Novel Pharmacokinetic Effects of POLARIS-101™, Solid Biosciences' Rationally Designed, Next-Generation Capsid

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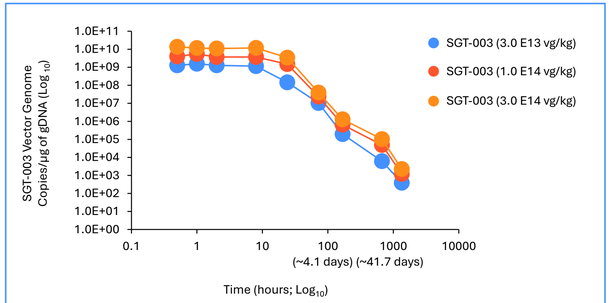
INTRODUCTION

- Adeno-associated virus (AAV) mediated gene therapy has emerged as a promising therapeutic for neuromuscular diseases; however, high systemic doses are required to achieve sufficient skeletal muscle and cardiac transduction
- POLARIS-101™ (formerly known as AAV-SLB101) was rationally designed as a vector with improved targeting capabilities to increase skeletal muscle and cardiac tropism through peptide insertions containing the RGD motif
- This capsid is under first-in-human clinical evaluation in the Phase 1/2 INSPIRE DUCHENNE trial (NCT06138639) and is also being evaluated in the Phase 3 IMPACT DUCHENNE trial (NCT07160634) of SGT-003, Solid Biosciences' investigational, next-generation gene therapy for Duchenne muscular dystrophy (Duchenne)
- To better understand the pharmacokinetics (PK) and pharmacodynamic (PD) effects of this novel capsid in comparison to first-generation capsids, a series of preclinical studies and early data from humans treated with SGT-003 were evaluated

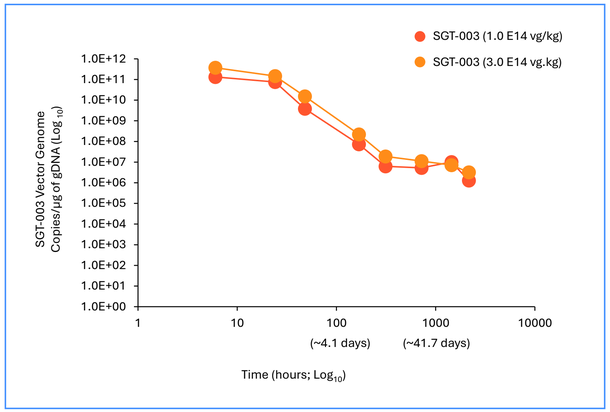
PRECLINICAL DATA PROVIDE INSIGHT INTO THE KINETICS OF POLARIS-101™

Figure 1. Whole Blood Concentrations of SGT-003 Declined Rapidly Within Days in *mdx* Mice



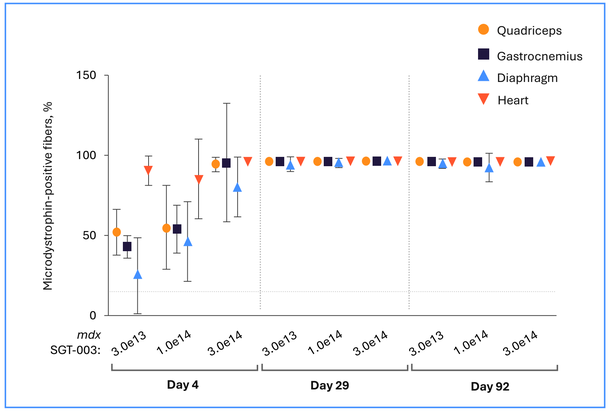
- The copies per microgram of genomic vector gDNA detected in blood are presented. Mean (n=5) for all study animals within a dose group and timepoint are plotted

Figure 2. Whole Blood Concentrations of SGT-003 Declined Rapidly Within Days in Male Cynomolgus Monkeys



- The copies per microgram of genomic vector gDNA detected in blood are presented. Mean (n=3) for study animals within a dose group and timepoint are plotted

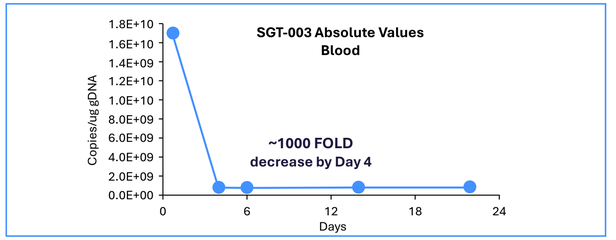
Figure 3. SGT-003 Treatment Exhibited Rapid and Robust Microdystrophin Expression



- SGT-003 dosed *mdx* mice demonstrate rapid tissue expression of SGT-003 microdystrophin at or near 100% positive fibers by Day 4

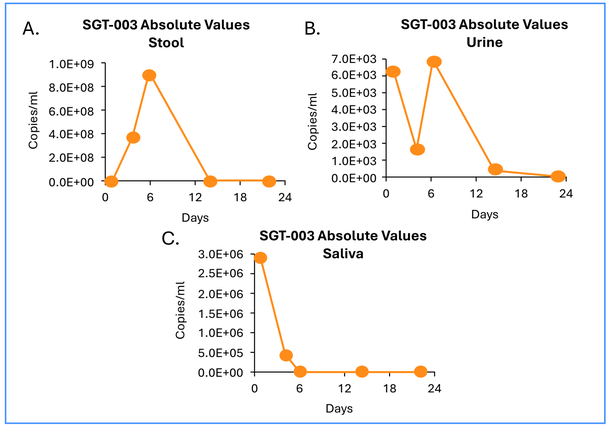
CLINICAL DATA PROVIDE INSIGHT INTO THE KINETICS OF POLARIS-101™

Figure 4. Mean Clearance of POLARIS-101™ up to Day 24[1]



- By Day 4 post-dose, POLARIS-101™ clearance is rapid and reflects what has been seen in animal models.

Figure 5. Shedding of POLARIS-101™ across matrices[1]



- Results from stool, urine and saliva suggest a short shedding duration (**Figure 5. A, B, C**)

Table 1. PCR Analysis Demonstrated High-Vector Genome Copies in Muscle Post–SGT-003 Treatment[2]

Dose	Day 90 (N=20)	Day 360 (N=3)
1.0E14 vg/kg	**11**	**12**

- High tissue transduction in the context of rapid clearance suggests that this is due to rapid uptake into target tissues

COMPREHENSIVE ORTHOGONAL MEASUREMENTS SHOWED CONSISTENT MICRODYSTROPHIN EXPRESSION

Figure 6. Mean SGT-003 Microdystrophin Expression[2]

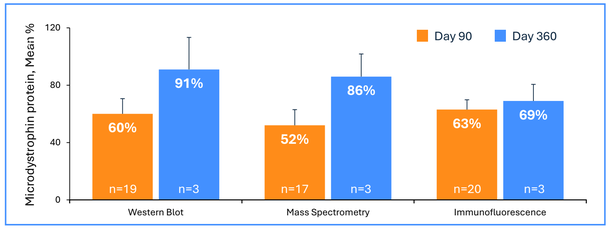


Table 2. SGT-003 Treatment-Related Adverse Events From the INSPIRE DUCHENNE Trial[2]

SGT-003 Participants With Treatment-Related Adverse Events (AEs) as of February 23, 2026 (n=39)		n (%)
Serious Adverse Events (SAEs)		1 (2.62)
Most Common Treatment-Related AEs	Nausea	24 (61.5)
	Vomiting	24 (61.5)
	Decreased appetite	14 (35.9)
	Thrombocytopenia	11 (28.2)

CONCLUSIONS

- POLARIS-101™ demonstrated rapid clearance, a limited shedding duration, and robust muscle transduction
- Early data from the INSPIRE DUCHENNE study demonstrated a similar PK/PD profile to that observed in preclinical studies with robust transduction and expression
- Rapid vector clearance may contribute to the encouraging safety and tolerability profile that continued to be seen in the INSPIRE DUCHENNE study as of a data cutoff of February 23, 2026
- Data suggest that the next-generation design of POLARIS-101™ may be a driving factor behind both the robust biological treatment effect and encouraging safety and tolerability profile observed in the INSPIRE DUCHENNE trial

REFERENCES
1. Data on File, Solid Biosciences. 2025 Data cutoff September 29, 2025. 2. Data on File, Solid Biosciences. 2026. Data cutoff February 23, 2026.

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