AAV-SLB101, a Novel Muscle-tropic Capsid, Increases Gene Delivery and Expression Versus AAV9 and AAVrh74 in Mouse Models of DMD and FSHD Muscle Disease

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SOLID BIOSCIENCES

Scan for Capsid Information

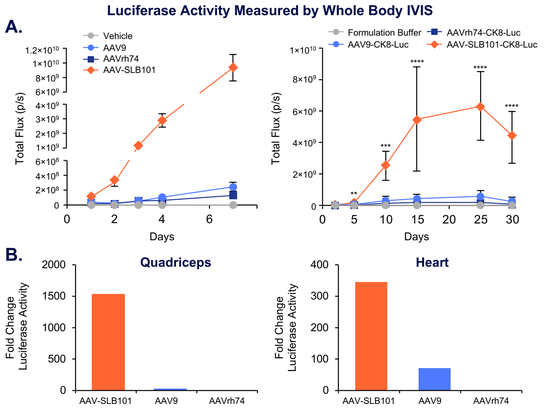
INTRODUCTION

- AAV-SLB101 is a proprietary rationally designed capsid used in Solid Biosciences' next-generation 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 (DMD).
- AAV-SLB101-mediated transduction and expression of various reporter and therapeutic transgenes were compared to first generation (AAV9 and AAVrh74) or next generation (MyoAAV) vectors in wild type and mouse models of muscle disease (DMD and FSHD).
- Muscle biopsy data from the first 3 participants reaching the Day 90 timepoint in the INSPIRE DUCHENNE clinical study and a safety overview with a data cutoff of March 7, 2025 are reported here.

RESULTS

AAV-SLB101 ACHIEVED FASTER AND HIGHER EXPRESSION VS AAV9 OR AAVrh74 IN WT MICE

Figure 1. Kinetics and Transduction Efficacy of AAV-SLB101 Compared to AAV9 and AAVrh74

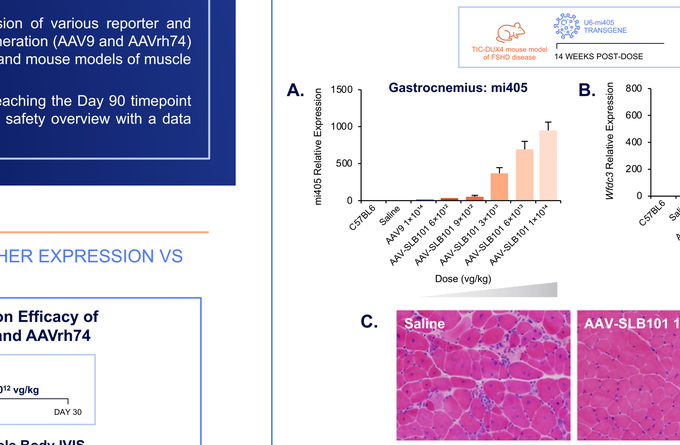


A. Luciferase activity (whole body IVIS) was detected as early as 2 days post-dose and remained significantly higher for AAV-SLB101 vs AAV9 or AAVrh74. At Day 15, expression plateaued for all capsids, with higher AAV-SLB101-directed levels maintained until Day 30. **B.** Ex vivo luciferase activity was significantly higher for AAV-SLB101 vs AAV9 or AAVrh74 in heart and quad tissues at Day 30.

RESULTS *(cont'd)*

AAV-SLB101: EFFICACIOUS AT LOWER DOSES VS AAV9 IN DUX4 MODEL OF FSHD

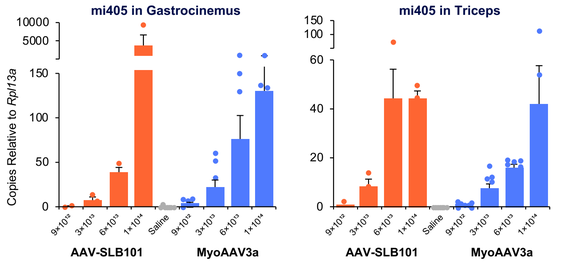
Figure 2. DUX4 Mouse Model of Facioscapulohumeral Muscular Dystrophy (FSHD)



A. Substantially higher levels of mi405 expression in gastrocnemius muscle of mice treated with AAV-SLB101 vs AAV9. **B.** Higher mi405 expression corresponded to lower levels of *Wfdc3*, a target gene of DUX4 and pre-clinical biomarker of FSHD in animal models. **C.** Hematoxylin and eosin show muscle histology improvements in AAV-SLB101-treated mice.

AAV-SLB101 ACHIEVED SIMILAR EXPRESSION AS MyoAAV3A IN DUX4 MODEL OF FSHD

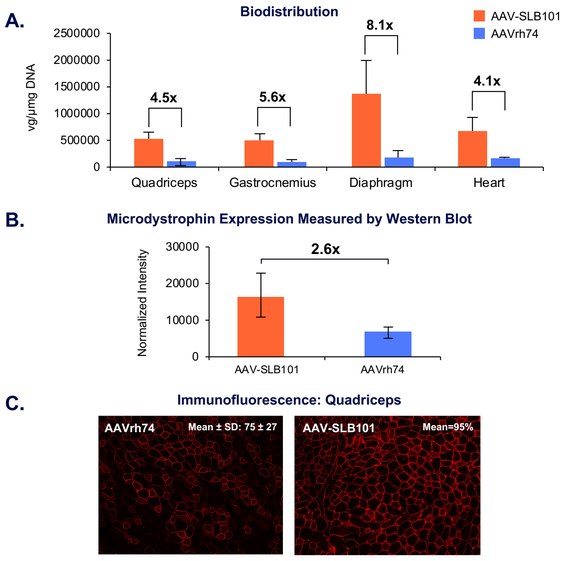
Figure 3. DUX4 Mouse Model of FSHD



Similar levels of mi405 expression from AAV-SLB101 vs next generation MyoAAV3a capsid in muscle tissues at 14 weeks post-dose. Dose unit is vg/kg.

AAV-SLB101: SUPERIOR TO AAVrh74 IN *mdx* MODEL OF DMD

Figure 4. *Mdx* Mouse Model of Duchenne Muscular Dystrophy (DMD)



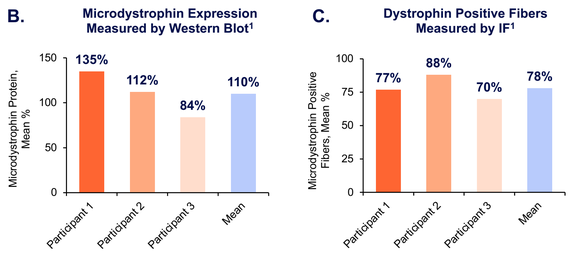
A. Higher biodistribution following AAV-SLB101 vs AAVrh74 treatment of *mdx* mice in disease-relevant quadriceps, gastrocnemius, diaphragm, and heart. **B.** Higher microdystrophin expression detected by Western blot in quadriceps of AAV-SLB101 vs AAVrh74-treated mice. **C.** Increased number of microdystrophin positive muscle fibers in quadriceps of AAV-SLB101 vs AAVrh74-treated mice. SD, standard deviation.

INSPIRE DUCHENNE CLINICAL STUDY OF SGT-003: AAV-SLB101-CK8-MICRODYSTROPHIN

Figure 5. INSPIRE DUCHENNE Clinical Study of SGT-003 in DMD Participants

A.

PARTICPANT	DOSE	COPIES/NUCLEUS
1	1.0×10¹⁴ vg/kg	19.8
2		28.6
3		7.6
Mean		**18.7**



A. Biodistribution following SGT-003 in first 3 DMD participants. **B.** Average (n=3) microdystrophin expression by western blot was 110% of normal. **C.** Average of 78% (n=3) microdystrophin positive muscle fibers by immunofluorescence.

[1]Baseline western blot was 0% mean normal dystrophin. Baseline mean dystrophin positive fibers were 1.5% measured by immunofluorescence. Dystrophin positive fibers are not adjusted for fat or fibrosis; these are absolute numbers.

SGT-003 TREATMENT-EMERGENT ADVERSE EVENTS (TEAEs) *Data cutoff March 7, 2025*		TOTAL PARTICIPANTS (N=7) n (%)
Serious Adverse Events (SAEs)		0 (0)
Adverse Events of Special Interest (AESIs)	Hepatotoxicity	0 (0)
	Thrombotic Microangiopathy	0 (0)
	Myocarditis	0 (0)
	Myositis	0 (0)

The most common treatment-related adverse events (AEs) reported: nausea (n=7), vomiting (n=6), headache (n=4), and thrombocytopenia/platelet count decreased (n=4).

CONCLUSIONS

- Higher biodistribution and transgene expression were achieved when using AAV-SLB101 vs AAV9 or AAVrh74 in wild type and mouse models of muscle disease.
- AAV-SLB101-mi405 delivery outperformed AAV9 in FSHD disease model and was efficacious at much lower doses, comparable to MyoAAV3a.
- Higher biodistribution and microdystrophin expression were achieved with AAV-SLB101-CK8-microdisytrophin vs AAVrh74 in *mdx* DMD mice.
- There were high levels of biodistribution and microdystrophin expression in muscle biopsies of 3 DMD participants treated with SGT-003 in the INSPIRE DUCHENNE clinical study.
- No treatment-emergent SAEs were reported and all treatment-related AEs resolved without sequelae in the weeks following dosing (data cutoff March 7, 2025; n=7).

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