Solid Biosciences Reports Positive Initial Clinical Data from Next-Generation Duchenne Gene Therapy Candidate SGT-003

February 18, 2025

— Day 90 biopsy data reported from first 3 participants dosed in Phase 1/2 INSPIRE DUCHENNE trial —

— Average microdystrophin expression of 110% (N=3) and significant improvements in multiple additional muscle health biomarkers observed support the potential of SGT-003 as a next-generation, best-in-class Duchenne muscular dystrophy gene therapy candidate —

— Encouraging early signals of potential cardiac benefit observed —

—SGT-003 has been well-tolerated in the 6 participants dosed as of February 11, 2025, with no serious adverse events observed —

— Participant enrollment continues, with the 7th participant dosed on February 17, 2025; Company expects to dose approximately 20 total participants by Q4 2025 —

— In mid-2025, Company plans to request an FDA meeting to discuss potential accelerated approval pathway for SGT-003 —

— Company to hold a conference call today at 8:00 AM ET —

CHARLESTOWN, Mass., Feb. 18, 2025 (GLOBE NEWSWIRE) -- Solid Biosciences Inc. (Nasdaq: SLDB), a life sciences company developing precision genetic medicines for neuromuscular and cardiac diseases, today announced positive initial data from the Phase 1/2 INSPIRE DUCHENNE trial evaluating SGT-003, a next-generation gene therapy product candidate intended for the treatment of Duchenne muscular dystrophy (Duchenne). Interim 90-day biopsy data reported in the first three participants showed an average microdystrophin expression of 110%, as measured by western blot, and improvements in multiple biomarkers that are indicators of muscle health and resilience.

“We are extremely pleased to present our initial clinical data from the INSPIRE DUCHENNE trial,” said Bo Cumbo, President and CEO, Solid Biosciences. “When starting this trial, we committed to comprehensively analyzing the effects of SGT-003. To that end, three different measurement methodologies showed what we believe to be potential best-in-class expression of our differentiated microdystrophin transgene. Significant reductions observed in all evaluated clinical biomarkers of muscle damage associated with Duchenne provide preliminary evidence of a beneficial effect in muscle integrity, including potential early signals of a positive cardiac benefit of SGT-003 in these young boys. In mid-2025, we plan to request a meeting with the FDA to discuss the potential for an accelerated approval regulatory pathway for SGT-003.”

SGT-003 was well-tolerated in the first six participants dosed as of the data cutoff date of February 11, 2025. As of the cutoff date, all six participants have reached at least 20 days post SGT-003 treatment. Adverse events (AEs) observed after SGT-003 treatment were typical of those observed in AAV gene therapy, including nausea, vomiting, fever and transient declines in platelets in some participants. No serious adverse events (SAEs) or suspected unexpected serious adverse reactions (SUSARs) were observed, and there was no evidence of thrombotic microangiopathy (TMA), atypical hemolytic uremic syndrome (aHUS), or hemolysis. Importantly, none of the AEs that were observed required the use of additional immunomodulatory agents such as eculizumab, sirolimus or rituximab.

“The robust microdystrophin expression, improvements in markers of muscle integrity and health, and favorable safety profile observed in this cohort of participants as of the data cutoff date of February 11, 2025, are very promising,” said Craig McDonald, MD, Chair, Department of Physical Medicine & Rehabilitation at UC Davis Health and investigator in the INSPIRE DUCHENNE trial. “In the landscape of genetic therapies for Duchenne, individual microdystrophin constructs likely have unique efficacy and safety profiles. I am very encouraged by the initial results reported today and look forward to seeing additional data and longer-term functional data that I believe will further inform our understanding of the role that the nNOS binding domain, which is unique to SGT-003, may play in improving clinical outcomes.”

“While loss of normal dystrophin is the defining molecular hallmark of Duchenne, there is growing understanding within the community that the success of microdystrophin gene therapy extends beyond expression, and will also depend on signals of restoration and preservation of muscle health, which were observed in these early clinical data,” said Gabriel Brooks, MD, Chief Medical Officer at Solid. “We are highly encouraged by the safety and tolerability profile observed, which has been consistent with AAV-based gene therapies. Additionally, though the trial was geared to follow cardiac measures for safety, we were gratified to observe early signs of cardiac benefit, including a decline in hs-troponin I levels in the participant with elevated levels at baseline, and improvements in cardiac function by echocardiography at day 180 in two participants with borderline low ejection fraction.”

INSPIRE DUCHENNE Trial Design
The INSPIRE DUCHENNE trial is a Phase 1/2 first in human, open-label, single-dose, multicenter trial designed to evaluate the safety, tolerability and efficacy of SGT-003 in pediatric patients with Duchenne at a dose of 1E14vg/kg. SGT-003 is administered as a one-time intravenous infusion. As of the data cutoff date of February 11, 2025, a total of six participants have been dosed in the INSPIRE DUCHENNE trial. Enrollment in the INSPIRE DUCHENNE trial is ongoing, with at least 10 total participants anticipated to be dosed by early in the second quarter of 2025 and approximately 20 total participants anticipated to be dosed by the fourth quarter of 2025.

INSPIRE DUCHENNE currently has a total of six active clinical sites in the United States and Canada and approved clinical trial applications (CTAs) in the United Kingdom and Italy. Solid expects to activate additional trial sites by the end of 2025.

90-Day Initial Data
The 90-day data reported today as of the data cutoff date of February 11, 2025, includes: microdystrophin expression, measures of restoration and activation of key elements of the dystrophin-associated protein complex, key muscle integrity biomarker evaluation, in each case, from the first three participants dosed in the INSPIRE DUCHENNE trial, and interim safety findings from the first six participants dosed in the INSPIRE DUCHENNE trial. The first three participants are two 5-year-old boys and one 7-year-old boy at the time of dosing. The second three participants are a 6-year-old boy

and two 7-year-old boys at the time of dosing.

Microdystrophin Expression and Other Measures at Day 90:

	Mean (N=3)	Participant 1	Participant 2	Participant 3
Microdystrophin Expression % Normal (Western Blot)	110%	135%	112%	84%
Microdystrophin Expression % Normal (Mass Spectrometry)	108%	119%	152%	53%
% Dystrophin Positive Fibers (Immunofluorescence)	78%	77%	88%	70%
Vector Copies/Nucleus	18.7	19.8	28.6	7.6
nNOS (neuronal nitric oxide synthase) % Positive Fibers	42%	48%	53%	25%
Beta Sarcoglycan % Positive Fibers	70%	60%	88%	63%

Muscle Integrity Biomarker Evaluation at Day 90 (N=3):

- Mean reductions observed in markers of muscle injury and stress:
  - Serum creatine kinase (CK) (IU/L): -57%
  - Serum aspartate aminotransferase (AST) (IU/L): -45%
  - Serum alanine transaminase (ALT) (IU/L): -54%
  - Serum lactate dehydrogenase (LDH) (IU/L): -60%
- Mean reductions observed in markers of muscle breakdown and dystrophic regeneration:
  - Serum titin (pmol/L): -42%
  - Embryonic myosin heavy chain (eMHC) positive fibers: -59%

Measure of Potential Cardiac Benefit:

- At Day 180, mean cardiac function increased by 8% (N=2) from baseline as measured by left ventricular ejection fraction
  - The third participant had not reached Day 180 follow up as of the data cutoff date of February 11, 2025
- Reduction in serum cardiac hs-troponin I (hs-cTnI) of -36% observed at Day 90 in one participant who entered the trial with elevated hs-cTnI levels
  - Two of the first three participants entered the study with normal baseline cTnI levels
  - Two participants in total (N=6) had elevated troponin at baseline that reduced below initial baseline values post-dose

Safety Update for the First Six Participants Dosed:

- SGT-003 was well-tolerated
  - No SAEs observed
  - No SUSARs observed
  - No hospitalizations reported
  - No evidence of TMA or aHUS observed
  - All treatment-related AEs resolved with no sequelae
  - None of the AEs required the use of additional immunomodulatory agents such as eculizumab, sirolimus or rituximab
  - No AEs of hepatic transaminitis observed, including no elevated gamma-glutamyl transferase (GGT) levels
  - One adverse event of special interest (AESI) was observed
    - Mild, transient hs-troponin I elevation observed (CTCAE Grade 1) that resolved without intervention

        - No clinical evidence of myocarditis observed
        - No EKG or echocardiographic changes observed
    - Most common AEs observed:
        - Nausea/vomiting
        - Transient thrombocytopenia
            - One CTCAE Grade 3 episode that resolved within days without intervention
            - No evidence of hemolysis observed
        - Infusion related hypersensitivity reaction
            - One CTCAE Grade 3 episode of prolonged fever that resolved within days without intervention
        - Fever

Conference Call
The Company will host a conference call today, February 18, 2025, at 8:00 AM ET to discuss the positive initial data from the Phase 1/2 INSPIRE DUCHENNE trial evaluating SGT-003. A live and archived webcast of the call will be available on Solid's website at www.solidbio.com under the "Events" tab in the Investor Relations section, or by clicking here.

Participants may also access the live call by dialing 877-407-2991 (toll-free) or 201-389-0925 (international).

About Duchenne
Duchenne is a genetic muscle-wasting disease predominantly affecting boys, with symptoms usually appearing between three and five years of age. Duchenne is a progressive, irreversible, and ultimately fatal disease that affects approximately one in every 3,500 to 5,000 live male births and has an estimated prevalence of 5,000 to 15,000 cases in the United States alone.

About SGT-003
SGT-003 is an investigational gene therapy containing a differentiated microdystrophin construct and a proprietary, next-generation capsid, AAV-SLB101, which was rationally designed to target integrin receptors, and has shown enhanced cardiac and skeletal muscle transduction with decreased liver targeting in nonclinical studies. SGT-003's microdystrophin construct uniquely includes the R16/17 domains, which localize nNOS to the muscle. Nonclinical studies have shown that nNOS can improve blood flow to the muscle thereby reducing muscle breakdown from ischemia and muscle fatigue. Together, these design features suggest that SGT-003 could be a potential best-in-class investigational gene therapy for the treatment of Duchenne.

About INSPIRE DUCHENNE
INSPIRE DUCHENNE is a first-in-human, open-label, single-dose, multicenter Phase 1/2 clinical trial to evaluate the safety, tolerability and efficacy of SGT-003 in pediatric participants with a genetically confirmed Duchenne diagnosis with a documented dystrophin gene mutation. INSPIRE DUCHENNE is a multinational trial designed to enroll participants in the United States, Canada, the United Kingdom and Italy.

About Solid Biosciences
Solid Biosciences is a precision genetic medicine company focused on advancing a portfolio of gene therapy candidates targeting rare neuromuscular and cardiac diseases, including Duchenne muscular dystrophy (Duchenne), Friedreich's ataxia (FA), catecholaminergic polymorphic ventricular tachycardia (CPVT), TNNT2-mediated dilated cardiomyopathy, BAG3-mediated dilated cardiomyopathy, and additional fatal, genetic cardiac diseases. The Company is also focused on developing innovative libraries of genetic regulators and other enabling technologies with promising potential to significantly impact gene therapy delivery cross-industry. Solid is advancing its diverse pipeline and delivery platform in the pursuit of uniting experts in science, technology, disease management, and care. Patient-focused and founded by those directly impacted by Duchenne, Solid's mission is to improve the daily lives of patients living with devastating rare diseases. For more information, please visit www.solidbio.com.

Forward-Looking Statements
This press release 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 ability to successfully achieve and execute on the Company's goals, priorities and achieve key clinical milestones; the anticipated benefits of SGT-003; the Company's SGT-003 clinical program, including planned enrollment and site activations in the INSPIRE DUCHENNE trial, planned regulatory interactions and the potential accelerated approval pathway; 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 Company's ability to advance SGT-003, SGT-212, SGT-501, SGT-601, SGT-401 and other preclinical programs and capsid libraries on the timelines expected or at all; obtain and maintain necessary approvals and designations from the FDA and other regulatory authorities; replicate in clinical trials positive results found in preclinical studies and early-stage clinical trials of the Company's product candidates; replicate preliminary or interim data from early-stage clinicals trials in the final data of such trials; obtain, maintain or protect intellectual property rights related to its product candidates; compete successfully with other companies that are seeking to develop Duchenne, Friedreich's ataxia and other neuromuscular and cardiac treatments and gene therapies; manage expenses; and raise the substantial additional capital needed, on the timeline necessary, to continue development of SGT-003, SGT-212, SGT-501, SGT-601, SGT-401 and other 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.

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