# IGNITE DMD Phase I/II Study of SGT-001 Microdystrophin Gene Therapy: Update on Pulmonary Outcomes

Oscar H. Mayer[1], Barry J. Byrne[2], Stephanie Salabarria[2], Julie Berthy[2], Manuela Corti[2], Susan Redican[3], Jeffry Lawrence[3], Kristy J. Brown[3], Courtney Shanks[3], Sidney Spector[3], J. Patrick Gonzalez[3], Joel S. Schneider[3], Carl A. Morris[3], Cathryn Clary[3]

[1] Children's Hospital of Philadelphia, Philadelphia, PA; [2] University of Florida, Gainesville, FL; [3] Solid Biosciences, Cambridge, MA

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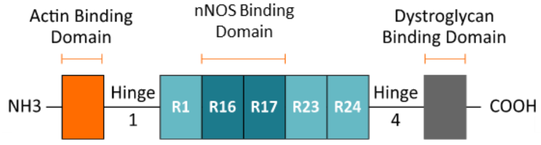
## Introduction / Objective

### 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 | SGT-001 Microdystrophin (µDys5) |




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

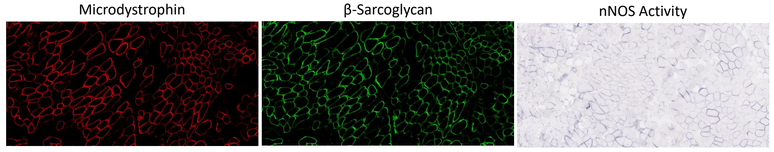
- SGT-001 is currently being evaluated in the IGNITE DMD Phase I/II clinical trial
- A single intravenous infusion of SGT-001 was administered to DMD patients in two ascending dose groups
- Following administration of 5E13 vg/kg to 3 subjects, all subsequent subjects received 2E14 vg/kg
- Three untreated DMD subjects served as controls
- Safety, microdystrophin expression, patient reported outcome measures, and motor and pulmonary function were assessed at baseline and the 1-year primary outcome timepoints
- Additional evaluations at the 1.5-year timepoint have been performed and long-term safety and efficacy continue to be evaluated

## Results

- Microdystrophin expression in the first 3 subjects in the 2E14 group ranged from approximately 5-17.5% of normal dystrophin by Western blot and 10-70% of positive muscle fibers by immunofluorescence at day 90 and were sustained or increased in long-term biopsies
- Microdystrophin positive fibers importantly demonstrated restored sarcolemmal β-sarcoglycan and nNOS in all biopsies evaluated
- Motor function in both dose groups showed stability or improvement after 1 year
- FVC % predicted after 1 year declined by a mean of 10.7% in untreated subjects but increased by 3.3% and 15.7% in the 5E13 and 2E14 groups, respectively
- PEF % predicted and FEV1 % predicted tracked similarly

### Durable Microdystrophin Expression and Protein Function are Observed Between Day 90 and Long-Term Biopsies

| | % 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) |

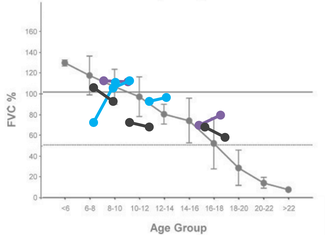



Pt 5 (18 months post-treatment)

### FVC % Predicted is Improved in SGT-001 Treated Subjects at 1 Year when Natural History Would Predict Declining Function

| Cohort | Subject | FVC % Predicted Baseline to 1 Year Change |
|---|---|---|
| Control | Ct 1 | -9.5% |
| | Ct 2 | -7.6% |
| | Ct 3 | -14.9% |
| Low Dose (5E13 vg/kg) | Pt 1 | +8.9% |
| | Pt 2 | n/a |
| | Pt 3 | -2.4% |
| High Dose (2E14 vg/kg) | Pt 4 | +3.1% |
| | Pt 5 | +36.7% |
| | Pt 6 | +7.3% |

**Pulmonary Function in IGNITE DMD Subjects Overlayed on Mayer et al 2015 DMD Natural History**




FVC: forced vital capacity
n/a values represent either baseline or endpoint assessments not available or identification of suboptimal maximal respiratory efforts during testing

## Results Continued

### SGT-001 Treated Subjects Similarly Show Improvements in PEF % Predicted and FEV1 % Predicted 1 Year Post-Treatment

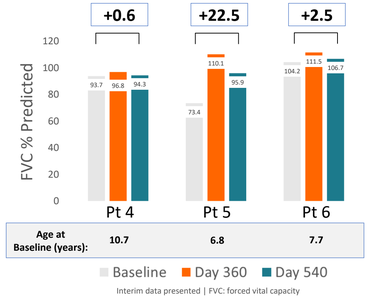
| Cohort | Subject | PEF % Predicted Baseline to 1 Year Change |
|---|---|---|
| Control | Ct 1 | -1.1% |
| | Ct 2 | n/a |
| | Ct 3 | -18.2% |
| Low Dose (5E13 vg/kg) | Pt 1 | +2.5% |
| | Pt 2 | n/a |
| | Pt 3 | +38.5% |
| High Dose (2E14 vg/kg) | Pt 4 | +15.9% |
| | Pt 5 | n/a |
| | Pt 6 | +26.7% |

| Cohort | Subject | FEV1 % Predicted Baseline to 1 Year Change |
|---|---|---|
| Control | Ct 1 | -8.7% |
| | Ct 2 | -17.0% |
| | Ct 3 | -12.0% |
| Low Dose (5E13 vg/kg) | Pt 1 | +13.4% |
| | Pt 2 | n/a |
| | Pt 3 | +4.3% |
| High Dose (2E14 vg/kg) | Pt 4 | +10.8% |
| | Pt 5 | +15.5% |
| | Pt 6 | +2.8% |

PEF: peak expiratory flow | FEV1: forced expiratory volume in one second
n/a values represent either baseline or endpoint assessments not available or identification of suboptimal maximal respiratory efforts during testing

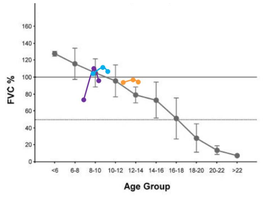
### Pulmonary Function Continues to Show Stability or Improvement 1.5 Years Post-Treatment

*Mean Change from Baseline to Day 540: +8.5 ±12.1% | **Difference of +16.0% Compared to Natural History over 1.5 Years***




Interim data presented | FVC: forced vital capacity

Individual Patient Trajectories




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

*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

## Conclusions

- Durable expression and function of microdystrophin protein are observed in biopsies collected at timepoints 12-24 months post-administration of SGT-001
- Encouraging evidence of motor function benefit is observed in 1-year post-treatment evaluations
- Pulmonary function is sustained or improved in 1 and 1.5-year post-treatment evaluations
- Interim data suggest the potential for SGT-001 to confer meaningful benefit for patients with DMD in multiple muscle groups