IGNITE DMD Phase I/II ascending dose study of SGT-001 microdystrophin gene therapy for DMD: Update on long-term outcomes

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Disclosures

- Advisory capacity: NS Pharma, Sarepta Therapeutics, Regenxbio, PTC Therapeutics, and Scholar Rock
- Speaker: Genentech/Roche, Biogen, Avexis

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This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding the Company’s IGNITE DMD clinical trial, ability of the Company to continue dosing patients in the IGNITE DMD trial, the implication of interim clinical data, the safety or potential treatment benefits of SGT-001 in patients with Duchenne, the Company’s expectations for reporting future data from the IGNITE DMD trial, the Company’s regulatory plans and timelines, the Company’s SGT-003 pipeline program and other statements containing the words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would,” “working” and similar expressions. Any forward-looking statements are based on management’s current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. These risks and uncertainties include, but are not limited to, risks associated with the Company’s ability to continue IGNITE DMD on the timeline expected or at all; obtain and maintain necessary approvals from the FDA and other regulatory authorities; obtain and maintain the necessary approvals from investigational review boards at clinical trial sites and the IGNITE DMD independent data safety monitoring board; enroll patients in IGNITE DMD; on the timeline expected; the Company’s dosing strategy; replicate in clinical trials positive results found in preclinical studies and earlier stages of clinical development; whether the interim data presented in this release will be predicative of the final results of the trial or will demonstrate a safe or effective treatment benefit of SGT-001; whether the methodologies, assumptions and applications we utilize to assess particular safety or efficacy parameters will yield meaningful statistical results; advance the development of its product candidates under the timelines it anticipates in current and future clinical trials; successfully optimize and scale its manufacturing process; obtain, maintain or protect intellectual property rights related to its product candidates; compete successfully with other companies that are seeking to develop Duchenne treatments and gene therapies; manage expenses; and raise the substantial additional capital needed, on the timeline necessary continue development of SGT-001, SGT-003 and other product candidates, achieve its other business objectives and continue as a going concern. For a discussion of other risks and uncertainties, and other important factors, any of which could cause the Company’s actual results to differ from those contained in the forward-looking statements, see the “Risk Factors” section, as well as discussions of potential risks, uncertainties and other important factors, in the Company’s most recent filings with the Securities and Exchange Commission. In addition, the forward-looking statements included in this presentation represent the Company’s views as of the date hereof and should not be relied upon as representing the Company’s views as of any date subsequent to the date hereof. The Company anticipates that subsequent events and developments will cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so. No representation or warranty is made as to the accuracy or completeness of the information or analysis in this presentation.

Agenda

- Overview of SGT-001 microdystrophin gene therapy for DMD
- IGNITE DMD study design
- Safety update
- Long-term muscle biopsy update
- Long-term functional data update
- Key takeaways

Duchenne Muscular Dystrophy Is a Devastating Muscle-Wasting Disease

Caused by Mutations in the *DMD* Gene

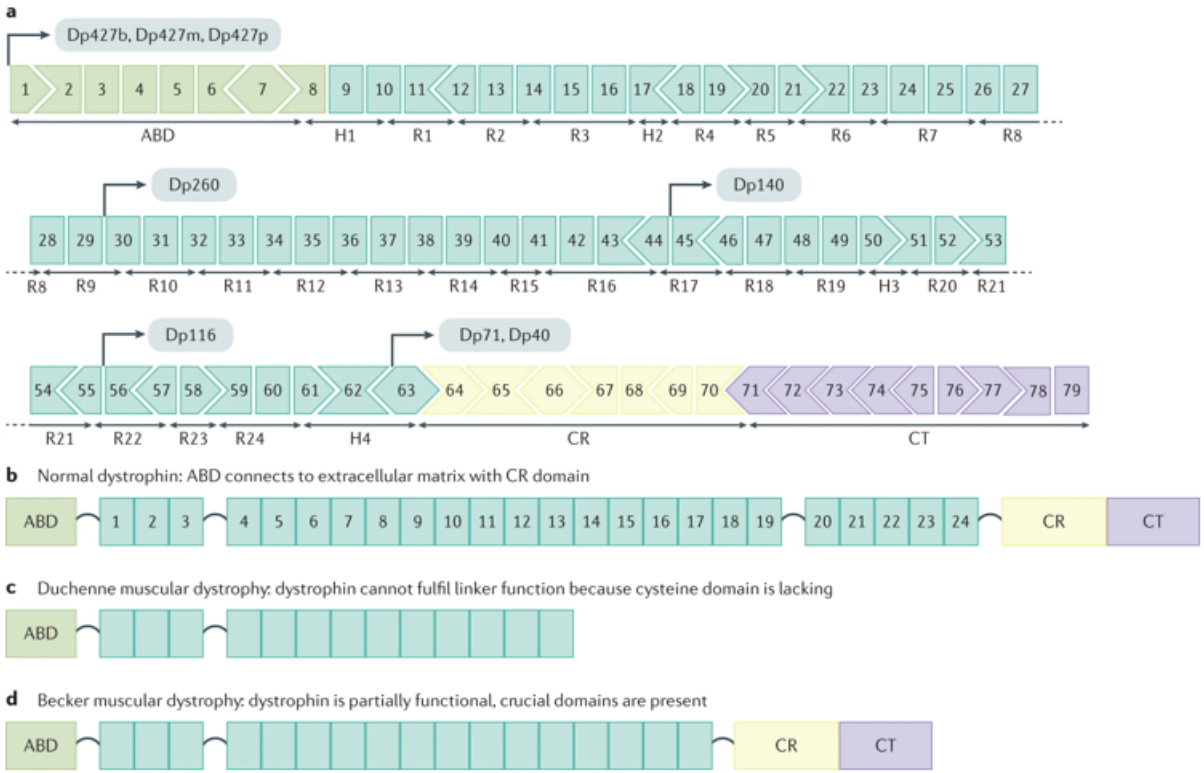
1:3500-5000 Newborn Males Affected

Skeletal and Cardiac Muscle Manifestations

100% FATAL

Progressive & Irreversible

No Meaningful Treatment Options



Schematic depiction of DMD gene and dystrophin protein. Duan et al. Nature Reviews Disease Primers 2021

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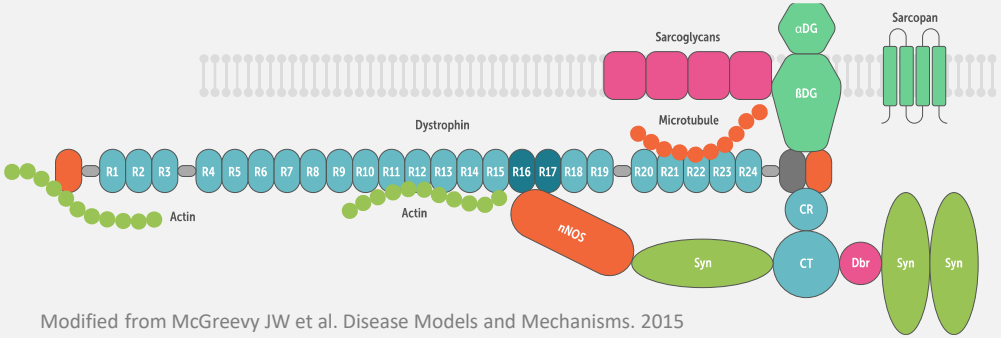
SGT-001 Microdystrophin Gene Therapy to Replace Absent Dystrophin

Dystrophin and the Glycoprotein Complex

- Stabilizes the muscle membrane
- Acts as a molecular shock absorber
- Prevents muscle tissue damage and death
- Absent in Duchenne muscular dystrophy (DMD)

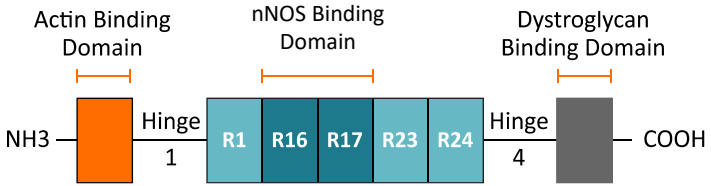


Modified from McGreevy JW et al. Disease Models and Mechanisms. 2015

SGT-001: AAV9-CK8-Microdystrophin

- AAV gene transfer therapy
- Systemically delivers a unique rationally designed microdystrophin
  - Shortened form of dystrophin able to be packaged into an AAV vector
  - **Uniquely includes the nNOS binding domain**
    - Important for prevention of activity-induced ischemia and associated muscle injury
    - Presence correlated with milder phenotypes of Becker muscular dystrophy (BMD)
  - Acts as a functional surrogate of full-length dystrophin

SGT-001 Microdystrophin
Retains key dystrophin protein functional domains



nNOS: neuronal nitric oxide synthase

IGNITE DMD Study Design: *Two Dose Levels Initially Assessed; 2E14 vg/kg Selected*

Interim Analysis of Subjects in IGNITE DMD

- n=3 subjects analyzed as controls
- n=3 subjects at 5E13 vg/kg*
- n=3 subjects at 2E14 vg/kg
  - 2 additional subjects dosed at 2E14 vg/kg**

Inclusion Criteria

- Ambulatory children; mutation agnostic
- Ages 4-17 years; upper weight limit of 18 kg for next two patients dosed; up to 30 kg (~66 lbs) for remainder of the clinical trial
- Primary focus on children with the potential to include adolescent patient population in the future
- Anti-AAV9 antibodies below protocol-specified thresholds
- For more information, please visit clinicaltrials.gov **NCT03368742**

*Data at 1.5 year timepoint not collected for 5E13 cohort subjects due to COVID-19
**One year and later timepoints not yet reached for additional subjects dosed

Dose Cohort	Patient #	Age at Baseline (years)
2E14 vg/kg	Pt 4	10.7
	Pt 5	6.8
	Pt 6	7.7

Primary Endpoints (Baseline to 1 Year):

- Incidence of adverse events
- Change in microdystrophin protein levels in muscle biopsies by Western Blot

Select Secondary Endpoints (Baseline to 1 Year):

- Six Minute Walk Distance
- North Star Ambulatory Assessment (NSAA)
- Pulmonary Function Tests
- Quality of Life as measured by Pediatric Outcomes Data Collection Instrument (PODCI)

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Overview of IGNITE DMD Safety Findings

Most Common Drug Related Clinical Adverse Reactions*

(updated to include Subjects 7 and 8)

Nausea	(8/8)
Vomiting	(7/8)
Fever	(6/8)

- The most common drug related laboratory abnormalities were thrombocytopenia/decreased platelets, anemia, proteinuria, and increases in fibrin, D dimer, soluble C5b9 and LDH**
- Activation of the terminal pathway (sC5b9) of the classical complement system occurred in all subjects resulting in 3 serious adverse events (SAEs) : Systemic Inflammatory Response Syndrome (2); thrombocytopenia (1).
- Two other SAEs: immune hepatitis 4 weeks post dosing which resolved rapidly after a transient increase of corticosteroids (1); Giardiasis, determined to be unrelated to SGT-001 (1)
- All SAEs are resolved
- No other drug-related adverse events have occurred in any of the 8 subjects after 90 days to 3.5 years of observation

*Less common adverse reactions include cytokine release syndrome, generalized edema, acute kidney injury and thrombotic microangiopathy

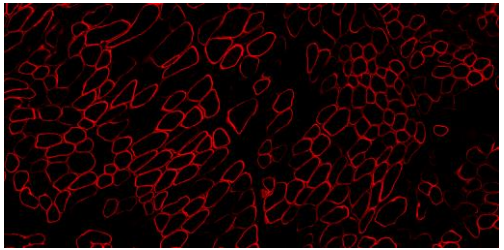
**Less common laboratory abnormalities include increased CPK, decreased complement, increased liver enzymes, increased troponin, decreased hemoglobin, increased haptoglobin urinary casts and leukocytosis

Durable Microdystrophin Expression and Protein Function Observed in Long-Term Biopsies

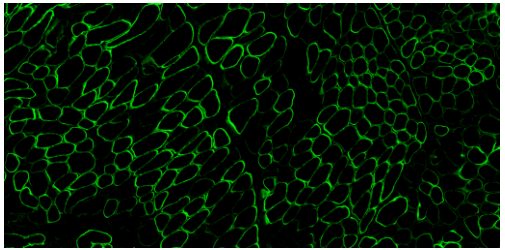
	Microdystrophin Expression			
	% Positive Fibers (Immunofluorescence)		% of Normal Dystrophin (Western Blot)	
	3 Months	Last Timepoint	3 Months	Last Timepoint
Pt 4	10-20%	10-30% (24 months)	BLQ	BLQ (24 months)
Pt 5	50-70%	85% (18 months)	17.5%	69.8% (18 months)
Pt 6	50-70%	50-60% (12 months)	8.0%	20.3% (12 months)

Pt 5
(18 months)

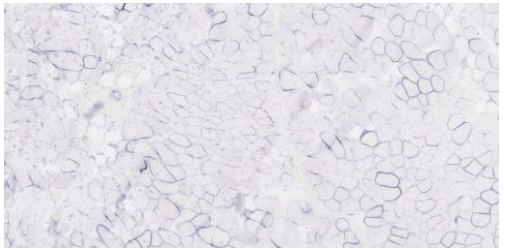
Microdystrophin



β-Sarcoglycan

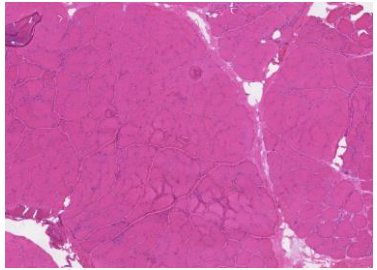
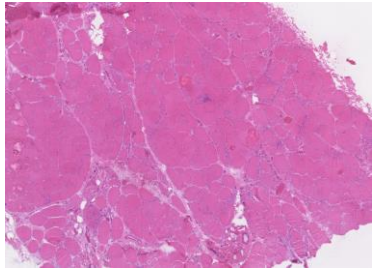
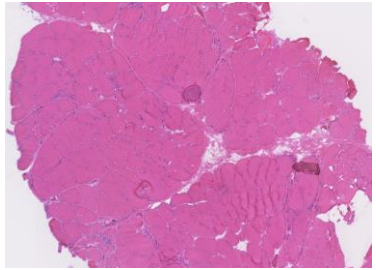
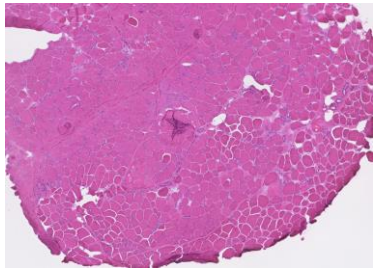
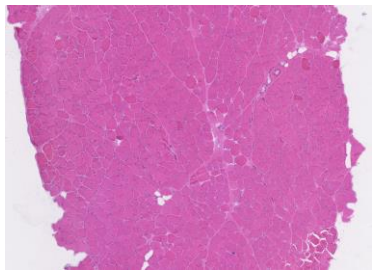
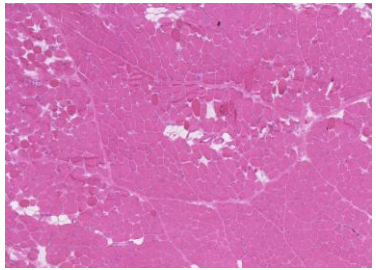
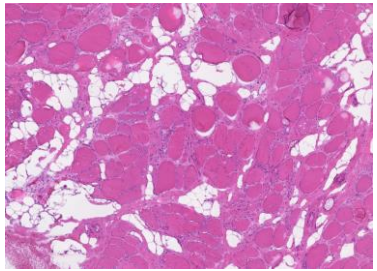
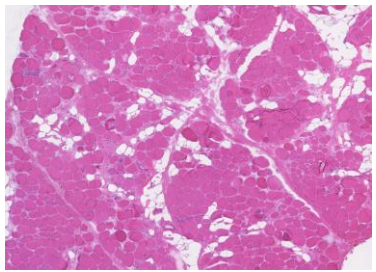
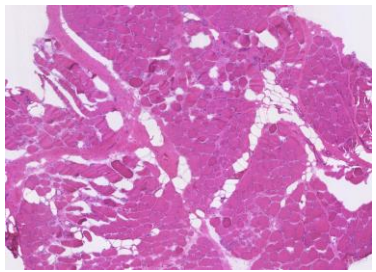


nNOS Activity



MUSCLE BIOPSY ANALYSIS

Limited Dystrophic Pathology Progression Over 12-24 Months

	Baseline	3 Months	Last Timepoint	
Pt 4 (24 months)				**Age at Last Timepoint: 12.7 yrs** *Very mild active dystrophic pathology*
Pt 5 (18 months)				**Age at Last Timepoint: 8.3 yrs** *No active dystrophic pathology*
Pt 6 (12 months)				**Age at Last Timepoint: 8.7 yrs** *Very mild active dystrophic pathology*

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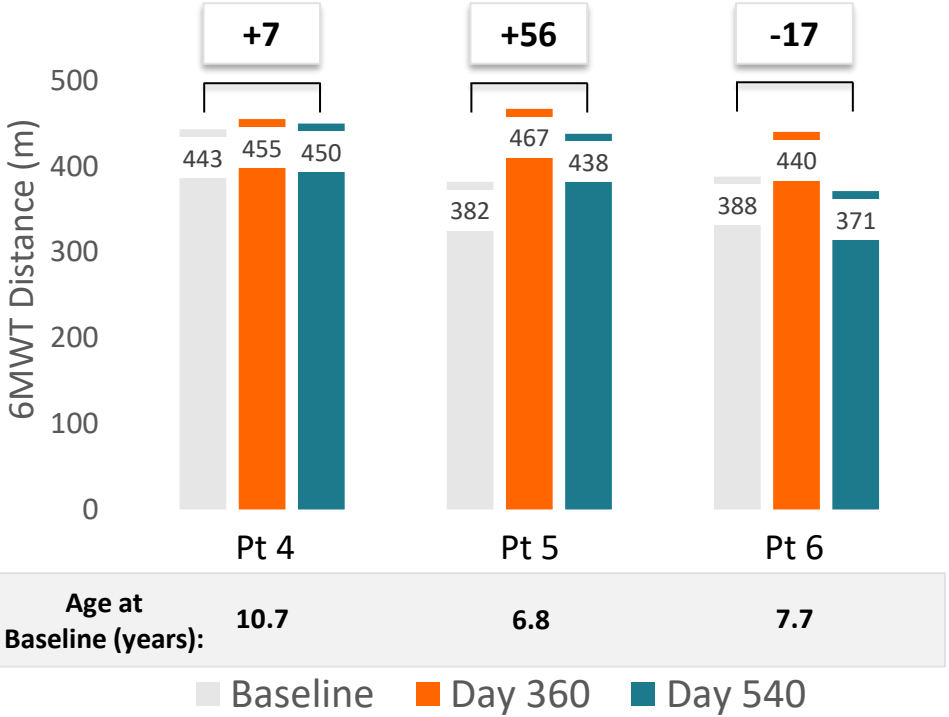
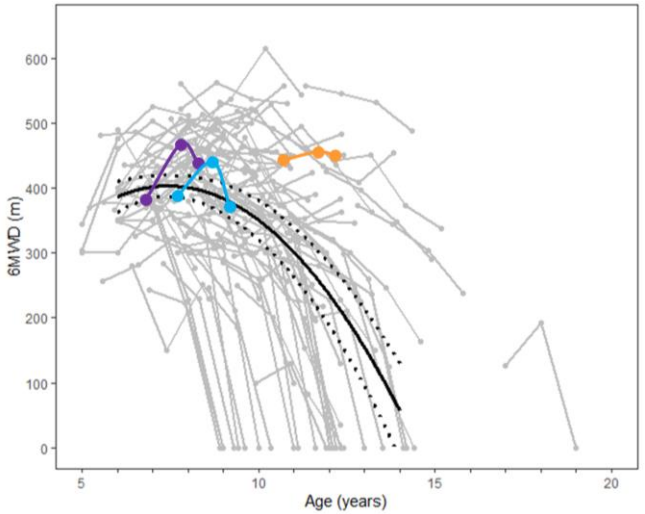
6MWT Distances are Maintained 1.5 Years Post-Treatment

*Mean Change from Baseline to Day 540: +15.3 ±37.2 m | **Difference of +78.8 m Compared to Natural History over 1.5 Years***



Individual Patient Trajectories



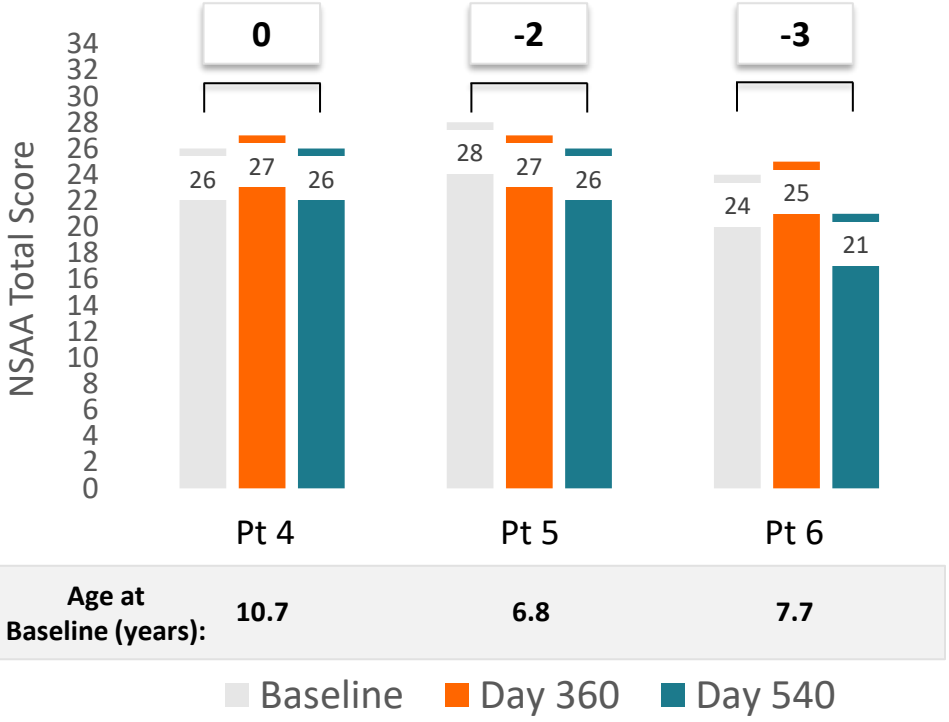
Data overlayed on Mercuri et al 2016
DMD Natural History
-63.5 m expected decline in 1.5 years after age 7

Interim data presented | m: meters

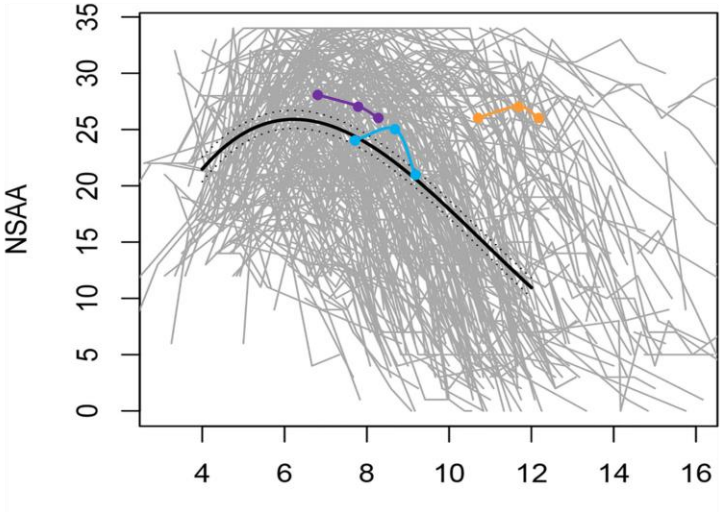
FUNCTIONAL ASSESSMENTS

NSAA Scores Show Minimal Change 1.5 Years Post-Treatment

Mean Change from Baseline to Day 540: -1.7 ±1.5 Units | ***Difference of +2.8 Units Compared to Natural History over 1.5 Years***



Individual Patient Trajectories



Data overlayed on Muntoni et al 2019
DMD Natural History
-4.5 unit expected decline over 1.5 years after age 6.3

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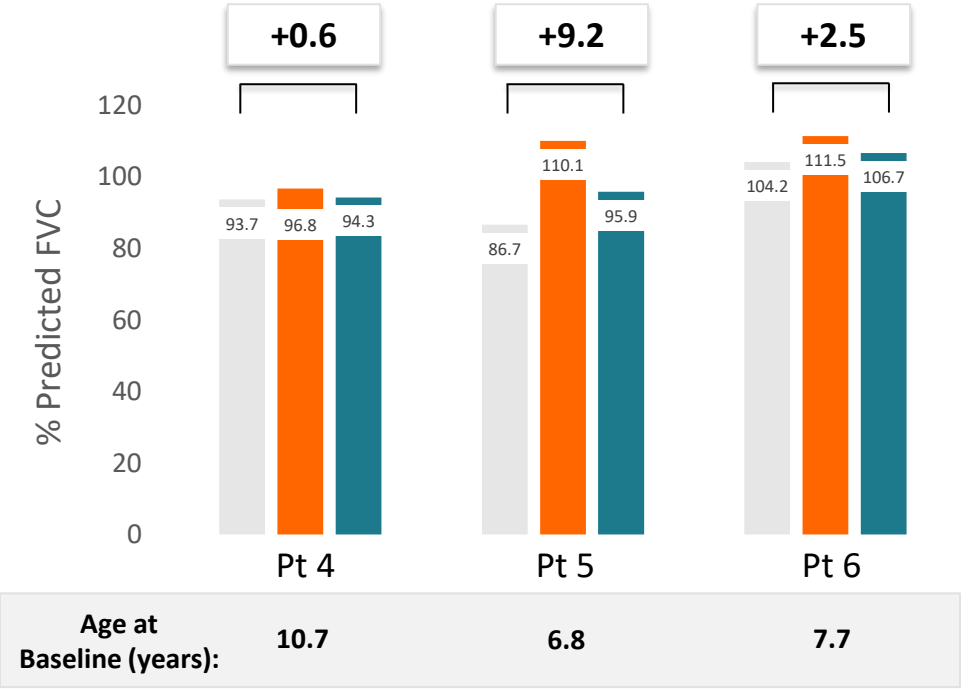
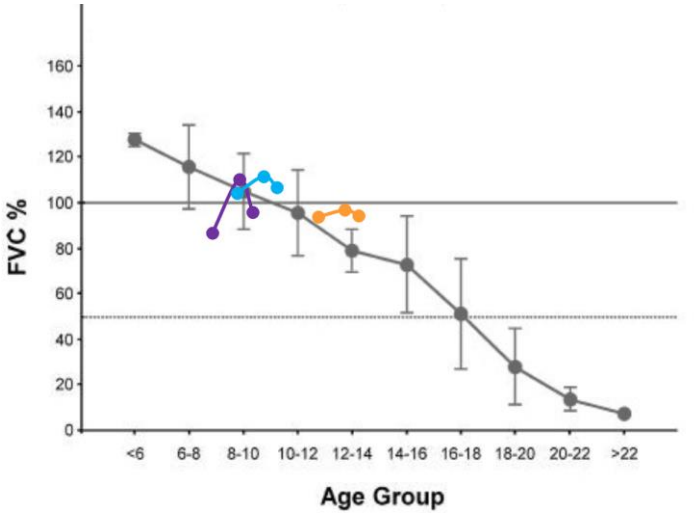
Interim data presented

% Predicted FVC Continues to Show Stability or Improvement 1.5 Years Post-Treatment

Mean Change from Baseline to Day 540: +4.1 ±4.5% | ***Difference of +11.6% Compared to Natural History over 1.5 Years***



Individual Patient Trajectories

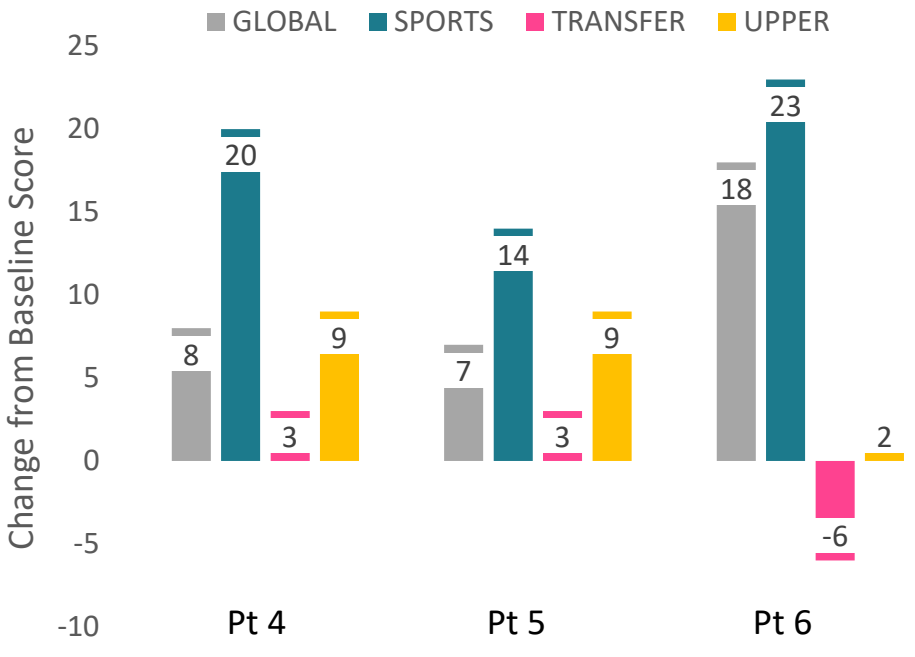


Data overlayed on Mayer et al 2015
DMD Natural History
-7.5% expected decline over 1.5 years after age 6

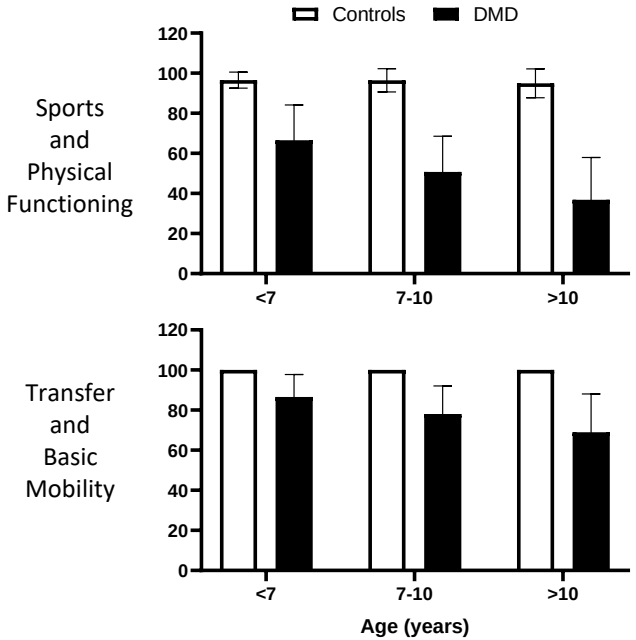
Interim data presented | FVC: forced vital capacity

PATIENT REPORTED OUTCOMES

Sustained Meaningful Improvements in SGT-001 Treated Subjects at 1.5 Years by PODCI



Age at Baseline (years):	**10.7**	**6.8**	**7.7**



Modified from McDonald et al 2010, Henricson et al 2013

DMD Natural History

-7.6 point expected decline over 1.5 years in Global scale

-4.7 point expected decline over 1.5 years in Sports scale

-14.9 point expected decline over 1.5 years in Transfer scale

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Interim data presented | Standardized scores calculated from pediatric and adolescent parent-reported responses

Key Takeaways From Interim Analysis of IGNITE DMD

Durable expression and function of microdystrophin protein in biopsies collected ≥12 months post-administration of SGT-001

- ✓ Sustained or increased microdystrophin protein levels and percent positive muscle fibers
- ✓ Sarcolemmal restoration of key dystrophin associated proteins β-sarcoglycan and nNOS

Encouraging evidence of functional benefit 1.5 years post-treatment vs natural history

- ✓ 6-Minute Walk Test (6MWT)
- ✓ North Star Ambulatory Assessment Total Score (NSAA)
- ✓ Forced Vital Capacity (FVC) normalized for age, height, and weight

Meaningful improvement in patient reported outcomes that assess motor function and fatigue

- ✓ Pediatric Outcomes Data Collection Instrument (PODCI)

Totality of data supports continued dosing in IGNITE DMD at 2E14 vg/kg dose

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Thank You

Questions & Answers