IGNITE DMD Phase I/II Study of SGT-001 Microdystrophin Gene Therapy for Duchenne Muscular Dystrophy

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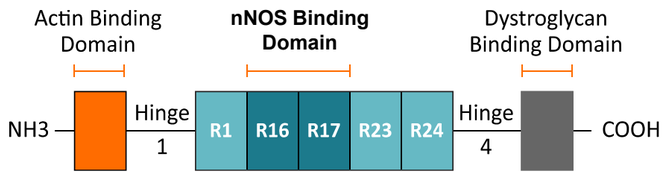
Introduction / Objective

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 evaluated for the safety, tolerability and efficacy in adolescents and children with DMD. SGT-001 was designed to deliver a unique, rationally designed dystrophin surrogate to replace absent protein in skeletal and cardiac muscles throughout the body

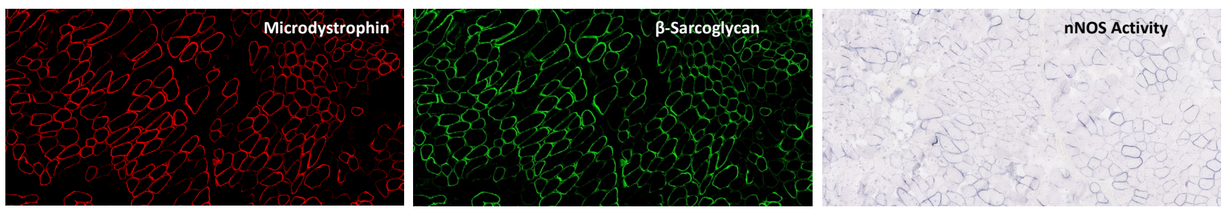
Methods

IGNITE DMD Phase I/II clinical trial to assess the safety and efficacy of SGT-001 (NCT03368742)

- Cohorts
  - n=3 control subjects analyzed
  - n=3 subjects at 5E13 vg/kg (Patients 1-3)
  - n=6 subjects at 2E14 vg/kg (Patients 4-9)
- Safety Assessments
  - Incidence of adverse events
- Biopsy Assessments
  - Microdystrophin expression in muscle biopsies (2E14 vg/kg cohort)
- Clinical Assessments
  - NSAA, 6MWT, FVC % Predicted, FEV1 % Predicted, PODCI
- Results presented as mean ± standard deviation for all control and treated subjects unless otherwise noted
- Enrollment in the study is complete and long term follow up to 5 years post-dosing continues

Results: Biopsy Analysis

Microdystrophin Expression and Protein Function in 3-Month and 12-Month Muscle Biopsies†



Biopsy from Pt. 5 at 18 months

Biopsy Results (2E14 vg/kg Cohort)	3 months (Mean % - Pts. 4-9)	12 months (Mean % - Pts. 6-9)	18 months (Pt. 5) †	24 months (Pt. 4) †
% Normal Dystrophin (Western Blot)	6.6%	7.0%	69.8%	BLQ*
% Positive Fibers (Immunofluorescence)				
Manual Assessment	31%	22%	85%	10%
Automated Assessment	40%	30%	84%	32%

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

†12-month biopsies for Pts. 4 and 5 collected at 24 months and 18 months, respectively, due to COVID-19.

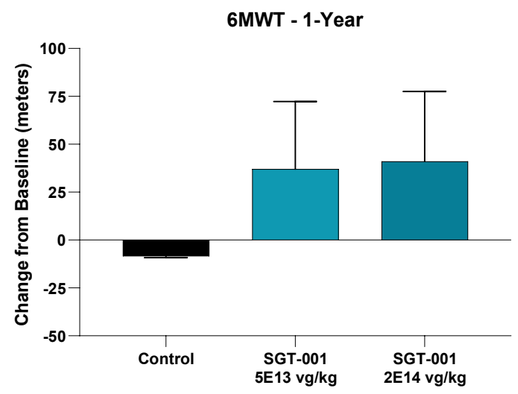
Results: 1-Year Assessments

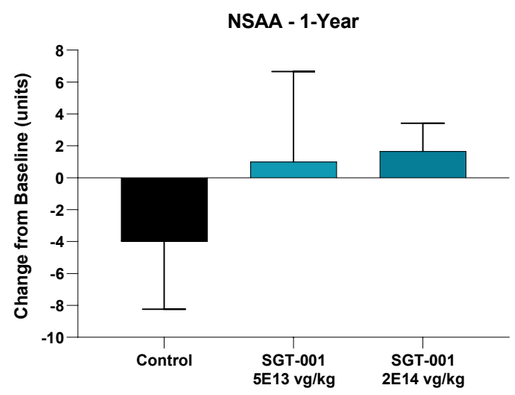
Cumulative Summary Tabulations of Safety Findings

Serious Adverse Events (SAEs)	All SGT-001 (n=9)	Related to SGT-001
Thrombocytopenia	1/9	Yes
Hepatotoxicity	1/9	Yes
Systemic Inflammatory Response Syndrome	2/9	Yes
Giardiasis	1/9	No

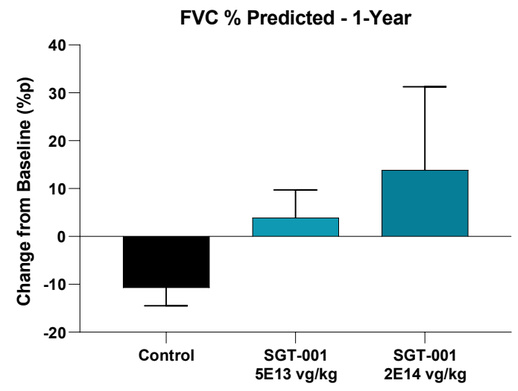
Most Common Treatment-Emergent Adverse Events (TEAEs)	All SGT-001 (n=9)
Nausea	9/9
Vomiting	9/9
Pyrexia	8/9
Thrombocytopenia	7/9
Headache	4/9
Viral Upper Respiratory Tract Infection	4/9

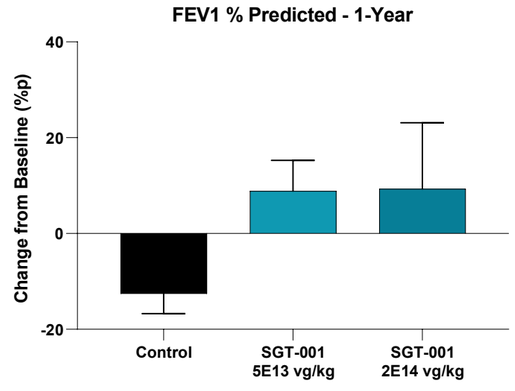
Motor Function Evaluated by 6-Minute Walk Test (6MWT) and North Star Ambulatory Assessment (NSAA)



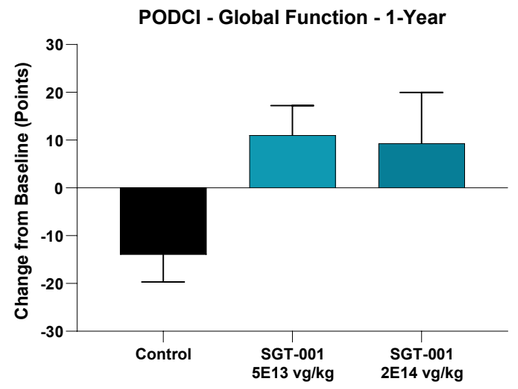


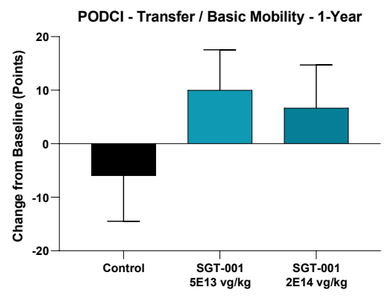
Pulmonary Function Tests Performed by Spirometry to Evaluate Forced Vital Capacity (FVC) and Forced Expiratory Volume in 1 Second (FEV1)

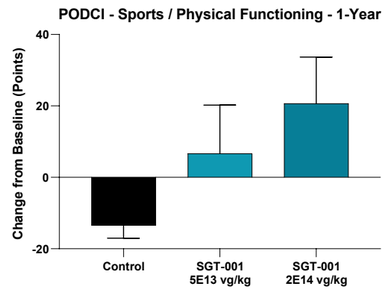




Patient Reported Outcome Measures Evaluated by the Pediatric Outcomes Data Collection Instrument (PODCI)







Conclusions

- All subjects in IGNITE DMD have reached the 1-year study time point
- Results show positive changes from baseline to 1-year for motor function, pulmonary function, and patient reported outcome measures
- Subjects continue to be monitored for safety and have not shown any new treatment-associated AEs after the first 90 days post-dosing
- Development of SGT-001 has concluded, with the next-generation SGT-003 program using an updated construct with novel muscle-tropic capsid currently in IND-enabling studies
- Additional updates on the IGNITE DMD study are expected to be provided following completion of the 5-year follow up timepoint for all subjects