Solid Biosciences Reports Additional Preclinical Data Demonstrating that its Novel Capsid, AAV-SLB101, Provides Superior Transduction Efficiency and Enhanced Distribution to Skeletal Muscle

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- AAV-SLB101 is the capsid used in SGT-003, Solid's next-generation Duchenne gene therapy, expected to enter the clinic in late-2023 -

- Additional novel capsids based on AAV-SLB101 binding protein data are also under evaluation and offer potential to improve safety and efficacy of Duchenne gene therapy -

- In vitro data evaluating agents for enhancing AAV transduction in muscle cells presented in an additional poster -

CHARLESTOWN, Mass., Oct. 17, 2022 (GLOBE NEWSWIRE) -- Solid Biosciences, a life sciences company focused on advancing meaningful therapies for Duchenne muscular dystrophy (Duchenne), presented additional data characterizing AAV-SLB101, a novel adeno-associated virus (AAV) vector designed for improved transduction efficiency and biodistribution to muscle cells. AAV-SLB101 is the capsid used in SGT-003, Solid's next-generation gene therapy for Duchenne. The data were presented in a poster (P011) at the European Society of Gene and Cell Therapy (ESGCT) 29th Congress, in Edinburgh, Scotland, October 11-14.

In studies in wild-type mice, the mdx mouse model of Duchenne (DMD^{mdx}), and non-human primates (NHPs) AAV-SLB101 demonstrated superior transduction efficiency compared with AAV9.

- In DMD^{mdx} mice, biodistribution of AAV-SLB101 to the quadriceps was significantly increased and biodistribution to liver and brain was decreased compared with AAV9.
- In DMD^{mdx} mice, microdystrophin protein expression by western blot and immunofluorescence was also significantly higher with AAV-SLB101 compared with AAV9.
- In NHPs, AAV-SLB101 demonstrated increased biodistribution (4.9x), reporter gene (luciferase) expression (2.8x), and luciferase activity (10x) in skeletal muscle and reduced biodistribution (0.60x), luciferase activity (0.67x), and luciferase activity (0.12x) in liver compared with AAV9.

Solid also presented new SGT-003 non-clinical data which reinforced previous comparative analyses that have demonstrated increased microdystrophin expression using the novel muscle-tropic capsid AAV-SLB101 compared to AAV9. Across multiple *in vivo* mdx mouse studies, muscle tissues collected 28 days post-dosing from animals treated with SGT-003 manufactured using a transient-transfection based process showed approximately 2- to 3-fold higher levels of microdystrophin protein, as measured by western blot, compared to animals treated at equivalent doses with SGT-001 manufactured using an HSV based process. We believe these data continue to suggest that the AAV-SLB101 capsid may be a superior candidate for muscle-targeted gene therapies, with the potential of achieving higher levels of efficacy with lower total doses, and support rapid advancement of the development of SGT-003 for the treatment of Duchenne.

Additional studies identified a protein on the surface of muscle cells to which AAV-SLB101 binds. Binding of AAV-SLB101 to this protein was more than 4x higher than binding of AAV9. The identification of this binding partner enables the rational design of additional capsids that may have even greater targeting to muscle tissue. Two novel capsids generated by this rationally designed platform demonstrate increased binding compared with AAV-SLB101.

"Enhancing outcomes that can be achieved with Duchenne gene therapy requires effective delivery and expression of therapeutic gene sequences to target muscle cells while reducing delivery to other cell types, especially the liver," said Carl Morris, Ph.D., Chief Scientific Officer at Solid Biosciences and senior author on the poster. "Solid has established a platform for rationally designing novel AAV capsids that achieve these critical goals. We are using AAV-SLB101 in SGT-003, our next-generation Duchenne gene therapy candidate, and believe that additional capsids under evaluation may provide new opportunities to improve the therapeutic index of gene therapies in Duchenne and other muscle disorders. These data also demonstrate the benefits of our new TT manufacturing process, which we expect will further increases microdystrophin expression in addition to the increases observed with AAV-SLB101."

The company expects to submit an investigational new drug application (IND) for SGT-003 in mid-2023 and, subject to IND clearance, initiate patient dosing in late-2023. SGT-003 includes AAV-SLB101 to deliver Solid's proprietary and differentiated neuronal nitric oxide synthase (nNOS) microdystrophin for the treatment of Duchenne. Solid's SGT-003 program incorporates improvements from both AAV-SLB101 and triple transfection manufacturing.

Solid also presented data from a small *in vitro* chemical screen in which six agents (neuraminidase, etoposide, teniposide, poloxamer 188, insulin, and DHBDC) significantly increased AAV9 transduction by greater than two-fold in dystrophin-deficient mouse myotubes. (Poster P693). Neuraminidase and topoisomerase II (topo II) inhibitors showed the greatest enhancement of transduction. Of the topo II inhibitors evaluated, mitoxantrone demonstrated the largest increase in AAV9 transduction. The studies also showed that agents from different drug classes (e.g., neuraminidase and mitoxantrone) may be combined to achieve a greater than additive increase in transduction.

About Solid Biosciences Inc.
Solid Biosciences is a life sciences company focused on advancing transformative treatments to improve the lives of patients living with Duchenne.

Disease-focused and founded by a family directly impacted by Duchenne, our mandate is simple yet comprehensive – work to address the disease at its core by correcting the underlying mutation that causes Duchenne with our gene therapy candidate SGT-003. For more information, please visit www.solidbio.com.

About SGT-003
SGT-003 is Solid's next-generation AAV gene transfer therapy candidate that utilizes a rationally designed, novel muscle-tropic AAV capsid, called AAV-SLB101, to deliver Solid's proprietary and differentiated nNOS microdystrophin for the treatment of Duchenne. AAV-SLB101 has demonstrated enhanced muscle biodistribution and transgene expression, as well as reduced liver tropism, compared with AAV9 in in vivo mouse models and, utilizing a reporter transgene, non-human primate in vivo models. SGT-003 has correspondingly demonstrated higher levels of microdystrophin expression in vivo in the mdx mouse model of Duchenne and in vitro in human Duchenne cell lines. Solid is targeting an IND submission for SGT-003 in mid-2023.

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 the Company's plans to present data, the implication of pre-clinical data, the safety or potential treatment benefits ofSGT-003 in patients with Duchenne, the Company's regulatory plans and discussions, the Company's SGT-003 program, including the Company's expectation for filing an IND, timelines, 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 its SGT-003 program 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 i data referenced in this release will be predicative of the results of clinical trials or will demonstrate a safe or effective treatment benefit of SGT-003; 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 treatments and gene therapies; manage expenses; and raise the substantial additional capital needed, on the timeline necessary, to continue development of SGT-003 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.

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