

# Solid Biosciences

## 41<sup>st</sup> Annual J.P. Morgan Healthcare Conference

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JANUARY 12, 2023



# Forward Looking Statement

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This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding future expectations, plans and prospects for the company; the anticipated milestones, business focus and pipeline of the company; the cash runway of the company and the sufficiency of the company’s cash and investments to fund its operations; the company’s SGT-003 program, including expectations for filing an IND and initiating dosing, AVB-202 program, including expectations for filing an IND, and AVB-401 program; the company’s plans to present data from IGNITE DMD; the implication of preclinical data; and other statements containing the words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would,” “working” and similar expressions. Any forward-looking statements are based on management’s current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. These risks and uncertainties include, but are not limited to, risks associated with the ability to recognize the anticipated benefits of Solid’s acquisition of AavantiBio; the outcome of any legal proceedings that may be instituted against Solid or AavantiBio following the announcement of the acquisition and related transactions; the ability to obtain or maintain the listing of the common stock of the combined company on the Nasdaq Stock Market following the acquisition; the company’s ability to advance its SGT-003, AVB-202, AVB-401 and other programs on the timelines expected or at all; obtain and maintain necessary approvals from the FDA and other regulatory authorities; obtain and maintain the necessary approvals from investigational review boards at clinical trial sites and independent data safety monitoring board; replicate in clinical trials positive results found in preclinical studies and early-stage clinical trials of its product candidates; whether the methodologies, assumptions and applications the company utilizes to assess particular safety or efficacy parameters will yield meaningful statistical results; advance the development of its product candidates under the timelines it anticipates in current and future clinical trials; successfully transition, optimize and scale its manufacturing process; obtain, maintain or protect intellectual property rights related to its product candidates; compete successfully with other companies that are seeking to develop Duchenne and Friedreich’s ataxia treatments and gene therapies; manage expenses; and raise the substantial additional capital needed, on the timeline necessary, to continue development of SGT-003, AVB-202, AVB-401 and other product candidates, achieve its other business objectives and continue as a going concern. For a discussion of other risks and uncertainties, and other important factors, any of which could cause the company’s actual results to differ from those contained in the forward-looking statements, see the “Risk Factors” section, as well as discussions of potential risks, uncertainties and other important factors, in the company’s most recent filings with the Securities and Exchange Commission. In addition, the forward-looking statements included in this press release represent the company’s views as of the date hereof and should not be relied upon as representing the company’s views as of any date subsequent to the date hereof. The company anticipates that subsequent events and developments will cause the company’s views to change. However, while the company may elect to update these forward-looking statements at some point in the future, the company specifically disclaims any obligation to do so.

# 2023 Expected To Be a Year of Transformation and Meaningful Advancements for Solid

Strategic pipeline of programs continuing to evolve with anticipated key milestones in 2023-2024



## PEOPLE

Led by experienced team with deep expertise in precision genetic medicine



## PROCESS

Differentiated CMC expertise, building a robust, scalable manufacturing process utilizing transient transfection



## PIPELINE

Opportunity to become a leading precision genetic medicines company within neuromuscular and cardiac genetic medicine

**Solid has the people, process and pipeline to be a leader in precision genetic medicines for rare neuromuscular and cardiac diseases.**

# 2023: Solid Biosciences At a Glance

## Developing Genetic Medicines for Patients with Rare Neuromuscular and Cardiac Diseases

- Completed merger between AavantiBio and Solid Biosciences in December 2022
- Headquartered in Charlestown, MA
- Combined pipeline, novel capsid development, and expertise from both companies to drive growth

### SGT-003

SGT-003 utilizes AAV-SLB101 capsid which has demonstrated superior tropism to AAV9

- IND expected for DMD  $\mu$ Dys SGT-003 program with novel capsid and transient transfection process

### Friedrich's Ataxia and AVB-202

- AVB-202 rescued cardiac function and extended survival in preclinical models
- Drug candidate selection, and transition from HSV to TT has begun, and initiation of IND-enabling studies for AVB-202 expected in 2023

## BAG3 Dilated Cardiomyopathy

- Rh74 capsid and cardiac-specific promoter combination increased cardiac expression while reducing expression in the liver
- Additional studies to be conducted evaluating the potential of using SLB101 to develop a genetic medicine for BAG3-mediated DCM

## Cardiac and Skeletal Capsid Library

- Developing next-generation AAV capsid libraries with two strategies designed to enhance cardiac and skeletal muscle tropism
- AAV-SLB101 has demonstrated more than double the transduction and expression in skeletal and cardiac muscle and half reduction in expression in the liver compared with AAV9

## Solid is Positioned for Success

- Additional programs to be announced in 2023
- Approximately \$214 million in cash and investments as of December 31, 2022 expected to enable Solid to advance key strategic priorities into 2025.

# Led By Experienced Team With Deep Expertise in Precision Genetic Medicine

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**Bo Cumbo**  
*President and CEO*



**Ty Howton, J.D.**  
*Chief Administrative Officer*



**Kevin Tan**  
*Chief Financial Officer*



**Jessie Hanrahan, Ph.D.**  
*Chief Regulatory Officer*



**Carl Morris, Ph.D.**  
*Chief Scientific Officer  
Neuromuscular*



**Jenny Marlowe, Ph.D.**  
*Chief Scientific Officer  
Friedreich's Ataxia &  
Cardiac Pipeline*



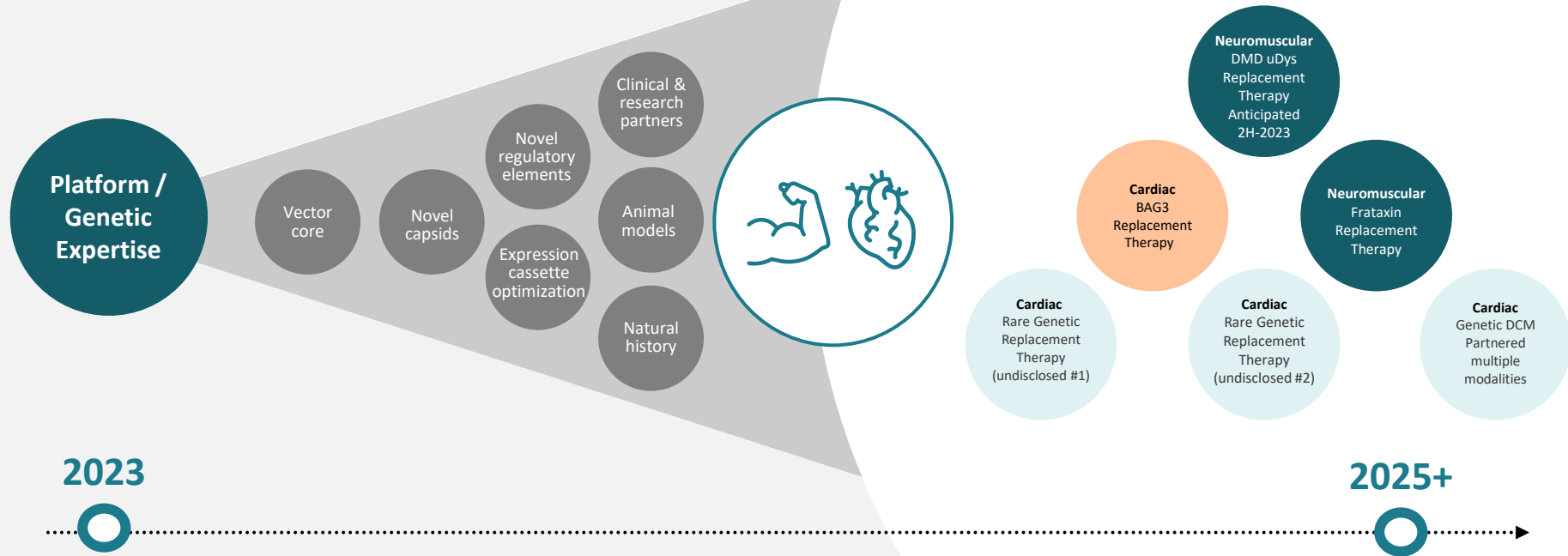
**Paul Herzich**  
*Chief Technology Officer*



**Roxana Donisa Dregheci, M.D.**  
*Head of Clinical  
Development*



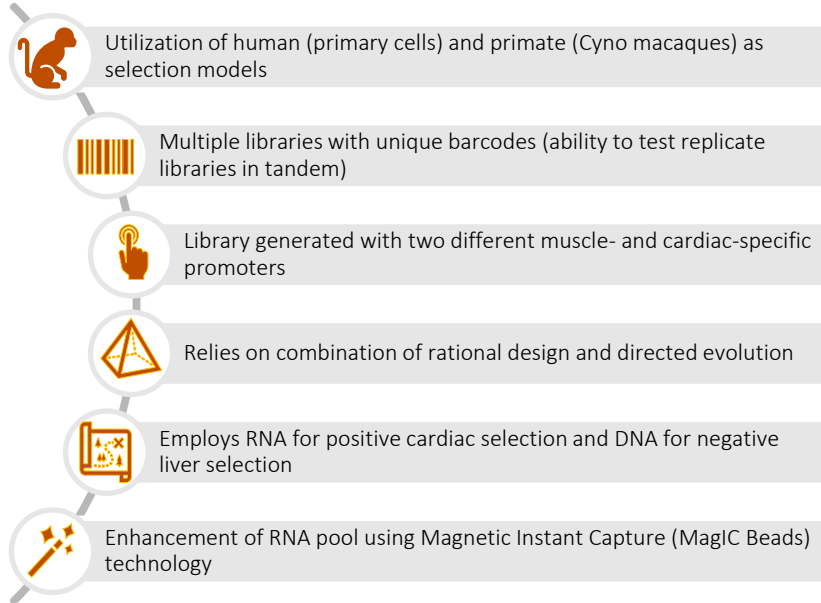
# Merger Solidifies Solid as a Gene Therapy Platform Technology Company



Solid is Well-Positioned to Execute on Multiple Programs in the Coming Years

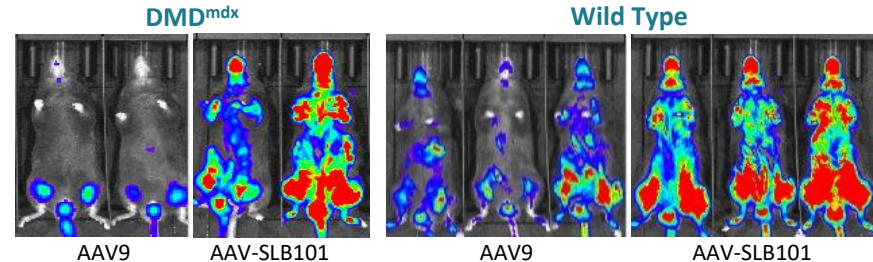
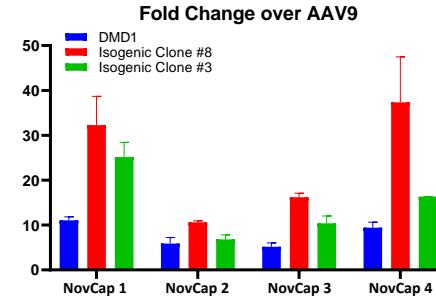
# Next Generation Therapies Start With Delivery Through Innovative Capsids

## AAV **CARDIAC** capsids enhance select cardiac tissue tropism and reduce liver targeting



## Rational Design approach used to engineer capsid candidates with the goal of improving **SKELETAL MUSCLE** tropism

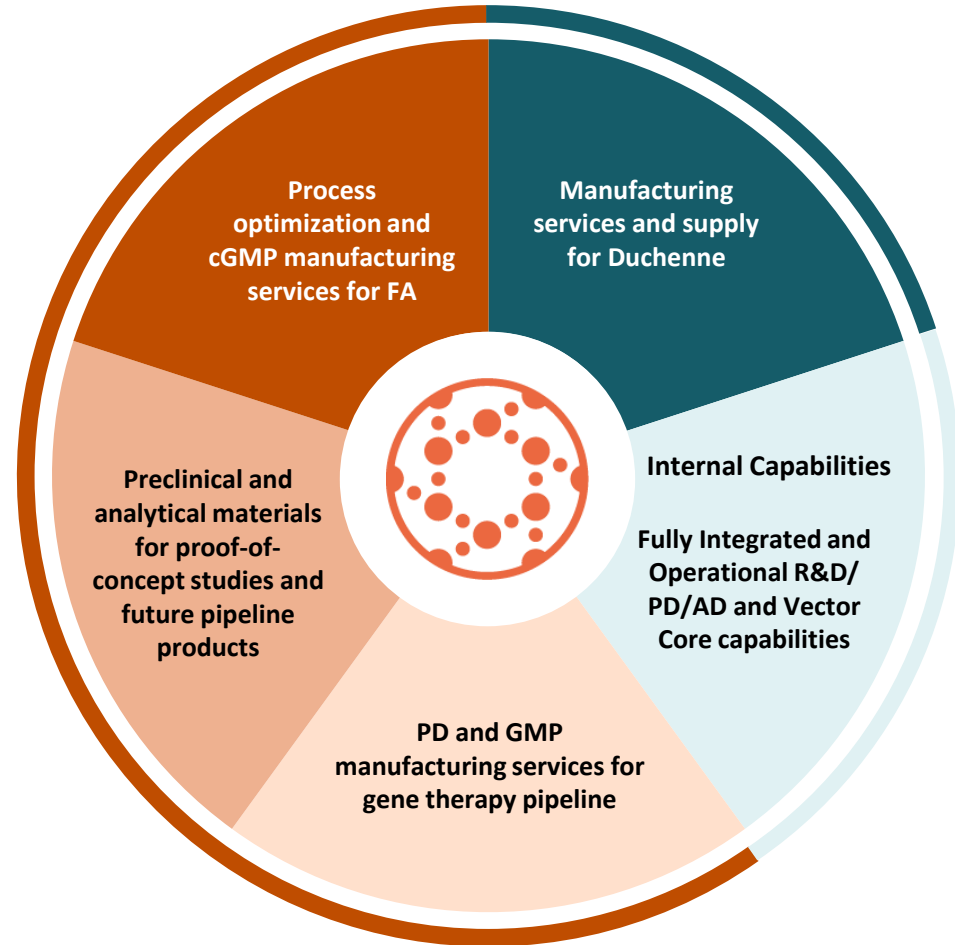
Human Duchenne Cell Microdystrophin Expression



# Combined Company Strengthens Process/Analytical Development & CMC Regulatory Team Capabilities

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Robust network of CDMO partners along with our internal MS&T expertise and dedicated resources support advancement of Solid's pre-clinical and early-stage pipeline programs

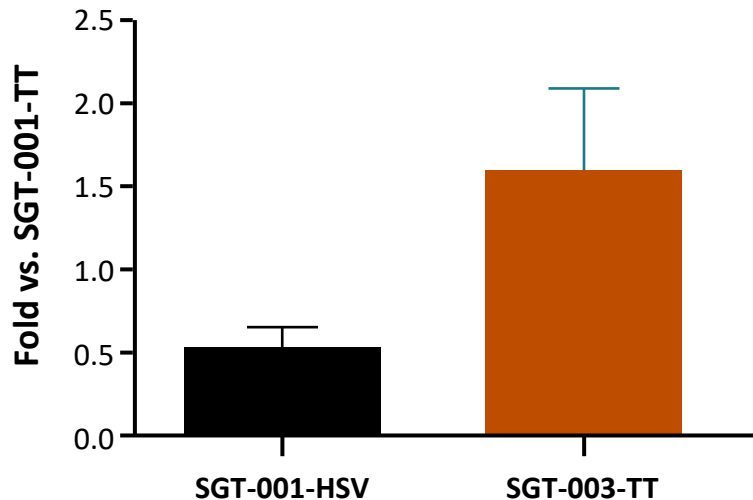




# Transition to Transient Transfection Manufacturing and Use of the AAV-SLB101 Capsid Yielded Additive Improvements in Expression

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## Microdystrophin Expression



28-day in vivo mdx mouse study. Microdystrophin expression measured in the quadriceps muscle using Western Blot (WB). Mean data are shown +/- SD relative a Reference of SGT-001 produced by the HSV process. n=5 per group.

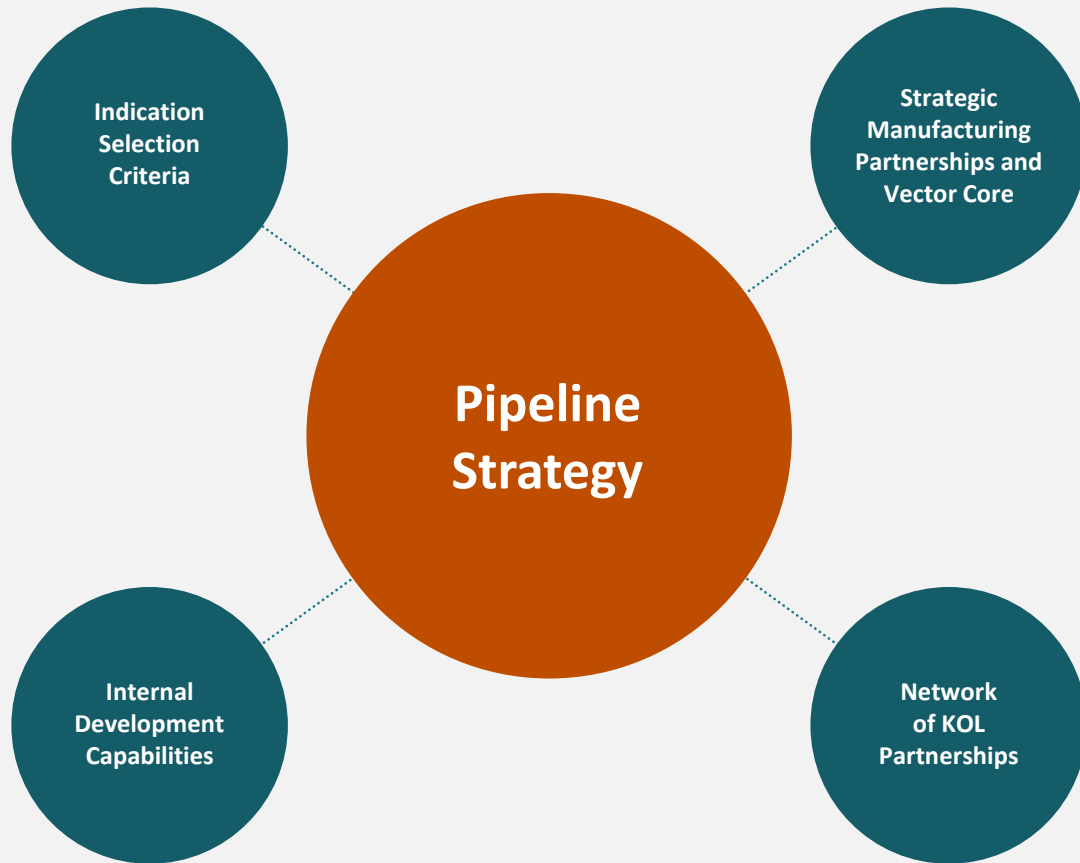


## Process change (HSV to TT) and AAV-SLB101 capsid combined to increase $\mu$ Dys by 2.3x vs SGT-001 HSV

- Product with desired quality attributes supported by analytical data with TT process
- Product demonstrated high levels of in vitro and in vivo transgene expression vs HSV material
  - In vivo expression increased by 1.4-2.0x in multiple mdx studies

## Solid is Well-Positioned for Strategic Pipeline Growth

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Leveraging and Integrating Learnings  
Across Indications



# Diversified Pipeline with Multiple Programs at Different Stages

## Indications With High Unmet Need and Significant Market Opportunities

Program	Indication	Research / Discovery	Preclinical	IND submission (Anticipated)
NEUROMUSCULAR				
SGT-003 (AAV-SLB101)	Duchenne	<div></div>	<div></div>	2H 2023
AVB-202 (cardiac and neuromuscular manifestations)	Friedreich’s Ataxia	<div></div>	<div></div>	
CARDIAC				
AVB-401 (Dilated Cardiomyopathy (DCM))	BAG3-Mediated DCM	<div></div>	<div></div>	
AVB-501 (Dilated Cardiomyopathy (DCM))	Undisclosed	<div></div>	<div></div>	
AVB-601 (Hypertrophic Cardiomyopathy)	Undisclosed	<div></div>	<div></div>	

**Notes:** In 2020, Solid entered into a collaboration agreement with Ultragenyx for the development of UX810, a next generation Duchenne construct comprised of Solid's proprietary nNOS microdystrophin and Ultragenyx's HeLa PCL manufacturing platform for use with AAV8 and Clade E variants thereof. Solid has the option to co-fund collaboration programs in return for a profit share or increased royalty payments at proof-of-concept

# Duchenne Muscular Dystrophy and Next Generation SGT-003

# Duchenne Represents A Large Global Market Opportunity With Significant Unmet Need

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## Next Generation and Potential For Best-In-Class With SGT-003

### Disease Overview

- Caused by mutations in the dystrophin gene, which leads to the absence of the dystrophin protein
- Due to progressive and irreversible muscle loss, patients typically lose the ability to walk by their early-teens and succumb to respiratory or heart failure in their 30's

### Epidemiology

- Most common life-limiting genetic disorder diagnosed in childhood
- Estimated 5,000 to 15,000 cases in the U.S.
- 1:3500-5000 newborn males affected
- Diagnosed between three and five years of age due to pronounced muscle weakness

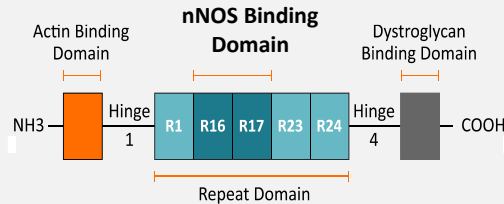
### Planned Approach

- Drive functional microdystrophin expression in patients' muscles and improve the course of the disease
- Deliver best-in-class microdystrophin transgene containing the nNOS binding domain via a novel, muscle-tropic capsid
- Utilize a transient transfection manufacturing process

# Next-Generation Therapies Utilize Optimized Transgene, Capsid and Manufacturing Process

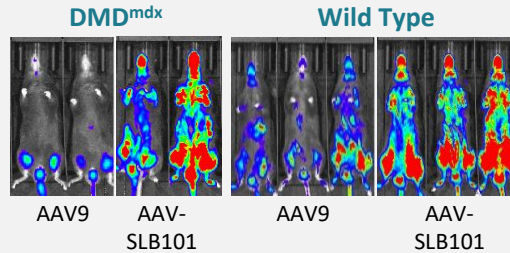
## Transgene

nNOS Microdystrophin uniquely includes the nNOS binding domain, important for prevention of activity-induced ischemia and associated muscle injury



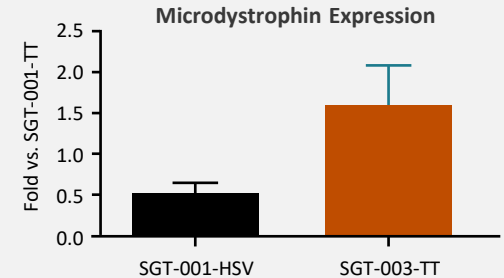
## Capsid

Rational design approach used to engineer capsid candidates with the goal of improving skeletal muscle tropism



## Manufacturing Process

Process change from HSV to TT-based manufacturing has yielded a greater than two-fold increase in microdystrophin expression in mice for SGT-003 (TT) compared with SGT-001 (HSV)



Next-Generation Construct Has Shown Promising Results in Preclinical Testing

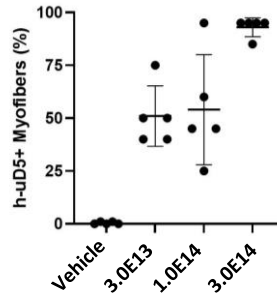
# Expression Achieved Early (Day 4) and Optimized by Day 29

## Observations:

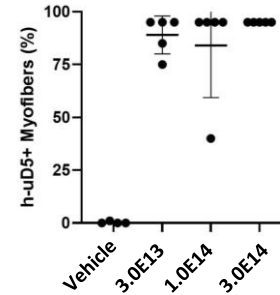
- Dose Dependent Expression
- Expression Localized to Functional Membrane
- All tissues reached 100% expression at all doses by day 29
- Quantitative MS analysis will be performed to evaluate full dynamic range of expression



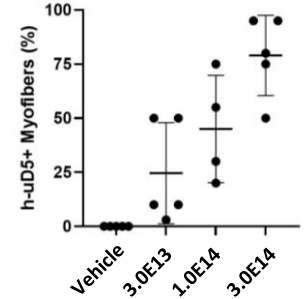
Quadriceps – Day 4



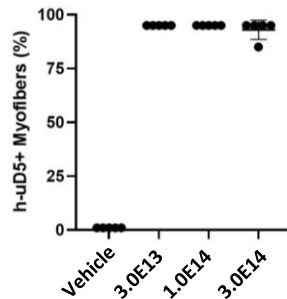
Heart – Day 4



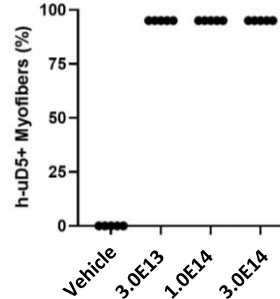
Diaphragm – Day 4



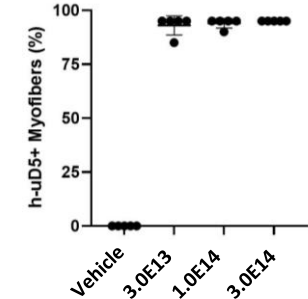
Quadriceps – Day 29



Heart – Day 29



Diaphragm – Day 29

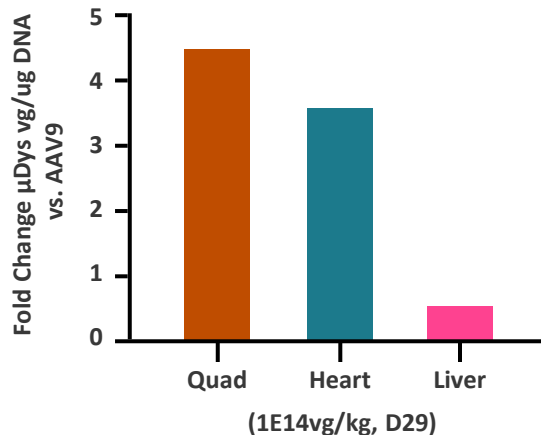


# SGT-003 with SLB101 Capsid Demonstrated Superior Tropism to AAV9

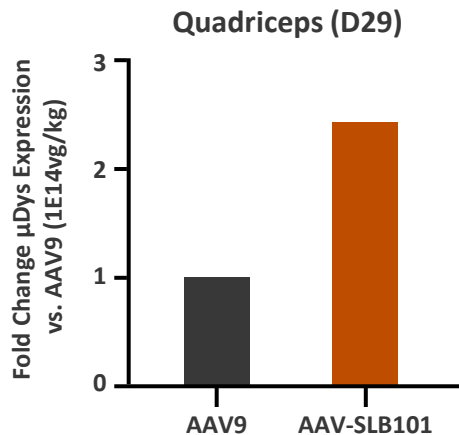
Positive biodistribution and expression data has the potential to translate into better efficacy

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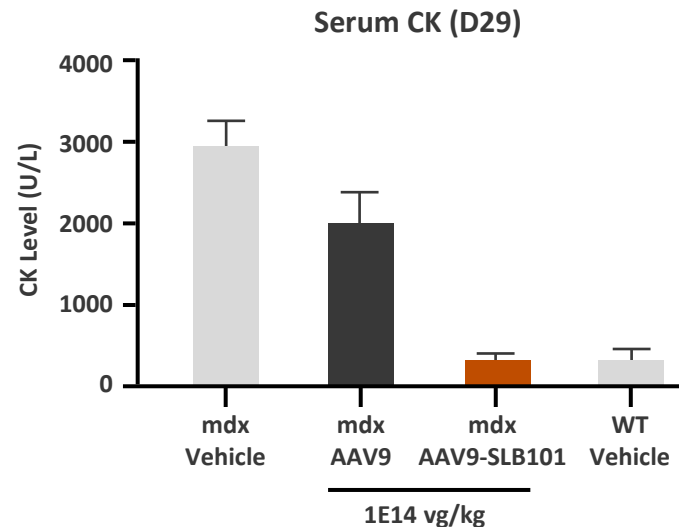
## Tissue Specific Biodistribution and Liver De-targeting in mdx Mouse



## Robust $\mu$ Dys Expression in mdx Mouse



## Reduced CK levels in Vivo in mdx Mouse



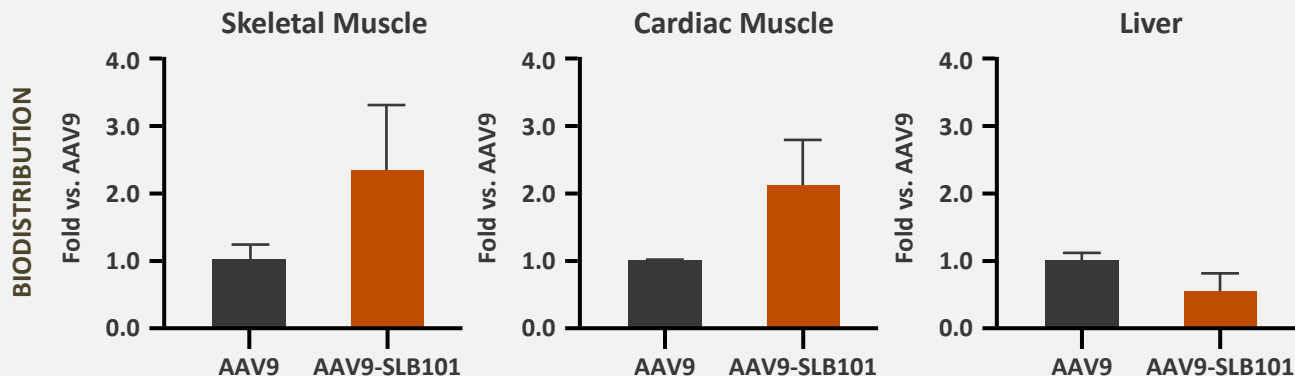


# NHP Data Utilizing AAV-SLB101 Showed Improved Biodistribution in Cardiac and Skeletal Muscle with Decreased Hepatic Transduction vs AAV9

- ✓ **Increased biodistribution to skeletal & cardiac muscle** resulted in increased transgene expression at lower doses\*
- ✓ **Reduced biodistribution in liver** suggests tissue de-targeting and improved safety profile\*



## NHP IV Administration of SLB101 with Constitutive Promoter and Reporter Gene



\* Average fold differences calculated from the five skeletal muscle tissues sampled, three cardiac muscles sampled, and the single liver sample

# Friedreich's Ataxia and AVB-202

# Friedreich's Ataxia Represents A Large Market Opportunity With Significant Unmet Need And No Approved Therapies

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AVB-202's dual route of administration is differentiated to treat the primary manifestations of morbidity and mortality

## Disease Overview

- Monogenic disease caused by loss of frataxin with both neurological and cardiac manifestations affecting muscle control and coordination with possible loss of vision and hearing, and slurred speech
- Cardiac complications are the primary cause of death
- Substantial unmet need with no disease-modifying standard of care for the broad population<sup>1</sup>

## Epidemiology

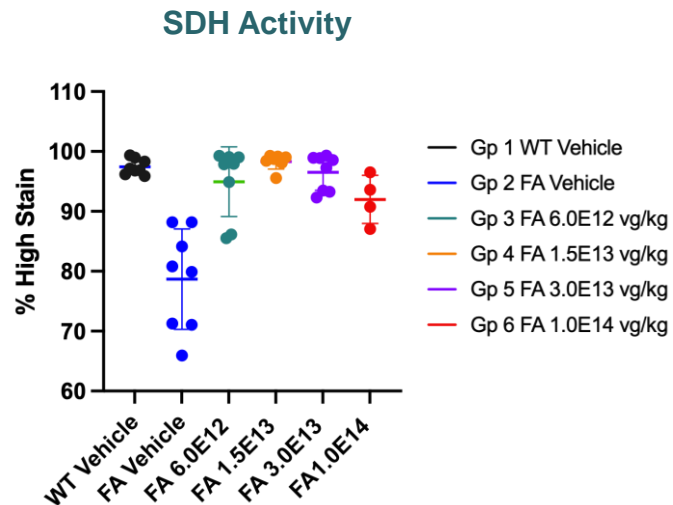
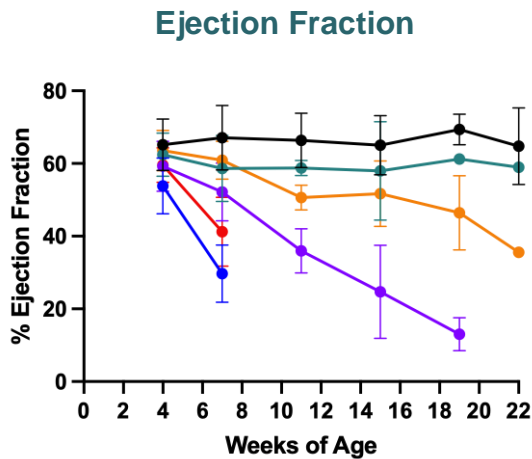
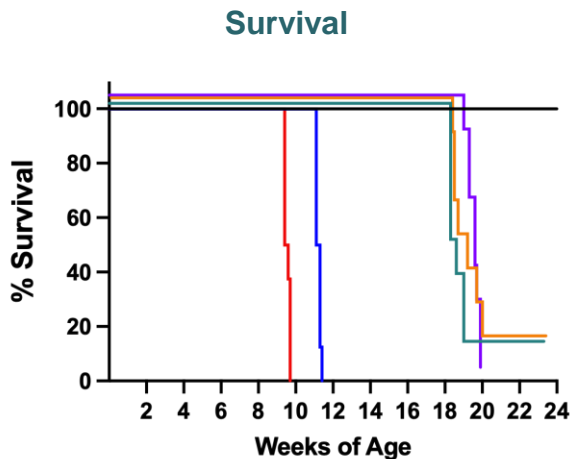
- 1 in every 40,000 to 50,000 people<sup>2,3</sup>
- Carrier rate between 1:60 and 1:100
- Average age of diagnosis is in the early-teens which leads to many undiagnosed patients<sup>1</sup>

## Planned Approach

- Aim to address neurological and cardiac manifestations via dual IV and IT routes of administration
- Drug candidate selection and transition manufacturing process to transient transfection

# AVB-202 Rescued Cardiac Function and Extended Survival in Cardiac FA Mouse

Robust frataxin expression levels suggest efficacy may be achieved at low doses

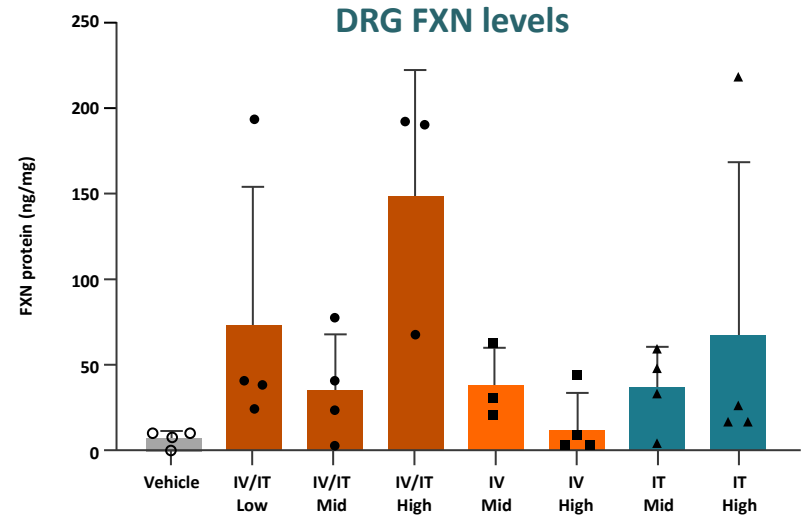
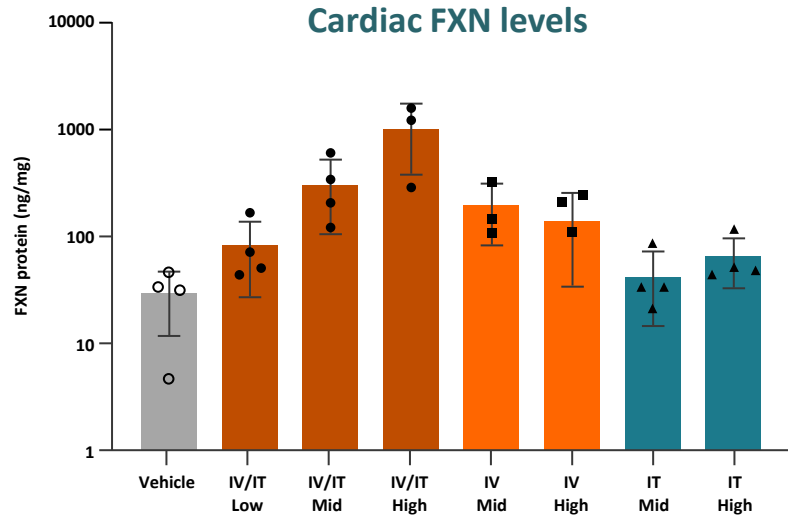


- SDH activity via histochemical stain on heart tissue sections. The percentage of tissue with high stain is quantified by image analysis software
- All groups analyzed 15-16 wks after dosing except for early euthanasia groups (FA vehicle = 11 wks; FA 1.0E14 vg/kg = 9.5 wks)



# NHP Study: Favorable Safety Profile and Utility of Dual Route of Administration

Using a dual route of administration allows for optimized expression at lower dose vs IT or IV alone



Dose Group	IV Dose (vg/kg)	IT Dose (vg/brain wt)
IV/IT Low	6.0E+12	6.00E+13
IV/IT Mid	1.5E+13	1.50E+14
IV/IT High	3.0E+13	3.00E+14
IV Mid	1.5E+13	-
IV High	3.0E+13	-
IT Mid	-	1.50E+14
IT High	-	3.00E+14



# BAG3 Mediated Dilated Cardiomyopathy

# Dilated Cardiomyopathy (BAG3) Is The First Program From Our Cardiac Pipeline

Attractive Indication with Clear Mechanistic Rationale, High Unmet Need, and Significant Market Opportunity

## Key Disease Highlights

- The BAG3 gene codes for the BCL-2-associated athanogene 3 protein
- Sufficient levels of functional BAG3 are required for healthy cardiac function
- BAG3 mutations lead to reduced BAG3 levels and dilated cardiomyopathy (DCM)
- Postulated mechanism: Decreased BAG3 leads to heat shock protein dysfunction, and a build-up of dysfunctional proteins in the sarcomere, causing myofilament damage, poor contraction and heart failure

## Epidemiology

- ~29,000 active patients in the US<sup>1, 2, 3</sup>
- Most common presentation is dyspnea but can range from dyspnea to sudden death
- Activities of daily life are severely impacted
- Eventually heart failure sets in and death ensues
- Once patients are symptomatic, mortality is approximately 25% at one year and approximately 50% at five years<sup>5</sup>
- No approved therapies address the underlying cause of disease. Symptomatic treatment is standard of care<sup>4</sup>

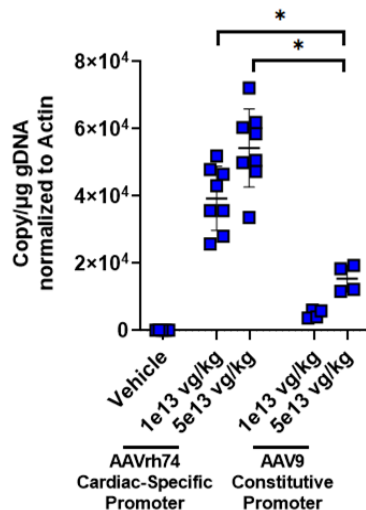
## Planned Approach

- AAVrh74-delivered optimized BAG3 transgene with cardiac-specific promoter for safe and specific expression
- Additional studies to evaluate the potential of using AAV-SLB101 to develop a genetic medicine for BAG3-mediated DCM
- Optimized transient transfection manufacturing process

# Data Illustrate Superior Cardiac Biodistribution and Transgene Expression Compared to AAV9

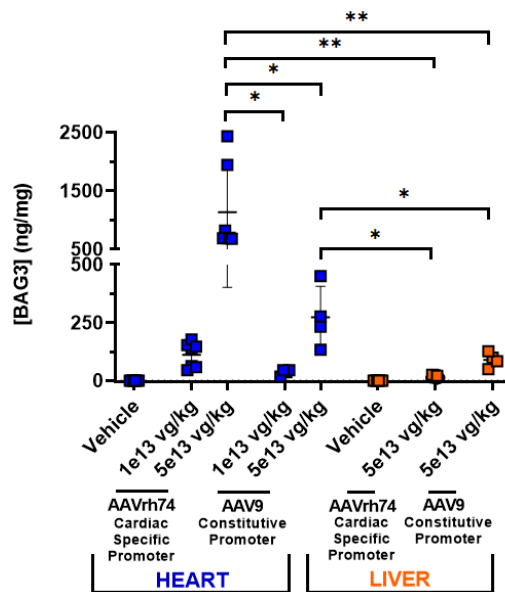
Data support Solid's targeted approach to genetic cardiomyopathies: BAG3

## Cardiac Biodistribution



rh74+cardiac specific promotor showed better BD in the heart over AAV9 with a constitutive promotor.

## hBAG3 Expression



rh74-cardiac specific promotor combination showed increased cardiac expression, and decreased liver expression.

**BAG3 DCM**  
Reducing liver expression while optimizing cardiac expression allows for a more targeted, lower dose AAV therapeutic.



# Driving the Future



## 2023 Anticipated Milestones

**Complete SGT-003 GLP tox for  
next-generation Duchenne  
therapy**  
1H 2023

**Report functional data  
from IGNITE DMD**  
Early-2023

**IND Submission  
for SGT-003**  
2H 2023

**Initiation of Patient Dosing  
for SGT-003**  
Late-2023

**Drug candidate selection and  
initiation of IND-enabling  
studies for AVB-202**

**Continue to diversify pipeline  
through BD transactions**

**Approximately \$214 million\* in cash and investments as of December 31, 2022  
expected to enable Solid to advance key strategic priorities into 2025**

# Thank You

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