Solid Biosciences

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No representation or warranty is made as to the accuracy or completeness of the information or analysis in this presentation.
Presentation Overview

• Introduction to Solid Biosciences
• Background on dystrophin
• Gene transfer for the treatment of Duchenne
• Solid’s SGT-001 microdystrophin gene therapy program and the IGNITE DMD clinical trial
• SGT-001 manufacturing
Purpose-Built to Solve Duchenne Muscular Dystrophy (DMD)

360-Degree Approach
Address all facets of DMD

Differentiated Lead Gene Transfer Program
Data from second dose cohort later this year

Scalable Manufacturing Process
Meet clinical and commercial needs
Solid Is Addressing the Full Spectrum of Duchenne

CORRECTIVE THERAPIES
Gene therapy to address the genetic cause of DMD

DISEASE-MODIFYING THERAPIES
Small molecules and biologics to address disease mechanisms

DISEASE UNDERSTANDING
Biomarkers and endpoints to improve development

ASSISTIVE DEVICES
Technology to support mobility
The Importance of Dystrophin
Dystrophin Function in Healthy Muscle

- Dystrophin protects the muscle from damage and stabilizes critical dystrophin-associated proteins.
Dystrophin is Missing in DMD Muscle

• In DMD, mutations in the dystrophin gene result in the absence of functional dystrophin protein

• Muscle fibers become damaged, cannot be repaired or replaced and are taken over by fat and scar tissue
Gene Transfer to Address the Genetic Cause of DMD

- Gene transfer brings instructions to the cell to make a new kind of dystrophin designed to replace the missing dystrophin protein.
Corrective Therapies

Microdystrophphin Gene Transfer
What Is Gene Transfer For DMD?

Gene transfer for DMD is made up of three essential elements:

1. Gene
2. Promoter
3. Vector

Vector *Carries the gene*

The combined product is then given to the patient.
Each Component of SGT-001 Was Carefully Selected

- **Transgene**: Restore key functions of a complex protein → **SGT-001 microdystrophin gene**
- **Promoter**: Expression in skeletal and heart muscle → **CK8 promoter**
- **Vector**: Targets skeletal and heart muscle → **AAV9 vector**
SGT-001 AAV-Mediated Microdystrophin Gene Therapy

Visual representation only.
Features of SGT-001 Microdystrophin

Full Length Dystrophin Protein

SGT-001 Microdystrophin Protein

- SGT-001 selection based on more than 30 years of research; confirmed through comparison experiments by Solid
Animal Studies Show SGT-001 Microdystrophin is Made Selectively in Muscle

Target Tissue

- **Diaphragm**
  - Dystrophin
  - Microdystrophin
  - Dose (vg/kg): 0, 1E14, 2E14, 2E13

- **Vastus Lateralis**
  - Dystrophin
  - Microdystrophin
  - Dose (vg/kg): 0, 1E14, 2E14, 2E13

Non-target Tissue

- **Liver**
  - Dystrophin
  - Microdystrophin
  - Dose (vg/kg): 0, 1E14, 2E14, 2E13

Company data. Three month efficacy study in GRMD canines. Representative only.
SGT-001 Microdystrophphin with nNOS Binding Domain Showed Greater Improvements in Muscle Strength in a Mouse Model of DMD

SGT-001 treatment led to force generation levels comparable to those in wild-type mice

Specific diaphragm force 6 months post-treatment. Data shown as mean ± SEM. n=5-7 per group.
Microdystrophin Expression Lasts at Least 2.5 years in an Animal Model of DMD

SGT-001 Clinical Program

IGNITE DMD
SGT-001 Phase I/II Clinical Study Ongoing

Cohort 1
Started at $5 \times 10^{13}$ vg/kg

Cohort 2
Escalated to $2 \times 10^{14}$ vg/kg

Matched control group

SGT-001

12 months primary endpoint

Primary Endpoints:
- Safety
- SGT-001 microdystrophin expression

Secondary Endpoints:
- Muscle function and strength
- Cardiac and respiratory function
- Muscle mass area and composition (MRI)

Ambulatory children, aged 4-11 and Non-ambulatory adolescents, aged 12-17 (n=16 to 32)

Visual representation only.
Announced preliminary three-month muscle biopsy data for first three patients receiving the starting dose of SGT-001 (5E13 vg/kg)

- All three biopsies showed low levels of microdystrophin protein expression via immunofluorescence
- In one patient, microdystrophin was detected via western blot (<5%) and in ~10% of muscle fibers via immunofluorescence

Necessary steps were completed to dose escalate SGT-001 to 2E14 vg/kg in a second cohort of patients

Announced dosing of first patient in second cohort (2E14 vg/kg) and initiation of clinical trial activities at two additional sites

- Transient decline in platelet count observed shortly after dosing, which fully resolved
- Also observed were transient abnormalities on laboratory tests that measure liver function, which quickly responded to an increased dose of oral steroids
- A gastrointestinal infection was also classified as unrelated to study drug

Data from second cohort expected later this year
Manufacturing

Producing SGT-001
Addressing the DMD Gene Therapy Supply Challenge

HIGH PATIENT NEED \times \text{HIGH AVERAGE PATIENT WEIGHT} \times \text{HIGH DOSES} \Rightarrow \text{SIGNIFICANT SUPPLY NEEDS}

Solid Manufacturing Capability

- Successfully scaled up to 250L in suspension and produced multiple batches
- Each 250L batch can dose multiple patients
- Create ability to potentially treat 1,000s of patients