Positive Preliminary Safety and Liver Toxicity Profile Using SGT-003, Solid Biosciences' Next-Generation Investigational Gene Therapy for Duchenne Muscular Dystrophy

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INTRODUCTION

- Adeno-associated viral vectors are a promising tool for gene therapy due to their ability to deliver genetic material with high precision. However, high vector doses have typically been required to achieve broad skeletal and cardiac muscle transduction. High systemic doses have been associated with dose-dependent safety risks, including hepatotoxicity.
- Rational capsid engineering offers an approach to improve muscle selectivity and reduce off-target liver exposure.
- POLARIS-101™ (formerly known as AAV-SLB101), Solid Biosciences' proprietary, rationally designed capsid, has demonstrated enhanced skeletal and cardiac muscle tropism with reduced liver biodistribution in preclinical studies.
- SGT-003, Solid's next-generation investigational gene therapy for DMD, incorporates POLARIS-101™ (AAV-SLB101) with the goal of enabling effective muscle transduction at lower systemic doses and improving the therapeutic index.
- INSPIRE DUCHENNE (NCT06138639) is a Phase 1/2 open-label, non-randomized multi-center clinical trial enrolling ambulatory boys with Duchenne aged 0 to < 12 years at 15 active clinical trial sites across the U.S., Canada, Italy, and the U.K.

OBJECTIVES

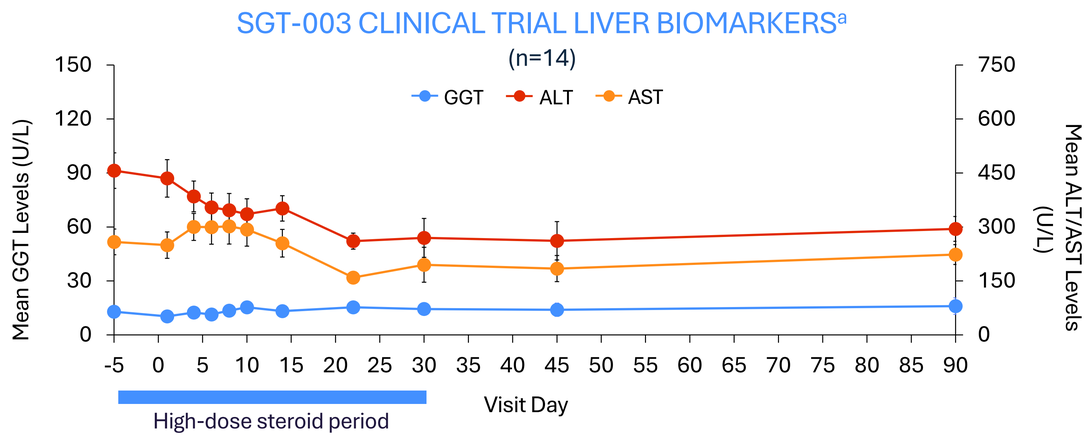
- To characterize and classify the liver-related biochemical profile in SGT-003-treated participants using predefined, FDA-aligned published criteria

METHODS

- Longitudinal tests of ALT, AST, GLDH and GGT were performed on samples collected from participants in the ongoing INSPIRE DUCHENNE study
- Results were plotted to assess potential trends across visits relative to baseline values
- Ratios of creatine kinase (CK) to ALT and AST were derived and similarly plotted to evaluate whether this more sensitive approach recently described would contribute to the assessment of potential trends

RESULTS

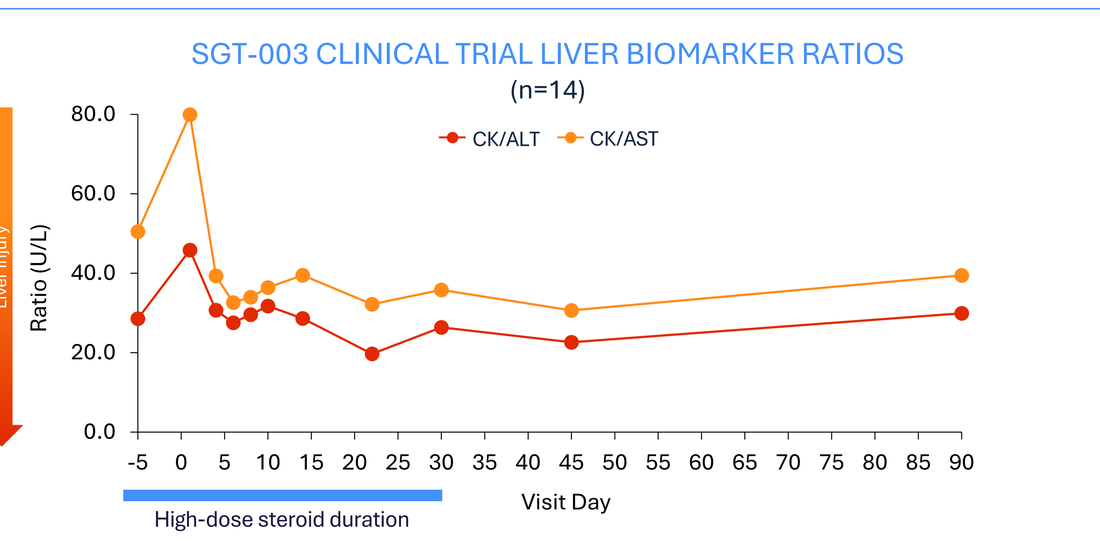
Figure 1. Liver Enzymes Declined or Remained Stable in the Peri-Dosing Period Following SGT-003 Administration[1]



GGT=gamma-glutamyl transferase, ALT=Alanine Aminotransferase, AST=Aspartate Aminotransferase
[a]Steroid tapering begins at Day 30 per INSPIRE DUCHENNE trial protocol.
1. Data on file. Data cutoff of September 29, 2025. Solid Biosciences.

- Mean ALT, AST, and GGT values decreased following administration and remained stable through Day 90, with no laboratory signal consistent with drug-induced liver injury

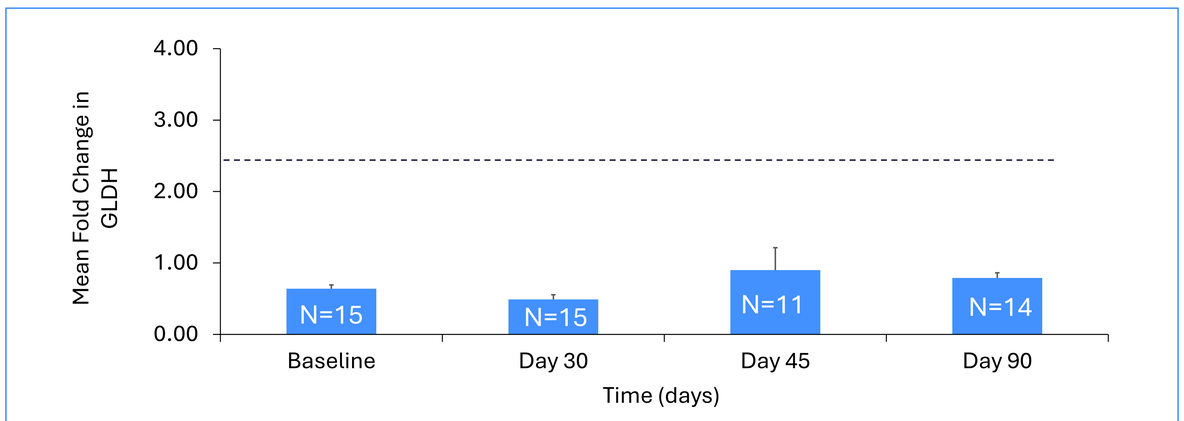
Figure 2. CK/ALT and CK/AST Ratios Demonstrate Stabilization After Dosing[1]



[a]Mean normal CK/AST ratio was 41.6 (SD: 15.5, 95% CI: 39.5-43.7). Mean normal CK/ALT ratio was 31.8 (SD: 26.1, 95% CI: 28.3-35.4).
1. Data on file. Data cutoff of September 29, 2025. Solid Biosciences. 2. Fequiere PR, et al. *Neuromuscul Disord*. 2008;18(9):806-807.

- Mean CK/transaminase ratios remained stable through Day 90, suggesting the changes in enzyme levels are due to muscle membrane improvements without injury to the liver
- The ratio of CK to ALT and AST has been demonstrated as an effective and sensitive early biomarker of liver injury in Duchenne. Trends observed after treatment with SGT-003 showed reassuring CK/AST and CK/ALT ratios, suggesting stabilization of muscle with no signal of injury

Figure 3. Mean Fold Change Relative to the Upper Limit of Normal in GLDH for Participants Receiving SGT-003, up to Day 90[1]



Hepatotoxicity has been defined as greater than 2.5x to 5.0x upper limit of normal (ULN)
1. Data on file. Data cutoff of September 29, 2025. Solid Biosciences.

Table 1. SGT-003 Treatment-Related Adverse Events From the INSPIRE DUCHENNE Clinical Trial[3]

SGT-003 Participants With Treatment-Related Adverse Events (AEs) as of January 13, 2026 (n=33)		n (%)
Serious Adverse Events (SAEs)		1 (3.0)
Drug-Induced Liver Injury[4]		0 (0%)
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)

DILI criteria defined as ALT/AST ≥3× ULN, ALP ≥2× ULN, or total bilirubin ≥2× ULN with elevated transaminases.
4. FDA. 2009. *Drug-Induced Liver Injury: Premarketing Clinical Evaluation*.

CONCLUSIONS

- As of January 13, 2026, SGT-003 has been generally well tolerated, demonstrating a favorable safety profile with no findings of drug-induced liver injury (DILI) across all participants who have received SGT-003 in the Phase 1/2 INSPIRE DUCHENNE trial (NCT06138639)
- Mean AST and ALT decreased overall, suggesting stabilization of muscle
- Novel methods of evaluating for liver injury suggested reassuring trends
- These findings demonstrated encouraging liver data following treatment with SGT-003 which may be attributed to the reduced liver biodistribution of the POLARIS-101™ (AAV-SLB101) capsid

REFERENCES

1. Data on file. Data cutoff of September 29, 2025. Solid Biosciences. 2. Fequiere PR, et al. Neuromuscul Disord. 2008;18(9):806-807. DILI criteria defined as ALT/AST ≥3× ULN, ALP ≥2× ULN, or total bilirubin ≥2× ULN with elevated transaminases. 3.Data on file. Data cutoff of January 13, 2026. Solid Biosciences. 4. FDA. 2009. Drug-Induced Liver Injury: Premarketing Clinical Evaluation.

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