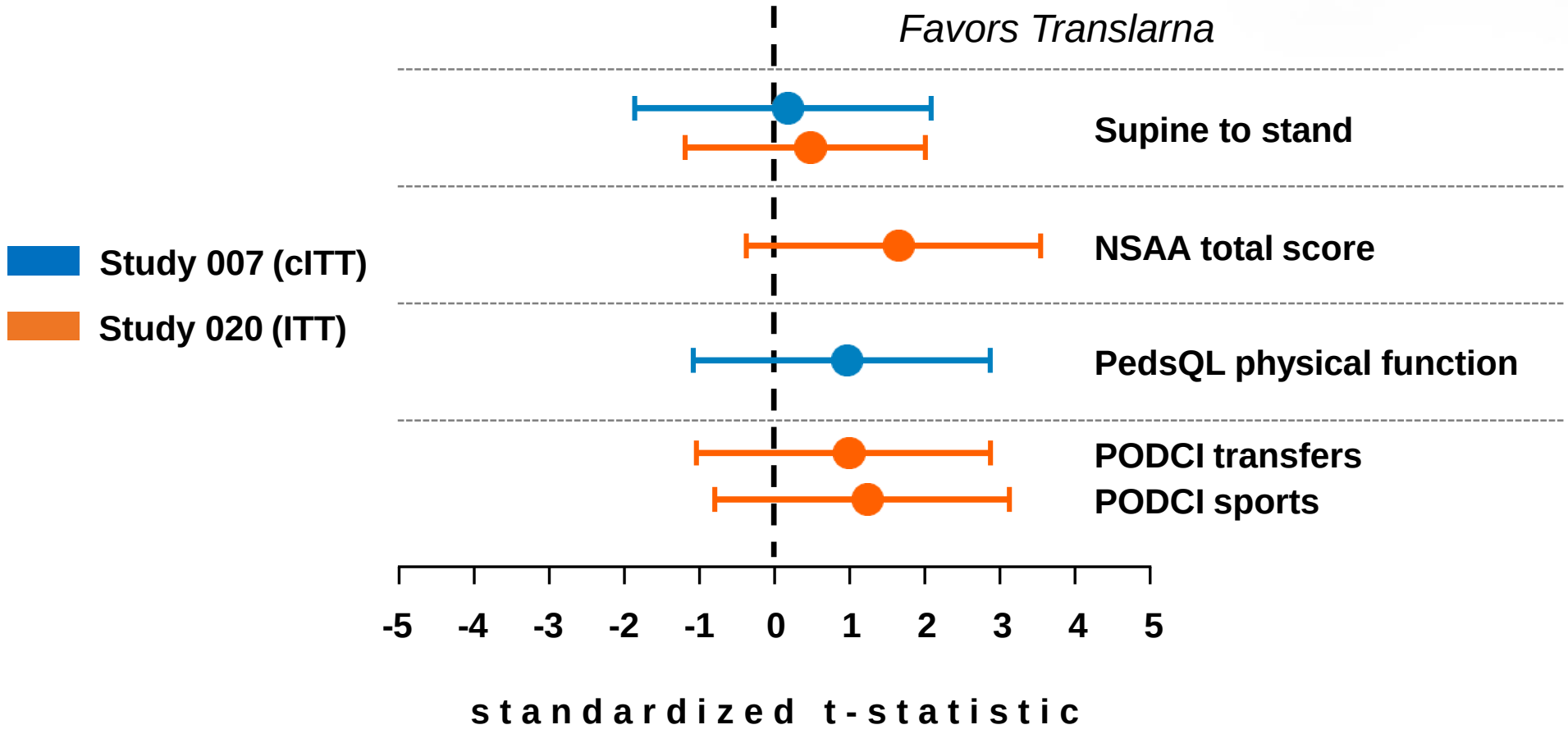

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STRIDE is a real-world registry of nmDMD patients that demonstrates Translarna meaningfully delays disease progression

Translarna treatment demonstrates a meaningful slowing of progression of DMD

- Multicentre registry study, evaluating the **long-term** safety and efficacy in a real-world setting
- Includes nmDMD patients with varied demographics, providing data that is representative of real-world patient experiences
- **Over ~250 patients to be followed for 5 years**

Mercuri E, *et al. J Comp Eff Res.* 2020;doi:10.2217/cer-2019-0171 [Epub ahead of print]

Translarna Summary of Product Characteristics.

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STRIDE is a real-world registry of nmDMD patients that demonstrates Translarna meaningfully delays disease progression

Translarna treatment demonstrates a meaningful slowing of progression of DMD

- Analysis of the STRIDE Registry shows that Translarna + standard of care (SoC) compared to SoC alone meaningfully delayed:
  - Loss of ambulation, providing an additional 3.5 years
  - Loss of physical function, as measured by delayed decline in time function tests (TFT)
  - Loss of pulmonary function, as measured by delayed decline in forced vital capacity (FVC)
- Findings indicate that long-term treatment with Translarna is well-tolerated by patients in the real world

Mercuri E, *et al. J Comp Eff Res.* 2020;doi:10.2217/cer-2019-0171 [Epub ahead of print]

Translarna Summary of Product Characteristics.

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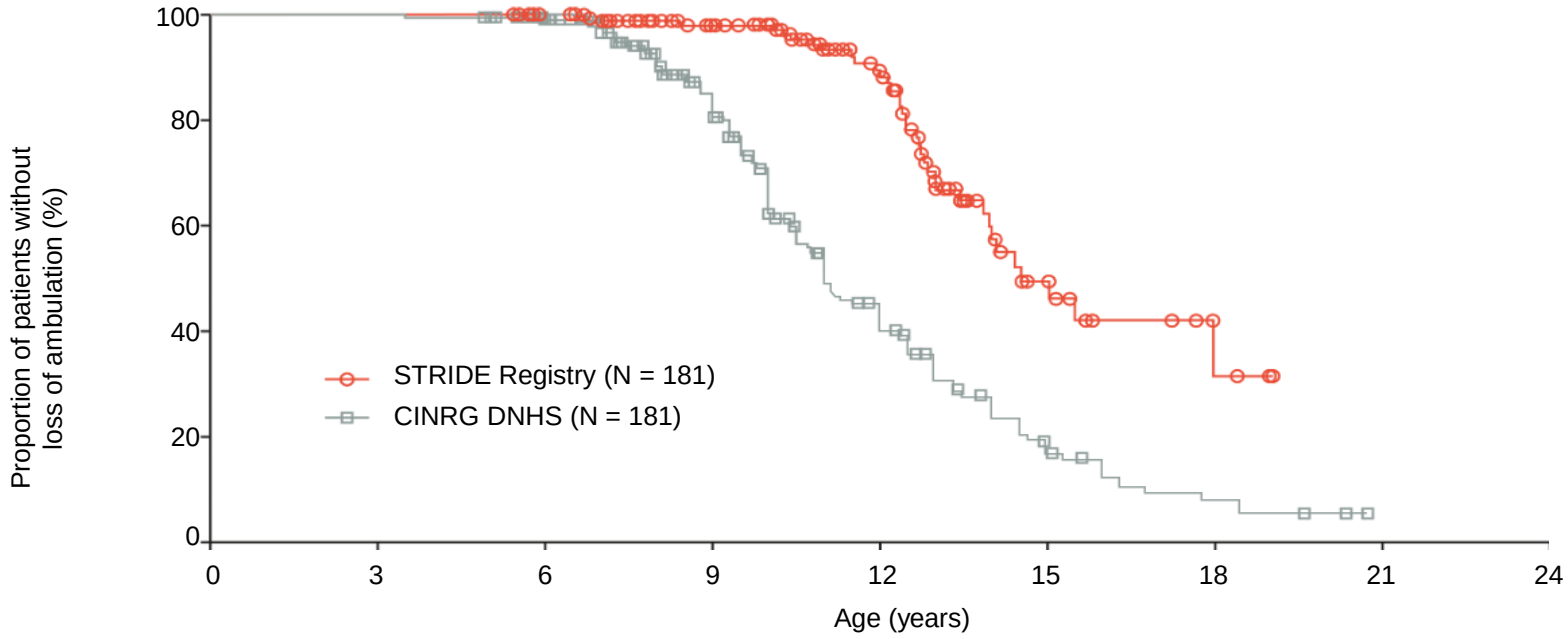
Translarna delays loss of ambulation by 3.5 years when compared to DMD natural history



Number of patients at risk									
STRIDE	181	181	170	124	67	16	3	0	0
CINRG	181	181	170	115	52	17	6	0	0

Number of patients	STRIDE (n = 181)	CINRG DNHS (n = 181)
Assessed, n	181	181
Loss of ambulation, n (%)	36 (19.9)	112 (61.9)
Censored, n (%)	145 (80.1)	69 (38.1)
Age at loss of ambulation, years		
Median (95% CI)	**14.5** (13.9, NA)	**11.0** (10.5, 12.0)
Min, max*	5.4+, 19.0+	3.5, 20.8+
P value†	**<0.0001**	
Hazard ratio (95% CI)	0.283 (0.190, 0.422)	

Figure adapted from Mercuri E, *et al. J Comp Eff Res* 2020;doi:10.2217/cer-2019-0171 [Epub ahead of print].

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Poor pulmonary function in DMD patients is directly linked to patient mortality

FVC ≤ 60% predicted

Need for lung volume recruitment (physical therapy)[1]

FVC < 50% predicted

Need for nocturnal assisted ventilation[1]

FVC < 1L

Predictive of mortality within 3 years[2]

FVC, forced vital capacity.

Birnkrant DJ, *et al. Lancet Neurol.* 2018;17(4):347–361
Philips MF, *et al. Am J Respir Crit Care Med.* 2001;164:2191–2194.

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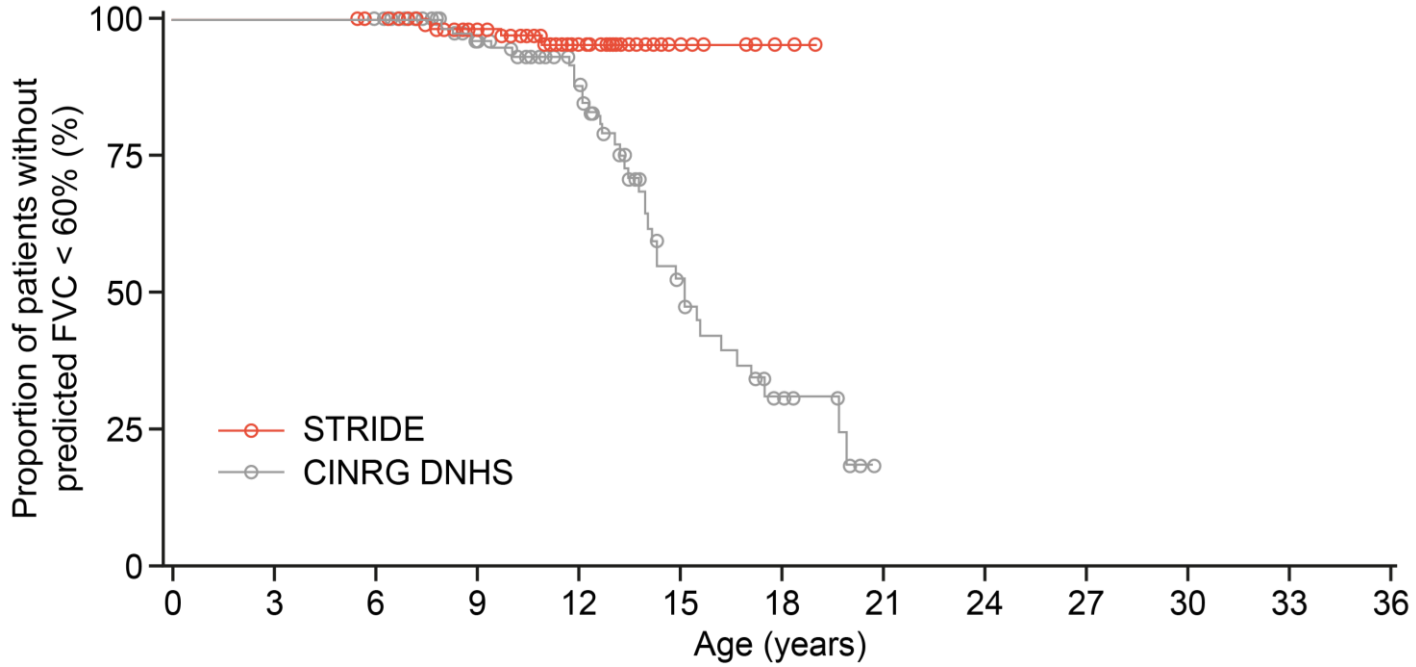
Translarna shows a significant benefit in preventing loss of pulmonary function in DMD patients

FVC < 60%



Number of patients at risk

STRIDE	123	123	119	90	46	14	3	0	0	0	0	0	0
CINRG	96	96	96	69	52	21	8	0	0	0	0	0	0

Number of patients	Predicted FV < 60% STRIDE (n = 181)	Predicted FV < 60% CINRG (n = 181)
Assessed, n	123	96
With events*	4 (3.3)	35 (36.5)
Censored	119 (96.7)	61 (63.5)
Age at event, years		
Median (95% CI)	NA (NA, NA)	15.1 (14.0, 17.1)
Min, max†	5.4+, 19.0+	6.0, 20.7+
P value‡	<0.0001	
Hazard ratio (95% CI)§	0.148 (0.052, 0.426)	

Figures adapted from Tulinius M, *et al.* 26th International Annual Congress of the World Muscle Society (WMS); 2019; Copenhagen, Denmark and Mercuri E, *et al. J Comp Eff Res* 2020;doi:10.2217/cer-2019-0171 [Epub ahead of print].

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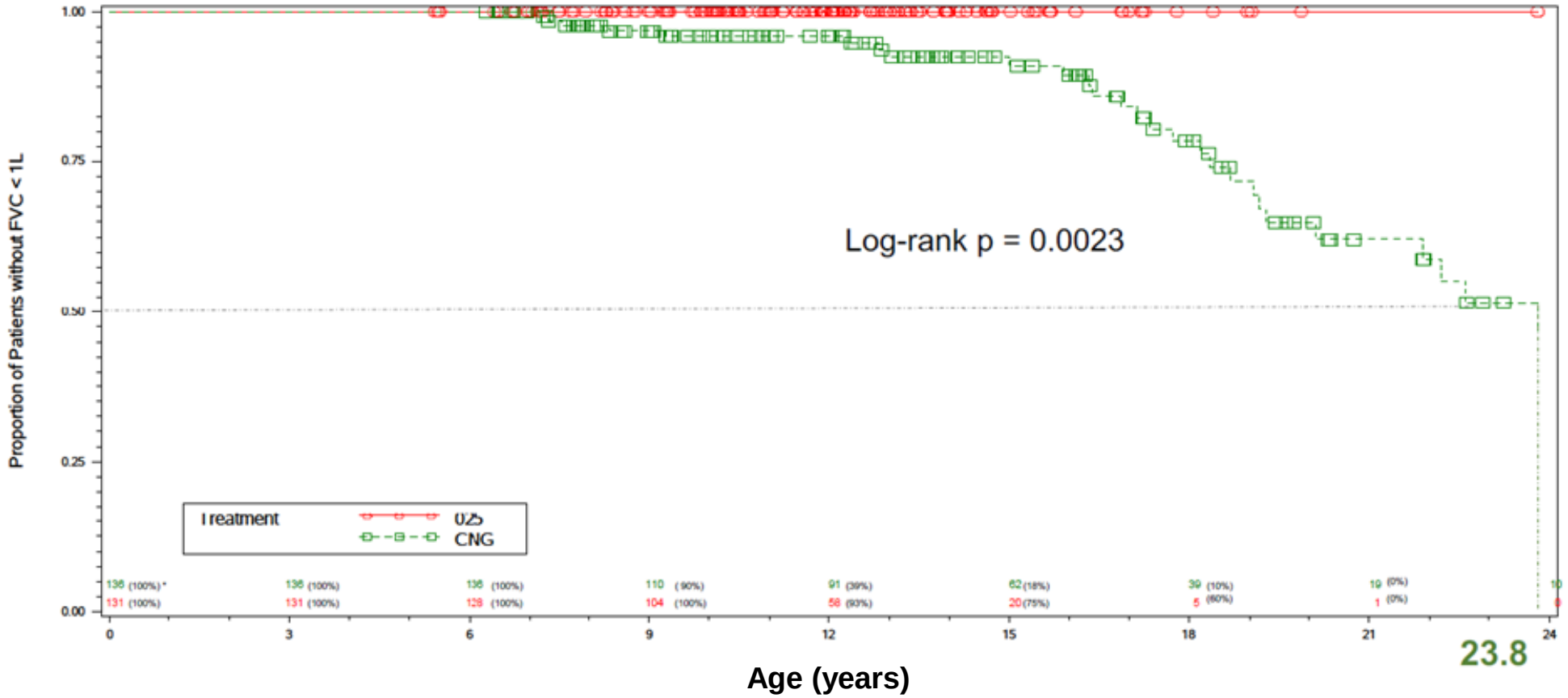
Translarna shows a significant benefit in preventing loss of pulmonary function in DMD patients

Age at FVC <1L



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Study 041 designed on PTC's developed knowledge of DMD

Eligibility Criteria

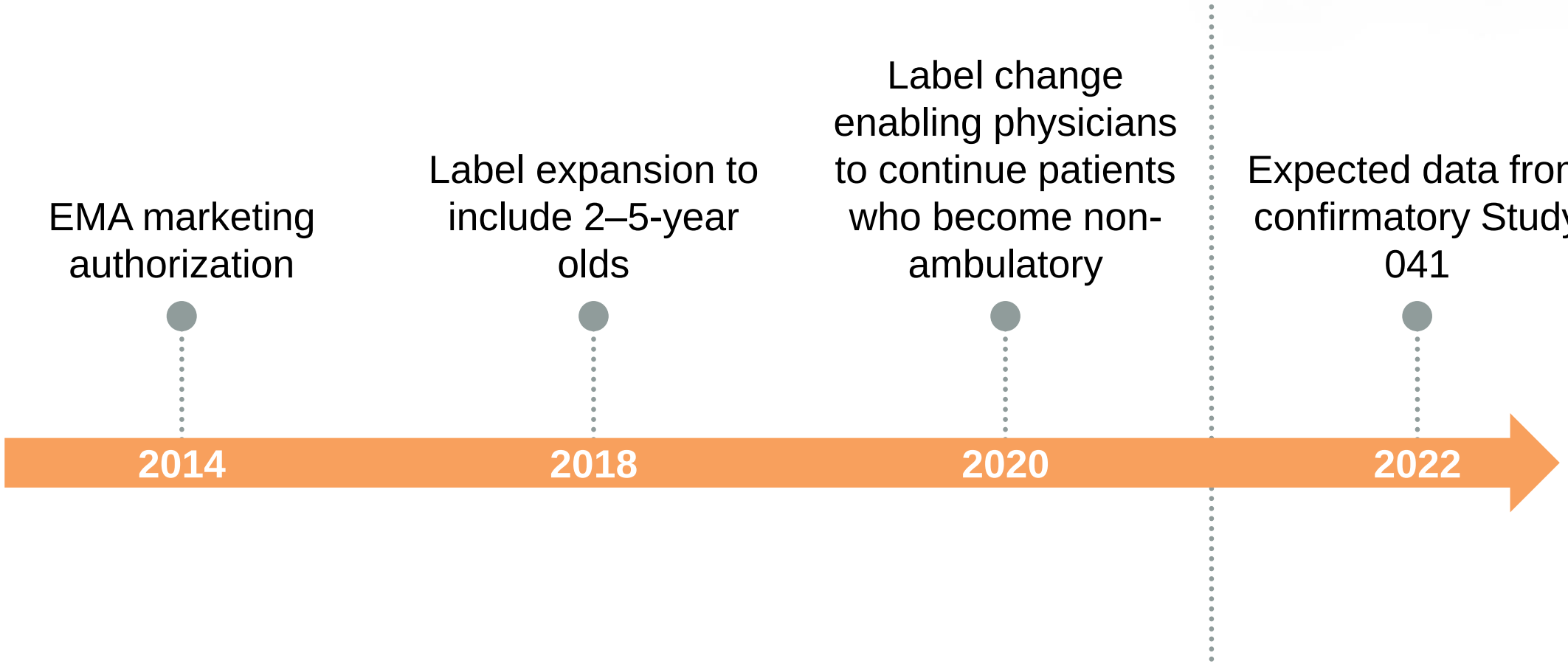
- ≥5 years old and 6MWD ≥150 meters
- Stand from supine and time function

Outcome Measures

- Primary endpoint: 6MWT
- Secondary endpoints: TFTs, NSAA, PFTs

- Broad population with comprehensive endpoints and 18-month trial duration (N=363)

EMA regulatory history continues to support the positive risk-benefit of Translarna



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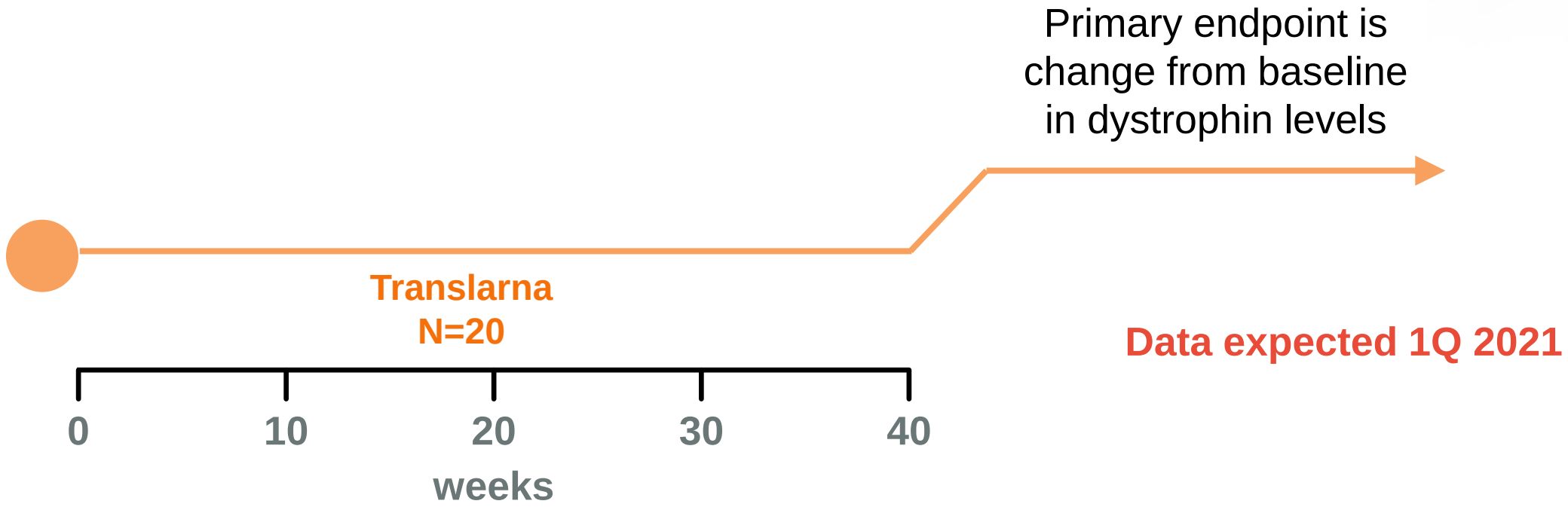
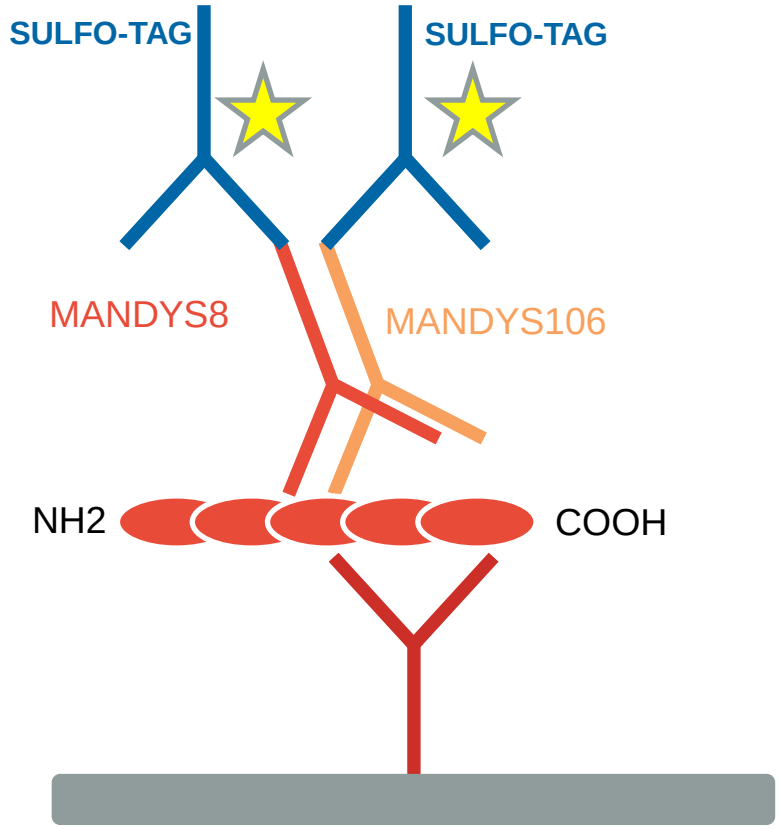
Study 045 provides a potential opportunity for accelerated approval in the US



Data expected 1Q 2021

Dystrophin detection done by ELISA assay

Electrochemiluminescence (ECL) provides sensitive and linear detection of dystrophin



- Assay developed in collaboration with FDA
- Intended to address challenges with western blot
- Able to detect lower levels of dystrophin
- Highly quantitative linear results

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Strategies for potential FDA approval

Biomarker Path → **Sub Part H**

Study 045

Data 1Q 2021

Clinical Data Path → **Part D**

Study 041

Data 3Q 2022

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Translarna's strong global commercial presence helps thousands of patients

2014
Approved by EMA

>Access
EMA label changes and additional approvals

>90%
Compliance rate in treated patients

Growth
Geographic expansion and increased penetration

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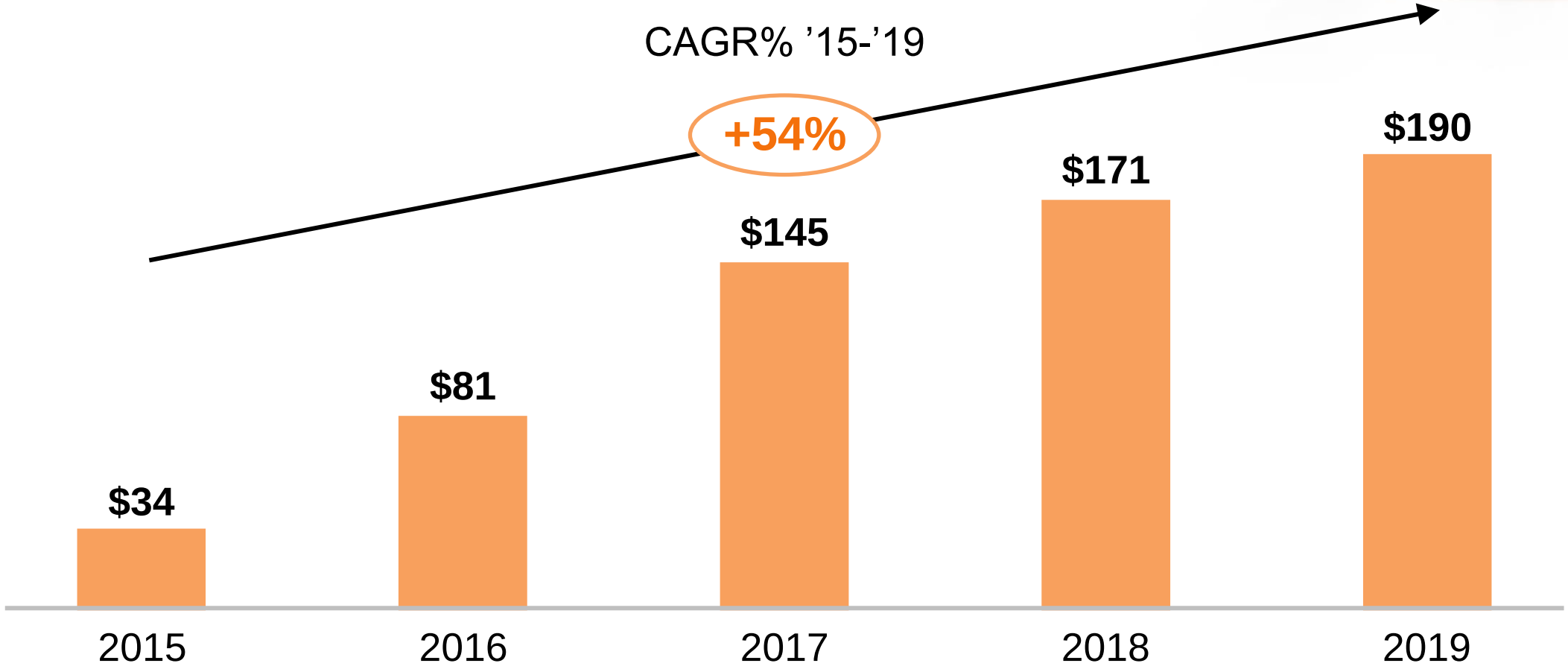
Strong global commercial growth since approval

Translarna Revenue 2015-2019

USD Millions



Translarna Approval 4Q 2014 – total revenue $1M

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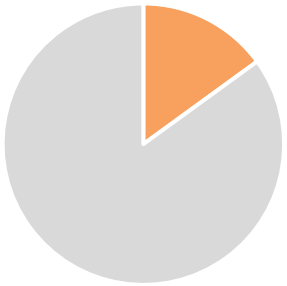
Well-positioned for rapid US launch



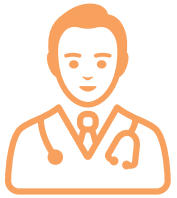
~10 - 15K

Total DMD patients in the US

10-15% have a nonsense mutation

Emflaza® (deflazacort)

Established US DMD leadership position with our commercial infrastructure



>20 years

of building relationships with DMD pediatric neurologists and patient advocacy groups

~150

US nmDMD patients from clinical trials on Translarna for over 10 years

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Q&A