



Analyst and Investor Call to Review DMD Gene Therapy Presentation at ASGCT

May 15, 2020

Breakthroughs that
change patients' lives

Disclaimer

This presentation includes forward-looking statements about, among other things, development of Pfizer's Rare Disease products and product candidates, including our investigational mini-dystrophin gene therapy (PF-06939926), a potential Phase 3 study, our manufacturing capabilities and capacity, and their potential benefits, that are subject to substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. These statements are subject to risks, uncertainties and other factors that may cause actual results to differ materially from past results, future plans and projected future results.

Additional information regarding these factors can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 and in our subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors that May Affect Future Results," as well as in our subsequent reports on Form 8-K, all of which are filed with the US Securities and Exchange Commission (SEC) and available at www.sec.gov and www.pfizer.com.

The forward-looking statements in this presentation speak only as of the original date of this presentation, and we undertake no obligation to update or revise any of these statements.



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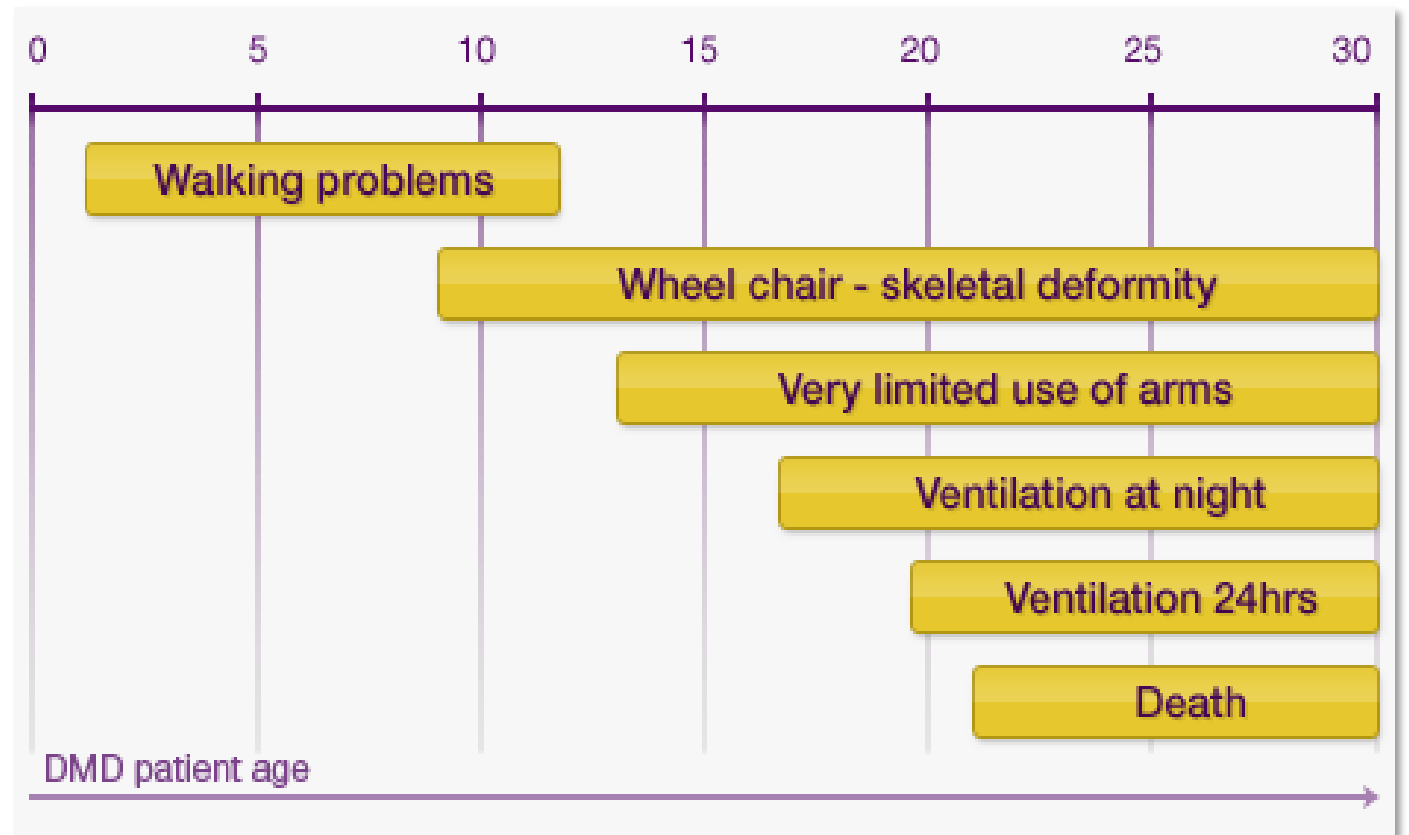
Introduction

Mikael Dolsten, M.D., Ph.D.

Chief Scientific Officer and President, Worldwide
Research, Development, and Medical, Pfizer

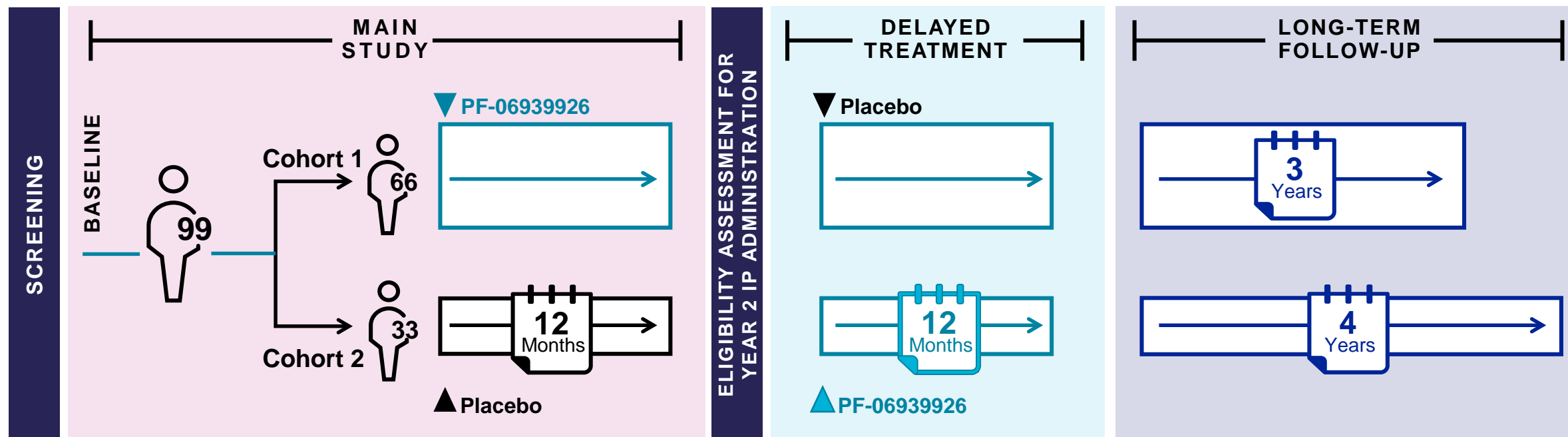
Duchenne Muscular Dystrophy

- **Hereditary severe X-linked muscular dystrophy**
 - incidence 1:3500-5000 / male live births
 - absent functional dystrophin protein reduces structural integrity of muscle fibers
- **Delays in motor milestones**
 - diagnosis at ~2-5 years of age
 - sometimes cognitive impairment
- **Loss of ambulation**
- **Progressive cardiac and respiratory failure**

















Study Design for Phase 3 Expected to Begin Dosing in 2H 2020

- A Phase 3, global, multicenter, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of PF-06939926 in ambulatory male patients with DMD
- Eligible patients will be randomized into 2 groups: either Cohort 1 or Cohort 2 in a 2:1 ratio
- All patients will be followed for 5 years after treatment with investigational gene therapy (PF-06939926)



A Leading Rare Disease Pipeline With 6 New Molecular Entities Expected to be in Phase 3 Studies by 2H 2020

	Rare Hematology	Rare Neurology	Rare Endocrine / Metabolic	Rare Cardiology
In line	  Antihemophilic Factor (Recombinant) 	 (tafamidis)	 (pegvisomant for injection)  (taliglucerase alfa) for injection 	 (tafamidis) 61 mg capsules
Phase 3	 Hemophilia B  Hemophilia A Pan Hemophilia		Growth Hormone Deficiency	LMNA-Related Dilated Cardiomyopathy
Phase 1 & 2	Sickle Cell Disease (E-Selectin)	 Duchenne Muscular Dystrophy Autoimmune Disease	Achondroplasia	
Pre-Clinical	Sickle Cell Disease (HbS)	 Amyotrophic Lateral Sclerosis	 Wilson Disease	



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Gene Therapy (GTx)

Significant Investment in Gene Therapy Manufacturing of Viral Vectors to Support Rapid Drug Development and Access

Leader in the Manufacture of AAV Vectors using Mammalian Cells:

- Three manufacturing facilities (~300,000 sq ft) designed to support DMD and multiple other gene therapy programs in parallel, depending on dose and product mix, by 2022; built for growth
- Internal end-to-end gene therapy manufacturing capabilities across research-development-commercial axis to support rapid access



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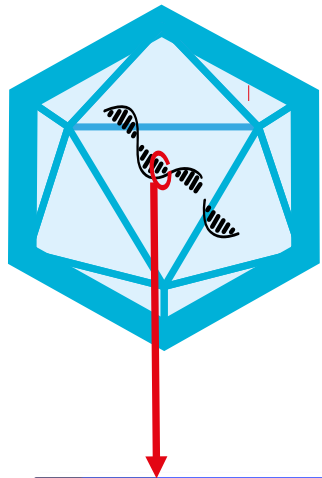
Safety and Tolerability of PF-06939926 in Ambulatory Boys with Duchenne Muscular Dystrophy

Tara McDonnell Moorehead, Florence Yong, Srividya Neelakantan, Katherine Beaverson, David Beidler, Michael Binks

Michael Binks, M.D.

Vice President, Rare Disease Clinical Research

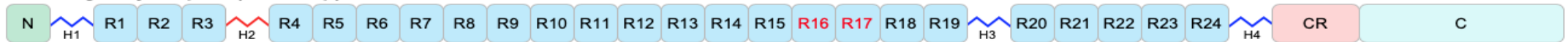
Developing a Gene Therapy for DMD



- PF-06939926 is an **AAV9** gene therapy vector containing a miniaturized dystrophin transgene
- Includes a **muscle specific promoter** to preferentially express in skeletal and cardiac muscle cells
- Contains **Δ3978 mini-dystrophin** transgene
- Clear dose response on Rat^{mdx} cardiac and skeletal muscle transduction with improved skeletal muscle strength and echo parameters
- Triple transfection suspension mammalian cell line manufacture

Mini-dystrophin Transgene – Derived From Mutation of Patient With Mild Phenotype BMD*

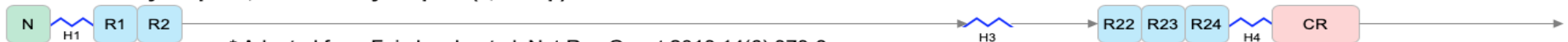
Full-length Dystrophin (11,058 bp)



Becker Muscular Dystrophy, Truncated Dystrophin (6,300 bp)



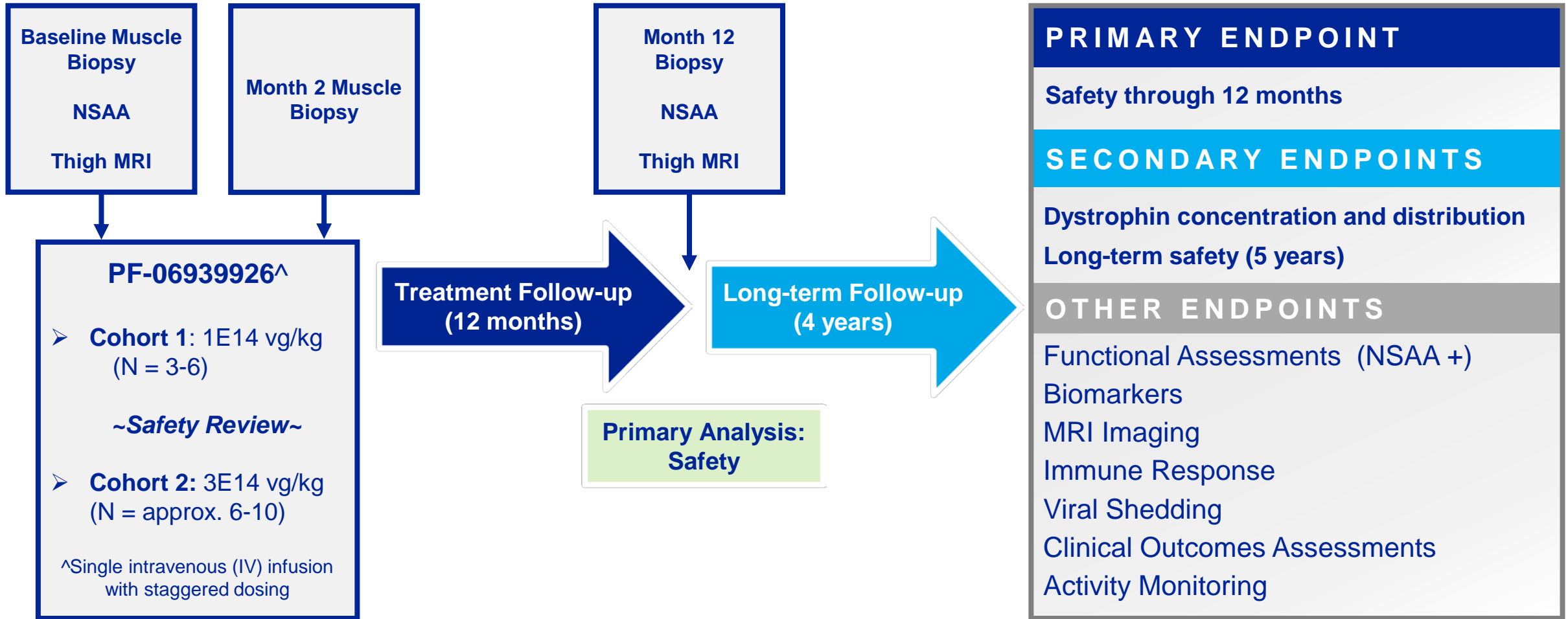
Pfizer's 'minidystrophin', truncated dystrophin (3,978 bp)



* Adapted from Fairclough, et al. Nat Rev Genet 2013;14(6):373-8.

C=C-terminal domain; CR=cysteine-rich domain; H=H-hinge; N=actin binding domain; R=rod domain

C3391001 (NCT03362502) Design: Ongoing Phase 1b Study



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C3391001 Study and Safety Status (as of 20th March 2020*)

Phase 1b Study Status

- **3 Sites in US**
- **9 Participants with DMD Enrolled:**
 - Ambulant and on daily glucocorticoids (GC)
 - Age mean: **8.8 years** (range: 6.2-12.8 years old)
 - Body weight mean: **27 kg** (range: 18-42 kg)
 - Rise from floor mean: **4 sec** (range: 3-7 sec)
 - Negative for neutralizing antibodies (NAb) to AAV9 and anti-dystrophin T-cell response
 - *10% excluded due to NAb positive test at screening*
- **9 Participants Dosed:**
 - **3** at 1E14 vg/kg
 - **6** at 3E14 vg/kg

* 3 additional patients have been dosed since March 20, 2020. No SAEs and no new safety signals have been observed in these patients to date.



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Preliminary Safety Summary

- **PF-06939926 intravenous (IV) administration well tolerated**
- **No evidence of hepatic dysfunction or clinically relevant anti-dystrophin response with daily GC regimen**
- **Adverse events occurring in >40% of participants (in ▼ order):**
 - *Vomiting, nausea, decreased appetite, pyrexia*
- **3 serious adverse events (SAEs)**
 - Persistent vomiting resulting in dehydration (required admission for IV anti-emetics and fluids)
 - Acute kidney injury with atypical hemolytic uremic syndrome (aHUS)-like complement activation (required hemodialysis and eculizumab)
 - Thrombocytopenia with aHUS-like complement activation (required platelet transfusion and eculizumab)

Monitoring and management regimen amended in protocol to mitigate risk



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Concentration of Dystrophin in Muscle Biopsy by LCMS

Novel LC-MS Assay: immunoaffinity liquid chromatography tandem mass spectrometry (IA LC-MS/MS)

High sensitivity and reproducibility

Wide dynamic range

GLP Quality

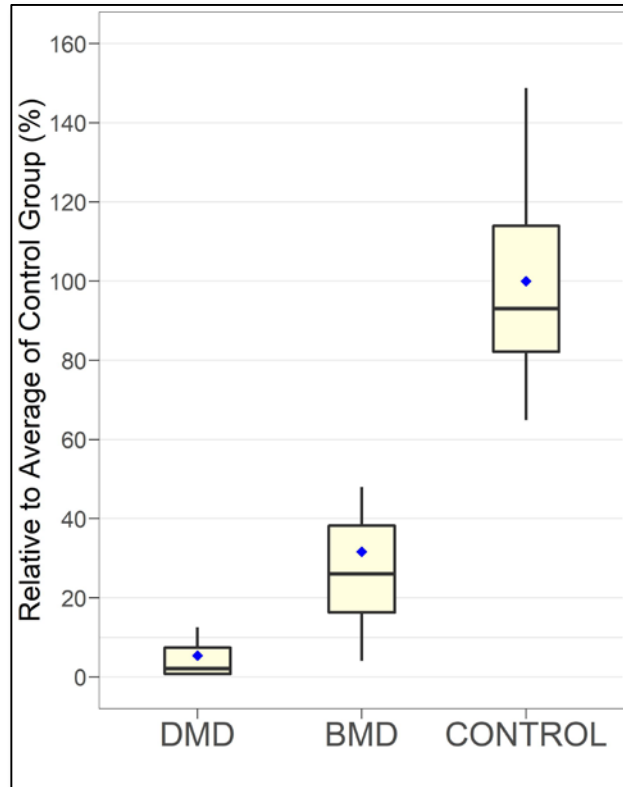
20 biopsies each from:

DMD patients (mean age 6yrs)

BMD patients (mean 8yrs)

Non-dystrophic,
pediatric control group
(mean 10yrs)

Clear distinction in expression levels between DMD and BMD



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Concentration of Dystrophin in Muscle Biopsy by LCMS

Significant and Sustained expression at 12 months

Novel LC-MS Assay: immunoaffinity liquid chromatography tandem mass spectrometry (IA LC-MS/MS)

High sensitivity and reproducibility

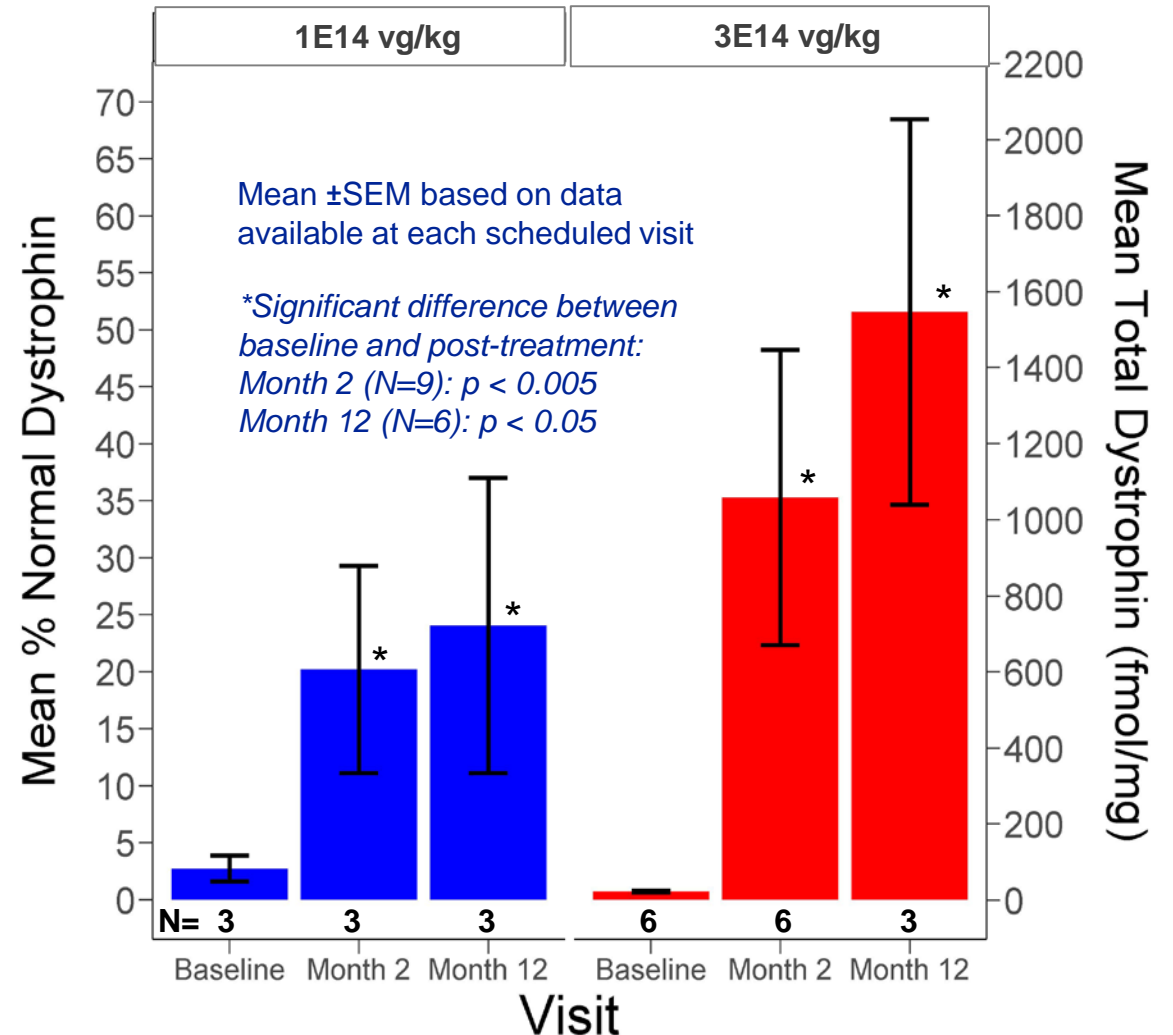
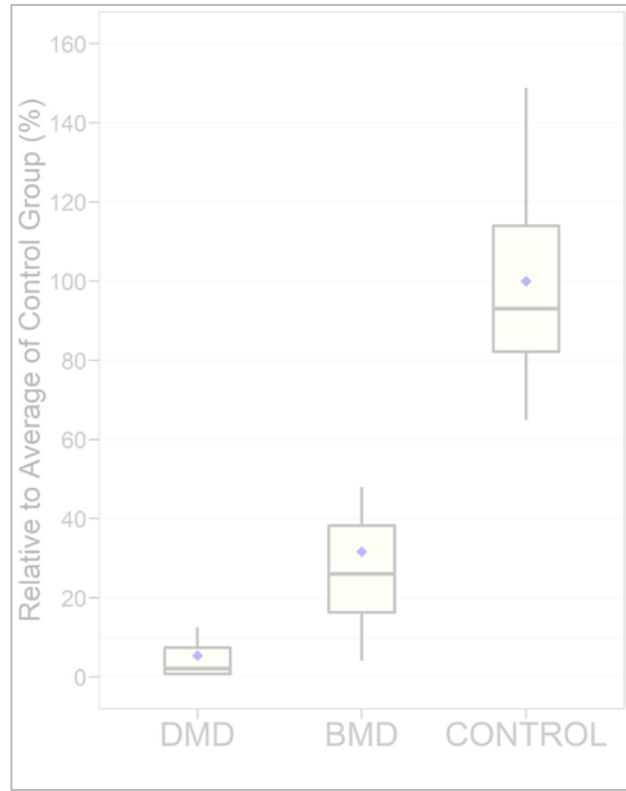
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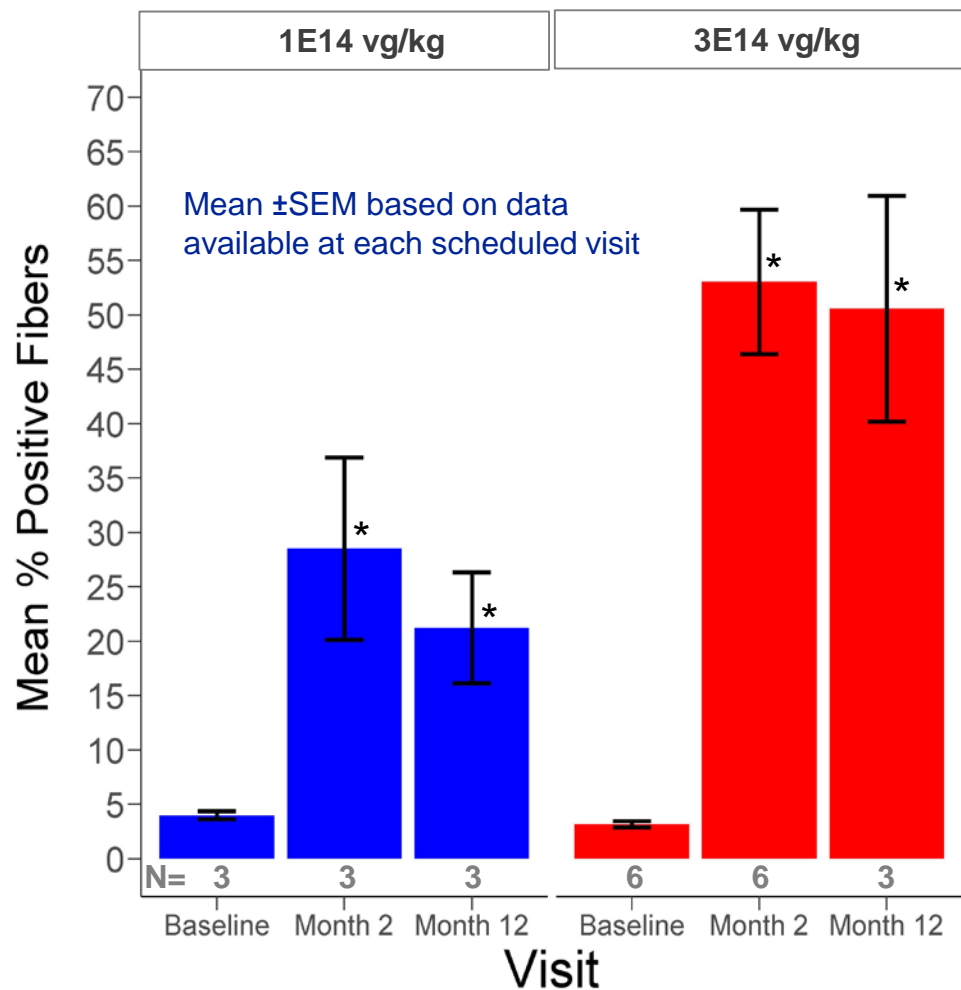
DMD (mean age 6yrs)
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Non-dystrophic, pediatric controls (mean 10yrs)

Clear distinction in expression levels between DMD and BMD



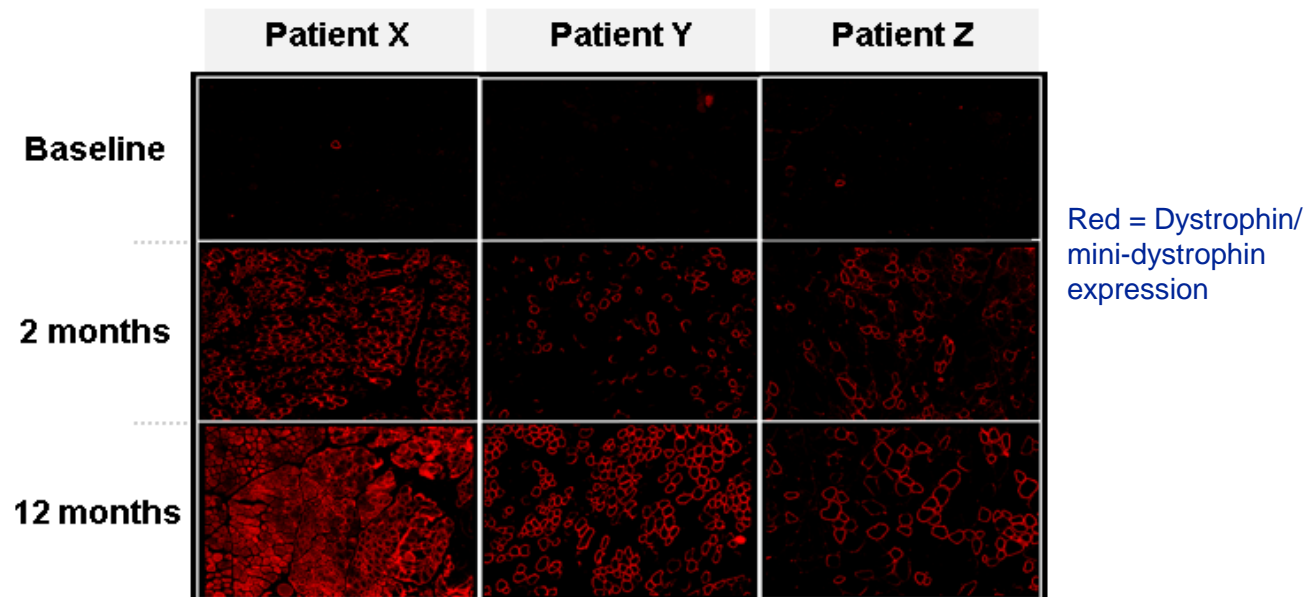
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Significant and Sustained Distribution of Dystrophin in Muscle Biopsy by Immunofluorescence



*Significant difference between baseline and post-treatment: Month 2 (N=9): $p < 0.005$ Month 12 (N=6): $p < 0.05$

Immunofluorescence Images for 3 High Dose Patients



3E14 vg/kg Dose: Mean %positive fibers = 53% at 2 months (N=6). At 12 months, Mean increased from 48% to 51% (N=3).

NOTE: All images acquired using an updated digital platform and analysis with a new quantitative imaging algorithm

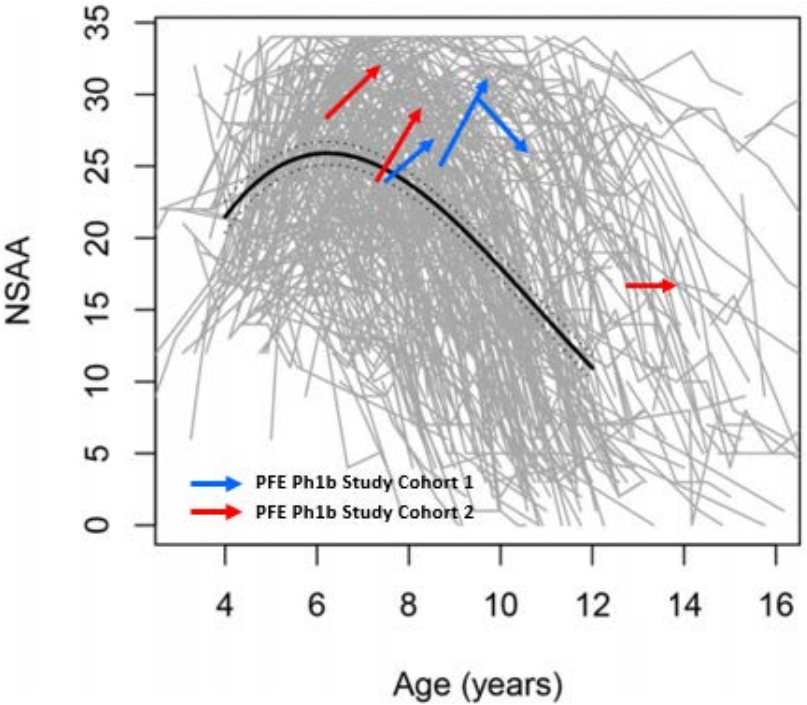


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NSAA Total Scores Show Improvement 12 Months After Treatment

Relative to Natural History and Clinical Trial Placebo Groups

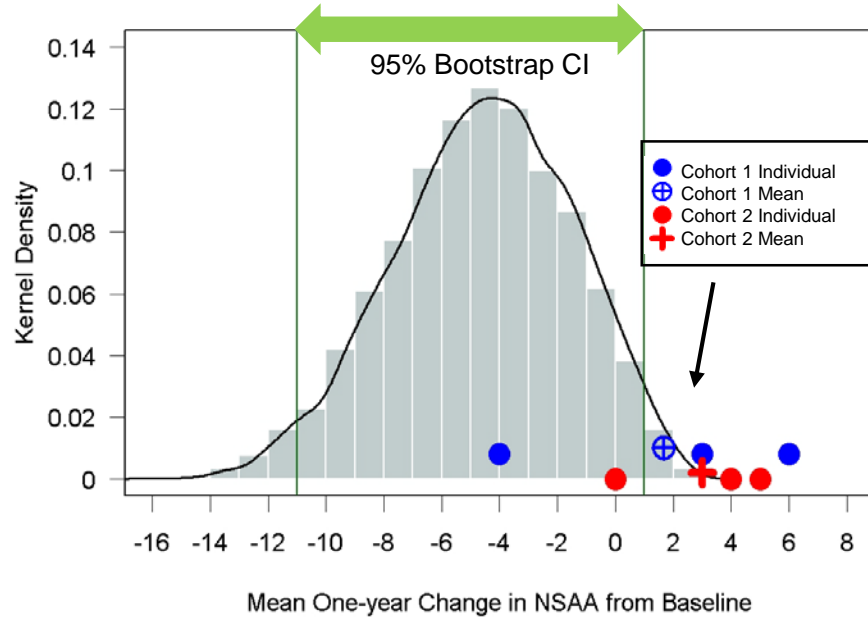
UK NorthStar Natural History



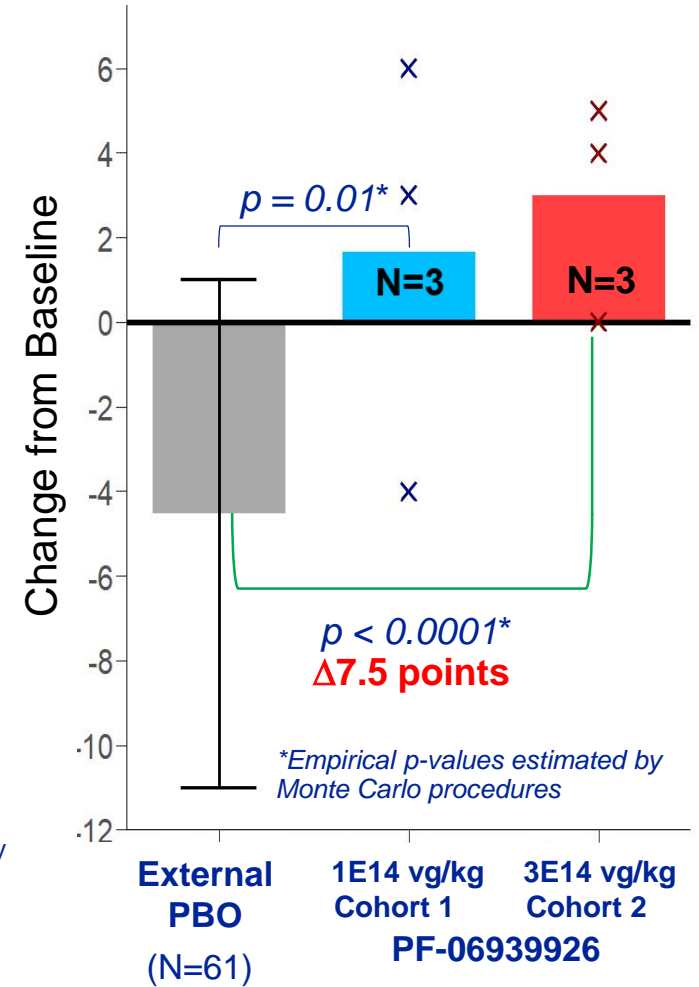
Background (N=395) from Figure 1 of Muntoni et al. (2019) PLoS ONE 14(9): e0221097. (cTAP consortium)

External Placebo (PBO) Control*

Bootstrap Distribution of the Mean Change from Baseline to 1-year Post Randomization



*External PBO (N=61) constructed from PBO of PFE domagrozumab study and PBO of another study in TransCelerate PSoc DB (N=142) matching key eligibility criteria (age, weight, function) of C391001 study. Black bars (right panel): 95% bootstrap confidence interval (CI) for the mean



Significant difference between External Placebo (N=61) and PF-06939926 study (N=6): median -4 vs 3.5, $p = 0.003$

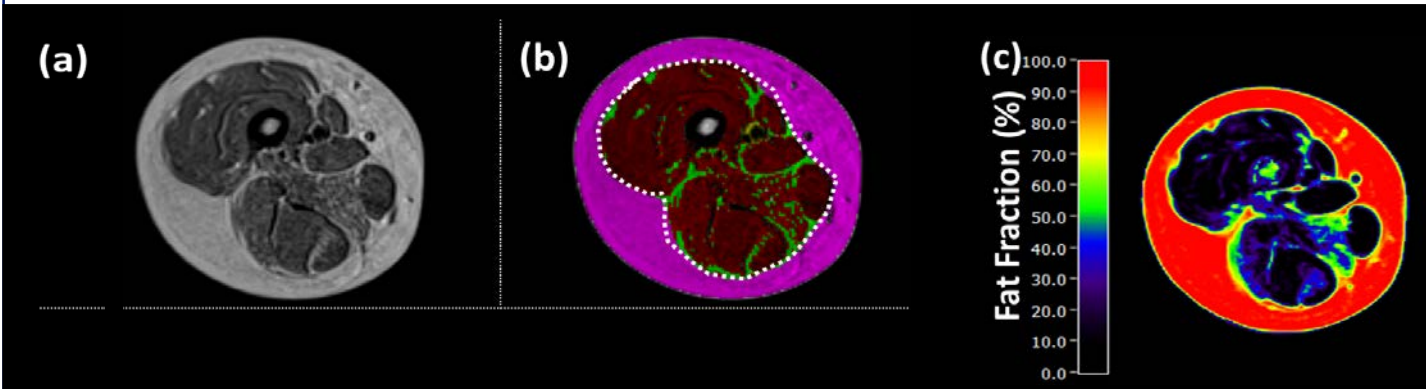


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Whole Thigh MRI – Significant Reduction in Fat Fraction at 12 months

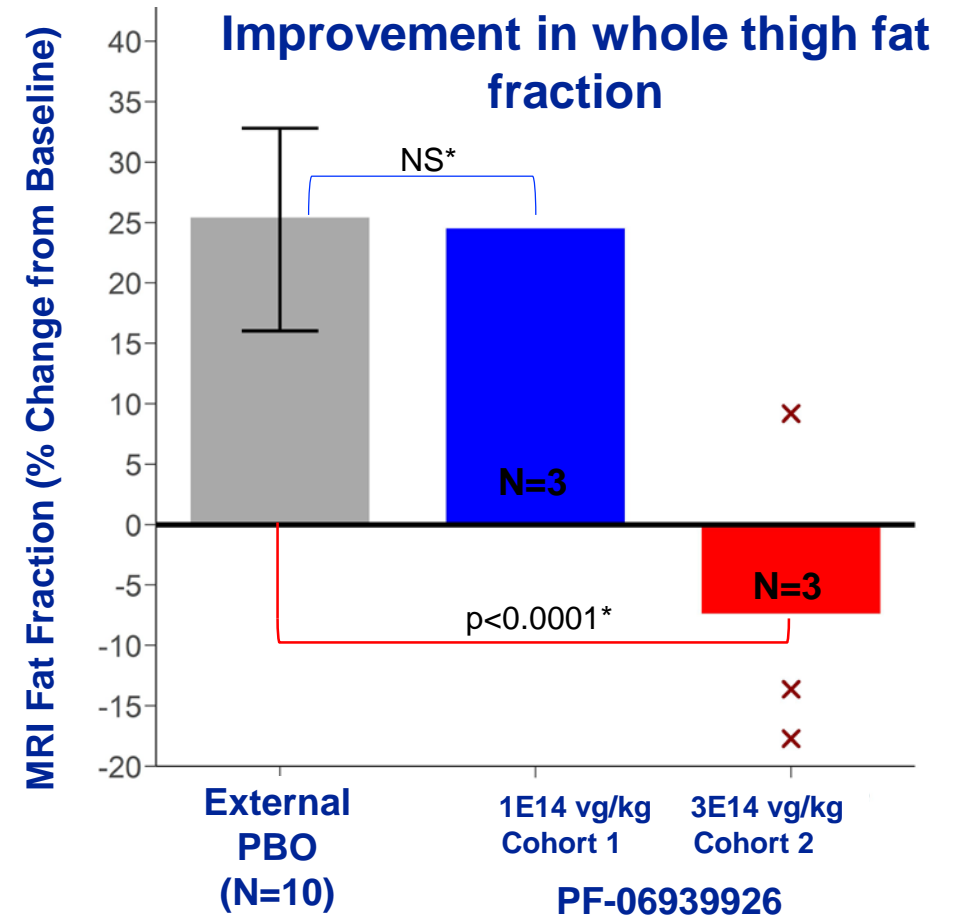
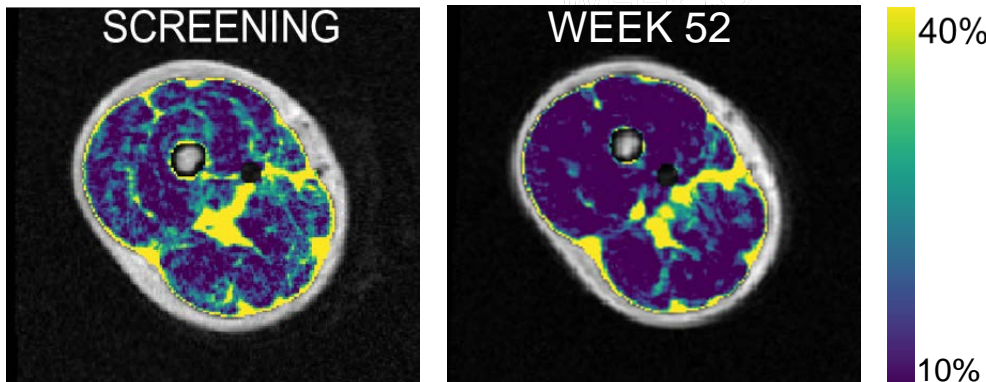
Relative to Recent Clinical Trial Placebo group (Domagrozumab)

Identical Dixon Method Applied to Both Studies



- a. MR scans acquired without compressing thigh tissue.
- b. Whole thigh were segmented to identify muscle and fat.
- c. Mean Dixon fat fraction computed over all voxels in entire segmented muscle.

MRI Fat Fraction Map of 1 Subject in High Dose



External PBO: PFE domagrozumab study placebo group matching key eligibility criteria (age, weight, function) of C3391001 study

Black Bars: 95% bootstrap confidence interval for the Mean %Change
 *Empirical p-values estimated by Monte Carlo procedures: NS = Not Significant



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Conclusions

- Preliminary results from the ongoing C3391001 Phase 1b study (NCT03362502) are encouraging
- For current Cohort 2 (PF-06939926 at 3E14 vg/kg ITR Dose)
 - PF-06939926 infusion well-tolerated, but complement activation ~5-10 days associated with aHUS-like phenomena
 - Increased monitoring and intervention regimen supports continued development at current dose level
 - Significant and sustained expression of mini-dystrophin in biceps muscle biopsy
 - Mini-dystrophin concentration at levels expected to translate into potential clinical benefit
 - Trend towards increased concentration between 2 and 12 months
 - No loss of mini-dystrophin expressing muscle fibers at 12 months
 - NSAA : Mean improvement in motor function score at 12 months exceeds expectations (given age and baseline function) by > 6 points
 - Thigh MRI Fat Fraction: Improvements at 12 months never observed in matched placebo control population
- Global Phase 3 randomized, multicentre, double-blind, placebo-controlled study is on track to start 2H2020 pending regulatory approval
 - Sample size = 99, sites will become active on a rolling basis, starting in the United States
 - C3391003 study is registered on ClinicalTrials.gov (NCT04281485)
 - Process for commercial manufacturing at 2,000 L scale was initiated in 2019



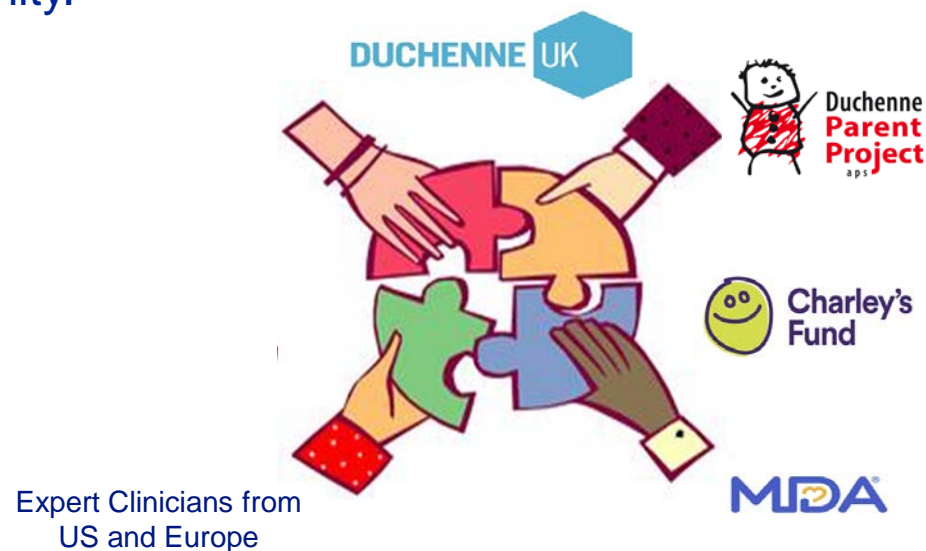
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Acknowledgments

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Special acknowledgements to:

- Study participants and their families
- Study investigators:
 - Russell J. Butterfield, MD, PhD
 - Perry B. Shieh, MD, PhD
 - Edward C. Smith, MD
- TransCelerate PSoC Data Sharing Initiative*



*The external control data was based in part on data from the TransCelerate BioPharma Inc. Placebo and Standard of Care (PSoC) Data Sharing Initiative, which includes contributions of anonymized or pseudonymized data from TransCelerate PSoC member companies including Abbvie, Allergan, Amgen, AstraZeneca, Astellas, Bristol-Myers Squibb, Boehringer Ingelheim, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, EMD Serono, NovoNordisk, Pfizer, Roche, Sanofi, Shionogi, and UCB Pharma ("Data Providers").

<https://transceleratebiopharmainc.com/assets/placebo-and-standard-of-care-data-sharing/>

Disclaimer: Neither TransCelerate Biopharma Inc. nor the Data Providers have contributed to or approved or are in any way responsible for Pfizer's research results



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Q&A

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