SGT-003 Demonstrates High Cardiac Tropism and Positive Preliminary Clinical Findings Using the Next-Generation Muscle-Tropic Capsid

J. Patrick Gonzalez, Jessica F Boehler, Jamie Marshall, Meghan Soustek-Kramer, Marie Ralff, Matthew Harmelink, Jessie Hanrahan, Nicolas Christoforou, Gabriel Brooks

Solid Biosciences Inc., Charlestown, MA, USA

INTRODUCTION

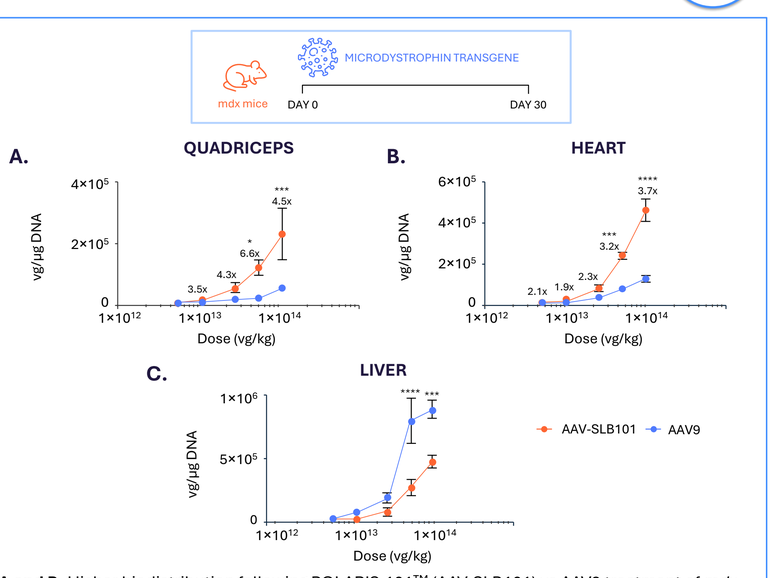
- Duchenne muscular dystrophy is a rare, X-linked recessive disease caused by the loss of functional dystrophin resulting in progressive, severe skeletal myopathy and cardiomyopathy, which is a leading cause of death
- Overt cardiomyopathy typically manifests late in the second decade
- However, intermittent and asymptomatic troponin I elevations and subtle declines in systolic function can be observed even before the age of 10
- This underscores the urgent need for therapies that not only restore dystrophin in skeletal muscle but also in the heart to preserve cardiac function
- POLARIS-101™ (formerly known as AAV-SLB101), Solid Biosciences' proprietary capsid, was rationally designed to improve cardiac and skeletal muscle tropism and is utilized in SGT-003, Solid's next-generation, investigational microdystrophin gene therapy for Duchenne
- POLARIS-101™ (AAV-SLB101) demonstrated increased muscle tropism and decreased liver uptake in both healthy animals and disease models (wild type and *mdx* mice, non-human primates, and human myotubes and iPSC-derived cardiac myocytes) when compared to first generation vectors (AAV9 and AAVrh74)
- In the *mdx* mouse model of Duchenne and in non-human primates, POLARIS-101™ (AAV-SLB101) -mediated transgene expression was several-fold higher than AAVrh74 in multiple muscle groups, and specifically four times higher in the heart

METHODS

- INSPIRE DUCHENNE is an ongoing open-label Phase 1/2 study evaluating a single IV dose of SGT-003 (1E14 vg/kg) in participants with Duchenne; primary endpoints include TEAEs through Day 360 and Day 90 microdystrophin expression, with secondary endpoints including evaluations of microdystrophin durability (Day 360) and function assessments
- SGT-003 transduction and microdystrophin expression were evaluated in muscle biopsies collected from INSPIRE DUCHENNE study participants
- Cardiac function and biomarkers of cardiac injury, were monitored

RESULTS

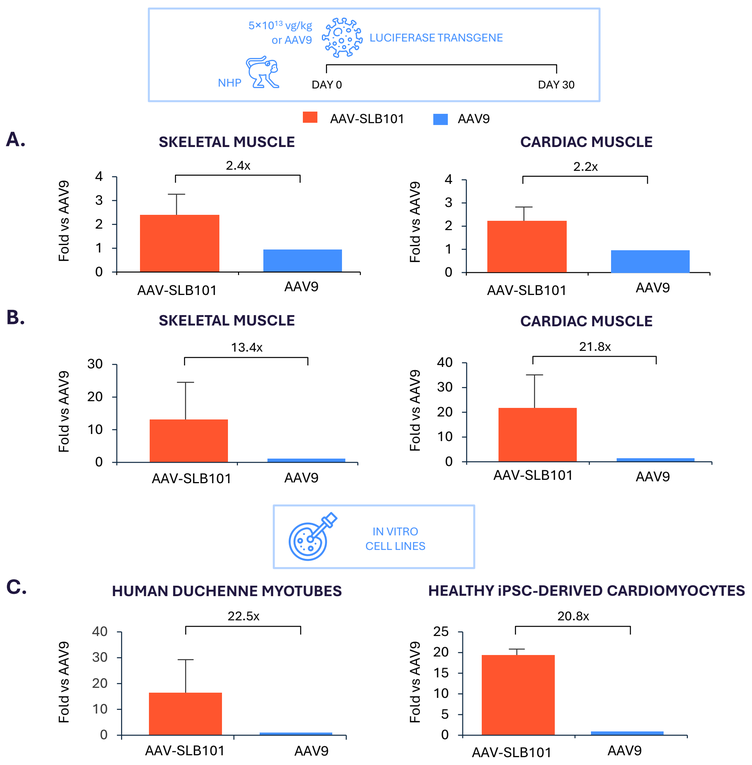
Figure 1. Head-to-Head Comparison in *mdx* Mouse Model of Duchenne



A and B. Higher biodistribution following POLARIS-101™ (AAV-SLB101) vs AAV9 treatment of *mdx* mice in disease-relevant tissues was observed in the quadriceps and heart. **C.** Decreased biodistribution of POLARIS-101™ (AAV-SLB101) vs AAV9 was observed in the liver. Asterisks indicate statistical significance (*P<0.05, ***P <0.001, ****P <0.0001) between groups with fold changes depicted.

POLARIS-101™ (AAV-SLB101) TRANSDUCTION EFFICIENCY IN THE HEART IS HIGH BASED ON DATA FROM HUMAN CELL LINES, MICE, AND NHPs

Figure 2. Transduction Efficiency of POLARIS-101™ (AAV-SLB101) Compared to AAV9 in Non-human Primates (NHPs) and Human Cell Lines



A. Higher biodistribution (vector DNA). **B.** Luciferase activity following POLARIS-101™ (AAV-SLB101) versus AAV9 treatment in nonhuman primates (n=3); average fold differences were calculated across five skeletal muscle tissues and three cardiac regions sampled. **C.** In vitro experiments demonstrated increased luciferase activity of POLARIS-101™ (AAV-SLB101) in Duchenne myotubes and healthy induced pluripotent stem cell–derived cardiomyocytes compared with AAV9. AAV9, adeno-associated virus serotype 9; Duchenne, Duchenne muscular dystrophy; iPSC, induced pluripotent stem cells; NHP, nonhuman primate.

REFERENCES

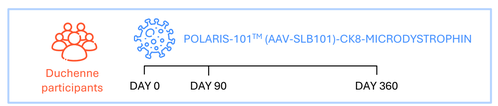
1. Data on file. Solid Biosciences. 2025. Data cutoff September 29, 2025. 2. Data on file. Solid Biosciences. 2025. Data cutoff January 13, 2026. 3. Romanowicz J, et al. J Am Soc Echocardiogr. 2023;36(3):310-323.

ACKNOWLEDGMENTS

This study was sponsored by Solid Biosciences Inc. (Charlestown, MA, USA). Medical writing and editing assistance were provided by the Propel Division of Woven Health Collective, LLC (New York, NY), and was funded by Solid Biosciences Inc.

COMPREHENSIVE ORTHOGONAL MEASUREMENTS SHOWED CONSISTENT MICRODYSTROPHIN EXPRESSION[a]

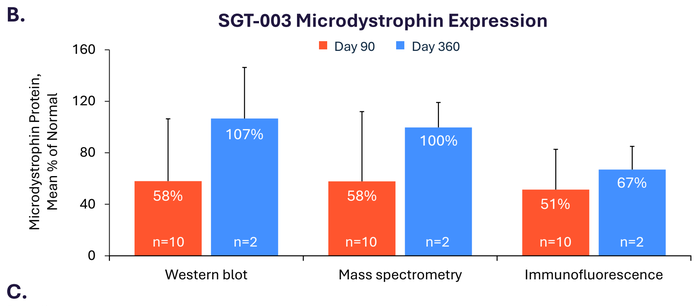
Figure 3. Data from INSPIRE DUCHENNE Clinical Trial of SGT-003[1]



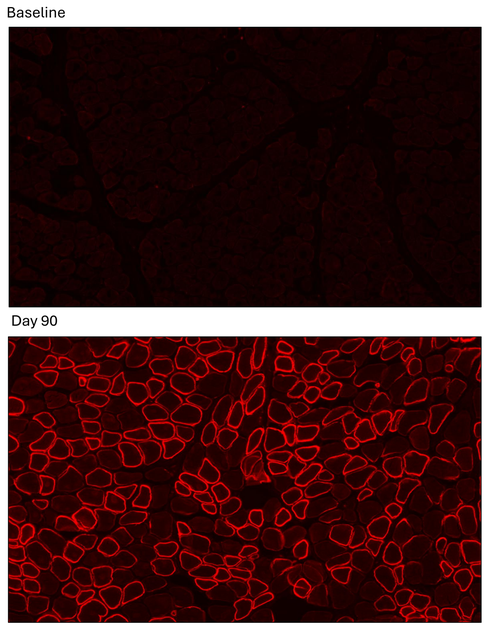
A.

DOSE (vg/kg)	VECTOR COPIES/NUCLEUS DAY 90 (n=10)	VECTOR COPIES/NUCLEUS DAY 360 (n=2)
1×10^{14}	13	12

B.



C.



A. Vector copies per nucleus at Day 90 and Day 360.
B. Microdystrophin expression measured by western blot, mass spectrometry, and immunofluorescence. [a]Baseline western blot and mass spectrometry were 0% mean normal dystrophin. Baseline mean dystrophin-positive fibers were 1.5% by immunofluorescence. Dystrophin-positive fibers are reported as absolute values and are not adjusted for fat or fibrosis.
C. Representative microdystrophin muscle biopsy images at baseline and Day 90; representative images are shown. Data on file. Data cutoff: September 29, 2025. Solid Biosciences. 2025.

33 PARTICIPANTS HAVE RECEIVED SGT-003 (1.0E14 vg/kg) AT AGES RANGING FROM 1 TO 10 YEARS AS OF 1/13/26[2]

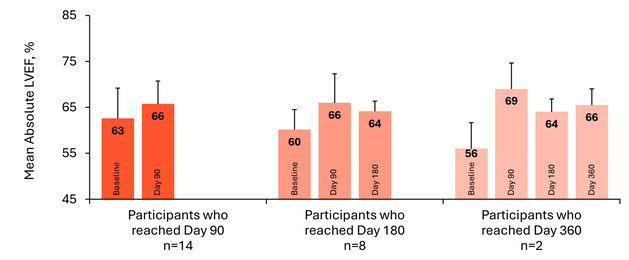
Table 1. Safety Summary, INSPIRE DUCHENNE Clinical Study of SGT-003: POLARIS-101™ (AAV-SLB101)-CK8-Microdystrophin

Cohorts	Eligible Age Range (years)	Ages at Enrollment (years)	Weights for Dosing (kg)	Participants Enrolled (n)
1-3	0 to <12	1 to 10	9.9 to 39.7	33

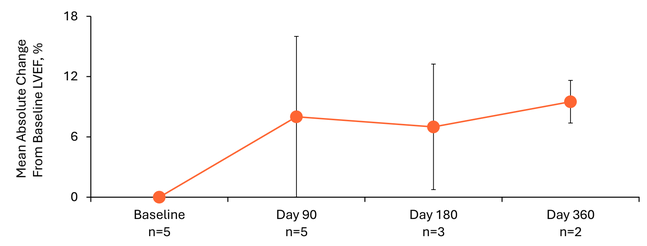
SGT-003 Participants With Treatment-Related Adverse Events (AEs) as of January 13, 2026 (n=33)		n (%)
Serious Adverse Events (SAEs)		1 (3.0)[a]
Most Common Treatment-Related AEs	Nausea	24 (72.2)
	Vomiting	21 (63.6)
	Thrombocytopenia	11 (33.3)
	Decreased appetite	11 (33.3)
	Headache	8 (24.2)
	Cough	8 (24.2)

Figure 4. Signals of SGT-003 Cardiac Treatment Effect from INSPIRE DUCHENNE[1]

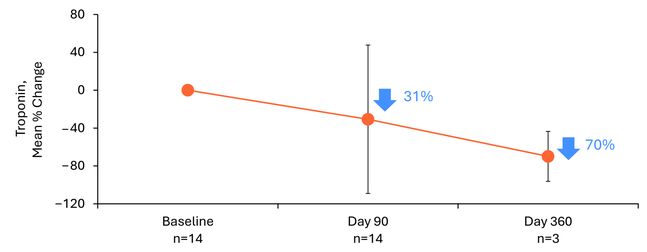
A. ABSOLUTE LEFT VENTRICULAR EJECTION FRACTION (LVEF) OVER TIME



B. ABSOLUTE CHANGE FROM BASELINE LVEF



C. PERCENT CHANGE FROM BASELINE TROPONIN



A. The mean ± SD normal LVEF range is 60% to 69% for this age-matched population.[3]
B. Observations of improved cardiac function, as measured by LVEF using echocardiography, in those with low to low-normal baseline LVEF.
C. A reduction of mean Troponin I was observed in participants after being dosed with SGT-003.

CONCLUSIONS

- Early findings in the Phase 1/2 INSPIRE DUCHENNE (NCT06138639) study investigating SGT-003 indicate a positive safety profile, high levels of microdystrophin expression, and potentially favorable changes in cardiac biomarkers as of a data cutoff of September 29, 2025
- The mean levels of troponin I were observed to have declined post-treatment with SGT-003.
- Improvements in systolic function, as measured by LVEF using echocardiography, were also observed and were largely driven by patients with low-normal systolic function at baseline
- These findings suggest that SGT-003 may not only slow skeletal muscle decline but may also mitigate the progressive cardiomyopathy that has increasingly becoming a leading cause of death for patients with Duchenne
- Together, these findings underscore the potential for POLARIS-101™ (AAV-SLB101) as a targeted gene therapy vector for neuromuscular and cardiac indications, such as Duchenne.

Presented at MDA Clinical and Scientific Conference, March 8–11, 2026, Orlando, Florida