AAV-SLB101: A Next-Generation Rationally Designed Capsid Demonstrates Highly Potent Cardiac Tropism and Initial Clinical Safety

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Acknowledgments

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DMD Community

- PPMD, Duchenne UK, TREAT-NMD, MDA, Jett Foundation

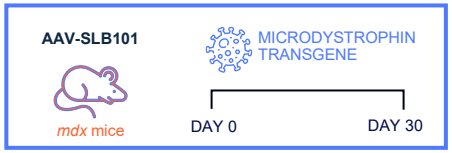
Solid Biosciences

- Preclinical and clinical development departments

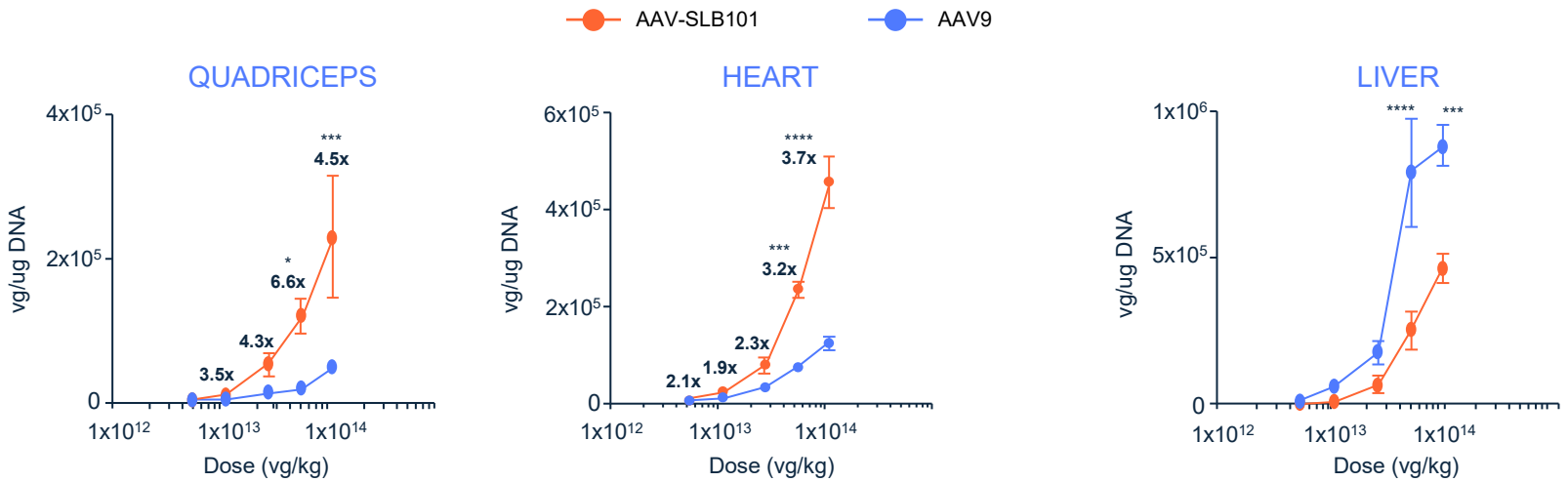
SGT-003 Is Solid's Next-Generation, Investigational Microdystrophin Gene Transfer Therapy That Uses AAV-SLB101

- AAV-SLB101 is a proprietary, rationally designed muscle-tropic capsid used in Solid Biosciences' investigational gene therapy, SGT-003
- SGT-003 is currently being evaluated in the INSPIRE DUCHENNE (NCT06138639) phase 1/2 clinical study for the treatment of Duchenne muscular dystrophy (Duchenne)
- AAV-SLB101–mediated transduction and expression of reporter and therapeutic transgenes were compared with first-generation vectors in wild-type and Duchenne mouse models
- SGT-003 transduction and microdystrophin expression were evaluated in muscle biopsies collected from INSPIRE DUCHENNE study participants
- Cardiac structure and function, and biomarkers of cardiac injury, were monitored

AAV-SLB101 Showed Improved Muscle Transduction and Lower Liver Distribution Compared With AAV9



Head-to-Head Comparison of Biodistribution in *mdx* Mouse Model of Duchenne[a]

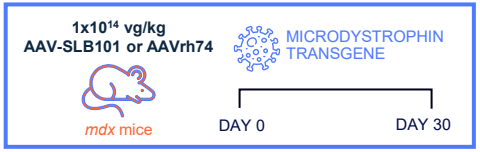


Higher biodistribution following AAV-SLB101 vs AAV9 treatment of *mdx* mice in disease-relevant tissues was observed in the quadriceps and heart

Decreased biodistribution of AAV-SLB101 vs AAV9 was observed in the liver

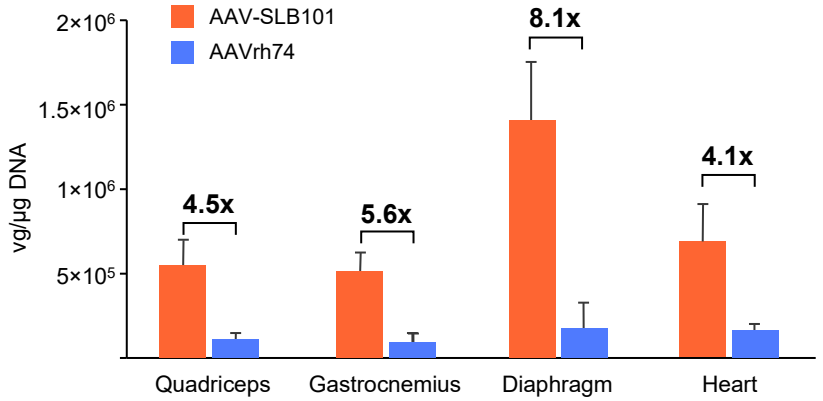
[a]Asterisks indicate statistical significance (*P<0.05, ***P<0.001, ****P<0.0001) between groups with fold changes depicted.
Data on file. Solid Biosciences. 2025.

AAV-SLB101 Resulted in Higher Biodistribution and Expression Compared With AAVrh74

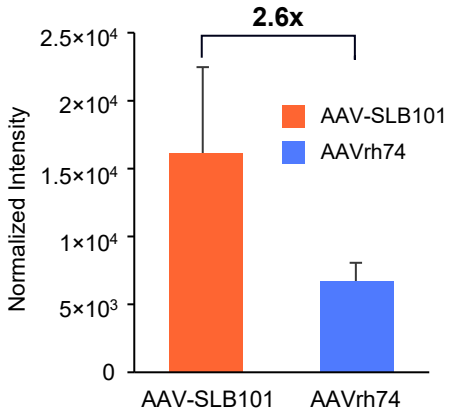


Head-to-Head Comparison in *mdx* Mouse Model of Duchenne

BIODISTRIBUTION



MICRODYSTROPHIN EXPRESSION (WB)

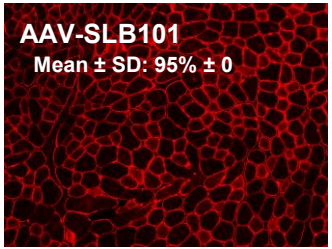


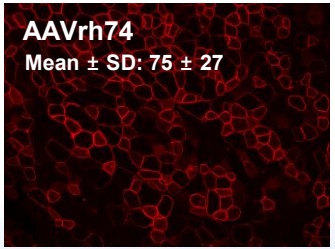
Higher biodistribution following AAV-SLB101 vs AAVrh74 treatment of *mdx* mice was observed in quadriceps, gastrocnemius, diaphragm, and heart

Higher microdystrophin expression was observed in quadriceps of AAV-SLB101 vs AAVrh74-treated *mdx* mice

Immunofluorescence

QUADRICEPS

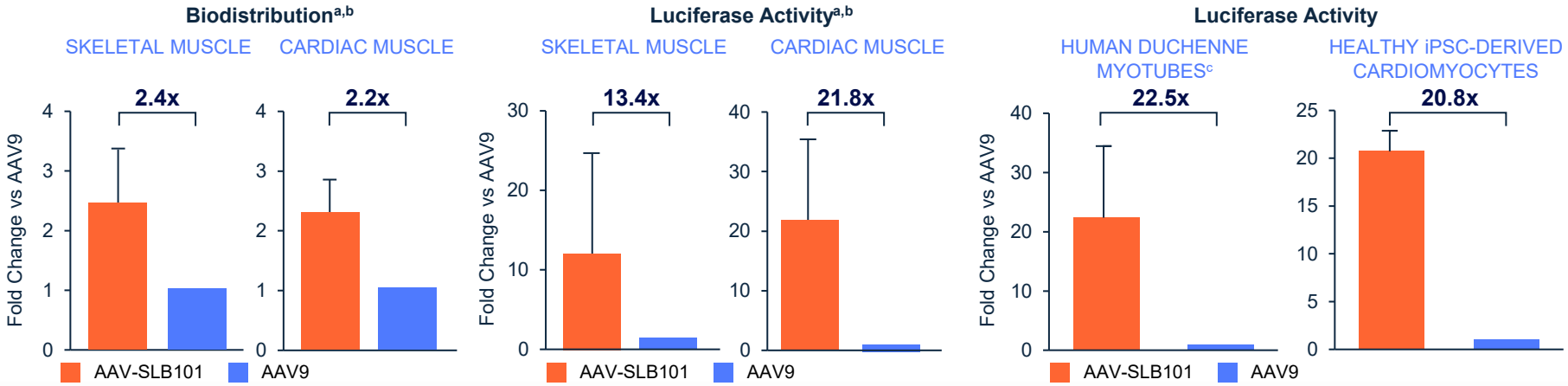




WB=western blot.
Data on file. Solid Biosciences. 2025.

AAV-SLB101 Transduction Efficiency Was Maintained in NHP Studies and Human Cell Lines Compared With Initial Results in Mice

Transduction Efficiency of AAV-SLB101 Compared With AAV9 in NHPs and Human Cell Models



Higher biodistribution (vector DNA) and luciferase activity were observed with AAV-SLB101 compared with AAV9 in NHPs

Increased luciferase activity was observed with AAV-SLB101 vs AAV9 in both Duchenne myotubes and healthy iPSC cardiomyocytes

NHP=non-human primate.
[a]n=2 per group. [b]Average fold differences calculated from the five skeletal muscle tissues sampled and three regions of cardiac tissue sampled. [c]n=3 cell lines per treatment.
Data on file. Solid Biosciences. 2025.

INSPIRE DUCHENNE Clinical Study of SGT-003: AAV-SLB101-CK8-Microdystrophin

Cohort	Eligible Age Range (years)	Ages at Enrollment (years)	Weights for Dosing (kg)	Participants Enrolled (n)
1	4 to <7	4 to 6	≤27.8	13
2	7 to <12	7 to 10	≤39.7	8
3	0 to <4	1 to 3	≤17.0	2
Total	**0 to <12**	**1 to 10**	**≤39.7**	**23**

SGT-003 Treatment-Related Adverse Events as of October 31, 2025 (N=23)		n (%)
Serious Adverse Events (SAEs)		1 (4.3)[a]
Most common treatment-related adverse events (AEs)	Nausea	17 (73.9)
	Vomiting	16 (69.6)
	Decreased appetite	11 (47.8)
	Thrombocytopenia/platelet count decreased	11 (47.8)
	Headache	6 (26.1)

[a]One (n=1) CTCAE Grade 3 serious adverse event of immune-mediated myositis. The myositis was not associated with muscle pain or weakness. The participant responded promptly to steroid treatment, with all clinical symptoms noted at presentation resolving and with creatine kinase levels declining well below baseline.
Data on file. Solid Biosciences. 2025. Data cutoff September 29, 2025.

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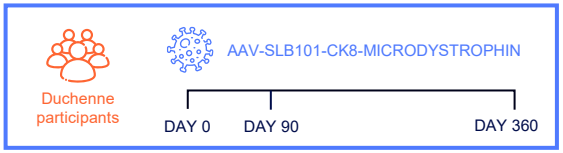
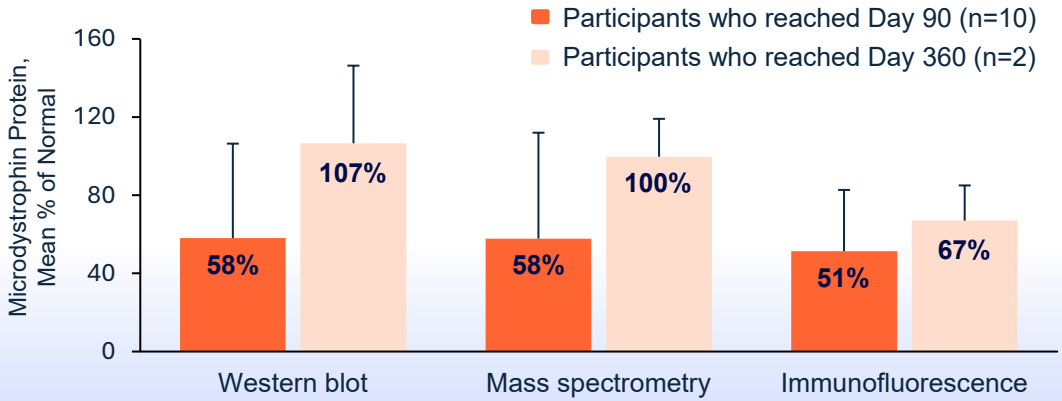
Data From INSPIRE DUCHENNE Clinical Trial of SGT-003



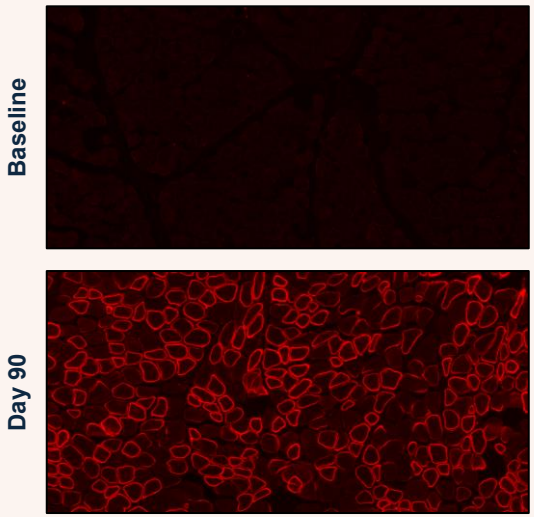
Vector Genome Copies/Nucleus

Dose	Day 90 (n=10)	Day 360 (n=2)
1x10^{14} vg/kg	13	12

SGT-003 Microdystrophin Expression



Example Microdystrophin Biopsy



Data on file. Solid Biosciences. 2025. Data cutoff September 29, 2025.

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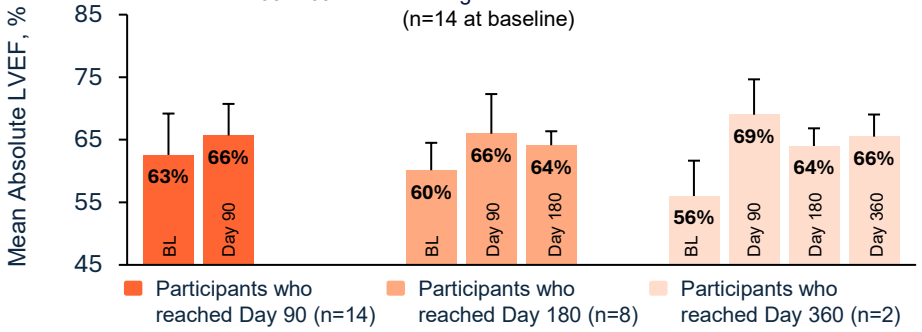
Reassuring-to-Promising Cardiac Function After SGT-003 Dosing[1]

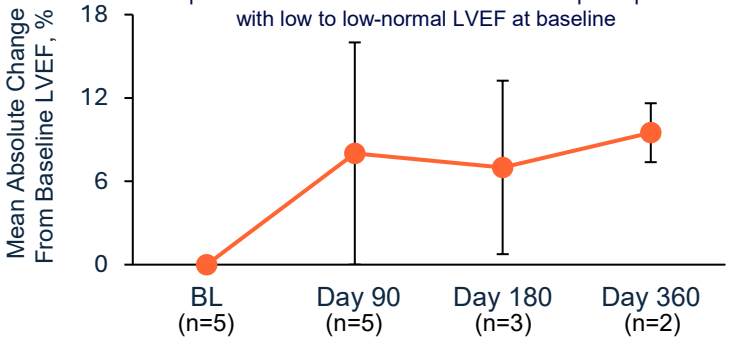
ABSOLUTE LVEF OVER TIME (%)

60%-69% normal range of LVEF = mean ± SD[2,a]
(n=14 at baseline)

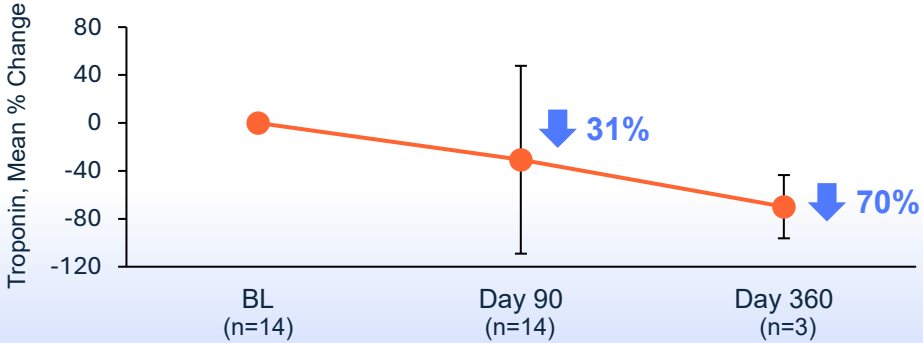


ABSOLUTE CHANGE FROM BASELINE LVEF (%)

Improved cardiac function was observed in participants with low to low-normal LVEF at baseline



CHANGE FROM BASELINE TROPONIN (%)



- Observations of improved cardiac function driven by participants with low to low-normal baseline LVEF
- Troponin reductions may indicate early signals of SGT-003 cardiac treatment effect

BL=baseline; LVEF=left ventricular ejection fraction.
[a]The mean ± SD normal LVEF range is 60% to 69% for this age-matched population.
1. Data on file. Solid Biosciences. 2025. Data cutoff September 29, 2025. 2. Romanowicz J, et al. *J Am Soc Echocardiogr.* 2023;36(3):310-323.

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AAV-SLB101 Overcomes the Challenges of First-Generation Capsids

- Higher biodistribution and transgene expression were achieved with AAV-SLB101 compared with AAV9 in animal (*mdx* mice, NHPs) and human cell models in key tissues for Duchenne, including skeletal muscle and heart
- Reductions in AAV-SLB101 liver biodistribution were observed compared with that of AAV9 in both mice and NHPs
- High levels of biodistribution and microdystrophin expression were observed in muscle biopsies collected from participants treated with SGT-003 in INSPIRE DUCHENNE
- Though collected for safety, early data from INSPIRE DUCHENNE study may indicate signals of potential benefit through reduction in cardiac troponin and increased systolic function, as measured by LVEF using echocardiography