FP.28

IGNITE DMD Phase I/II Study of SGT-001 Microdystrophin Gene Therapy for DMD: Long-Term Outcomes and Expression Update

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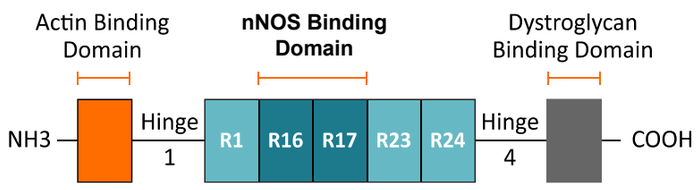
Introduction / Objective

Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is a fatal neuromuscular disease caused by mutations in the *DMD* gene that lead to the absence of functional dystrophin protein

SGT-001

Capsid	→	Skeletal and cardiac muscle tropism	→	AAV9
Promoter	→	High skeletal and cardiac muscle expression	→	CK8
Transgene	→	Retains critical elements of full-length dystrophin including the nNOS binding domain	→	nNOS Microdystrophin



nNOS: neuronal nitric oxide synthase

SGT-001 is an AAV microdystrophin gene transfer therapy being evaluated for the treatment of DMD that delivers a unique, rationally designed dystrophin surrogate to replace the absent protein in skeletal and cardiac muscles throughout the body

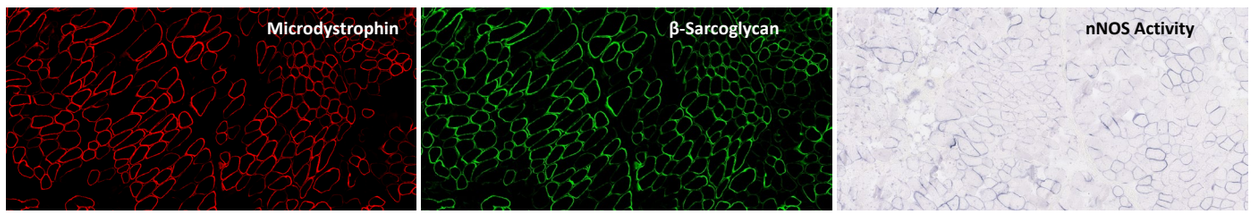
Methods

IGNITE DMD Phase I/II clinical trial to assess the safety and efficacy of SGT-001

- Cohorts
  - n=3 subjects analyzed as controls
  - n=3 subjects at 5E13 vg/kg (Patients 1-3)
  - n=6 subjects at 2E14 vg/kg (Patients 4-9)
- Primary Endpoints (Baseline to 1 Year)
  - Incidence of adverse events
  - Change in microdystrophin protein levels in muscle biopsies by Western blot
- Select Secondary Endpoints
  - NSAA, 6MWT, PFTs, PROMs (PODCI)
- Additional evaluations performed at the 1.5-year timepoint and annually up to 5 years to assess long-term safety and efficacy
- Enrollment in the study has concluded and subjects continue to undergo safety monitoring and efficacy evaluations

Results

Durable Microdystrophin Expression and Protein Function are Observed Between 3-Month and Long-Term 12 to 24-Month Biopsies



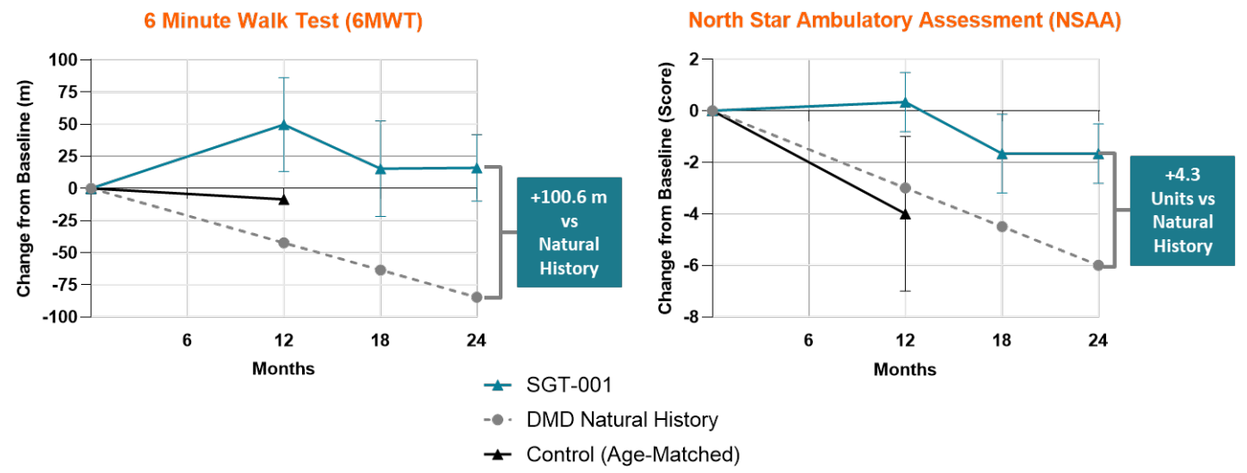
Biopsy from Pt. 5 at 18 months

Biopsy Results (2E14 vg/kg Cohort)	3 months (Mean % - Pts. 4-9)	12 months (Mean % - Pts. 6-8)	18 months (Pt. 5)	24 months (Pt. 4)
% Normal Dystrophin (Western Blot)	6.6%	8.4%	70%	BLQ*
% Positive Fibers (Immunofluorescence)				
Blinded Assessment (Pathologist)	31%	30%	85%	10%
Automated Assessment (Flagship)	40%	40%	84%	32%

*BLQ: Below the 5% limit of quantification by Western blot
BLQ values assigned 0.5*LLOQ for Mean calculations (=2.5%)

Results

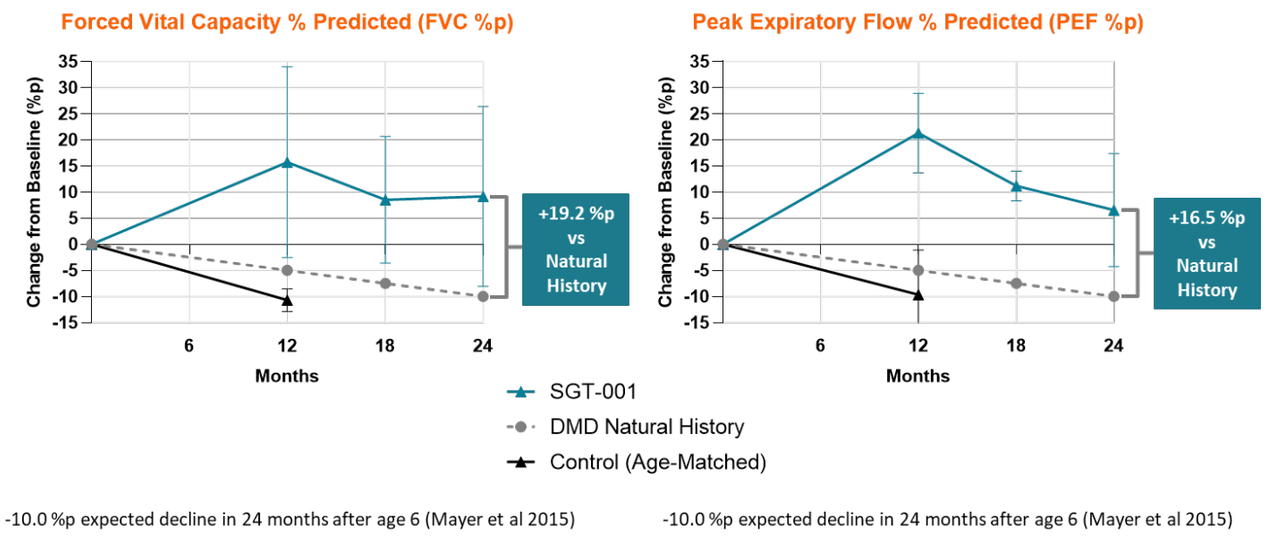
SGT-001 Treated Patients 4-6 Continue to Show Consistent, Stable Motor Function by 6MWT and NSAA at 2 Years Post-Dosing Compared to Natural History



-84.6 m expected decline in 24 months after age 7 (Mercuri et al 2016)

-6.0 unit expected decline in 24 months after age 6.3 (Muntoni et al 2019)

Pulmonary Function Tests Show Durable Improvements in SGT-001 Treated Patients 4-6 across 2 Years after Dosing



-10.0 %p expected decline in 24 months after age 6 (Mayer et al 2015)

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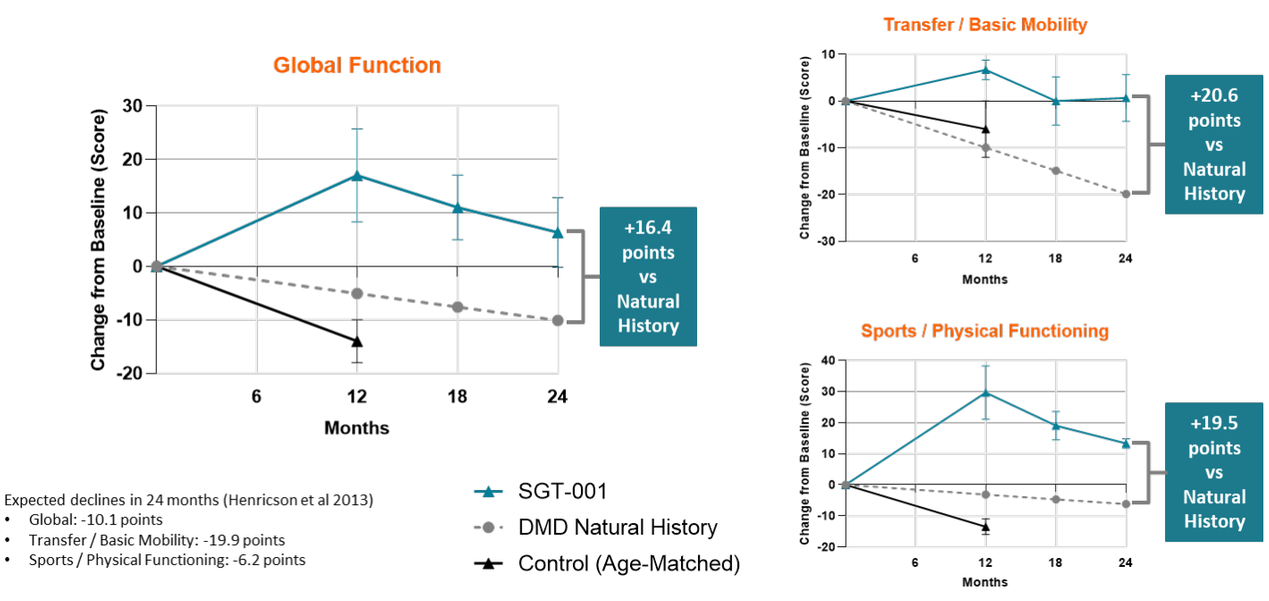
SGT-001 Treated Patients 4-6 Report Stability or Improvements in Key Functional Domains of the PODCI after 2 Years



Expected declines in 24 months (Henricson et al 2013)
- Global: -10.1 points
- Transfer / Basic Mobility: -19.9 points
- Sports / Physical Functioning: -6.2 points

Conclusions

Sustained motor function
- Stable 6 Minute Walk Test (6MWT) distances and North Star Ambulatory Assessment (NSAA) scores compared to natural history

Improved pulmonary function
- Improvements in Forced Vital Capacity (FVC %p) and Peak Expiratory Flow (PEF %p) compared to baseline and natural history

Continued meaningful improvements in patient reported outcomes
- Stable or improved scores across functional domains of the Pediatric Outcomes Data Collection Instrument (PODCI) compared to baseline and natural history

All patients dosed with SGT-001 in the high dose cohort have demonstrated microdystrophin expression and localization
- Long-term biopsy data from Patients 4-8 demonstrate durable microdystrophin expression at 12-24 months post-dosing

SGT-001 treated patients show consistent, durable improvements in function across assessments 2 years after dosing compared to expected natural history declines