Sio Gene Therapies Announces CSF Reductions in GM1 Ganglioside from Clinical Trial of AXO-AAV-GM1 Gene Therapy

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- GM1 ganglioside in CSF reduced in 4 out of 5 children treated with the lowest dose at 6 months follow-up
- Direct evidence of biochemical effect in the CNS suggests intravenous gene therapy may address both the systemic and neurological manifestations of GM1 gangliosidosis
- Dr. Cynthia Tifft to deliver oral presentation at the 24th Annual ASGCT conference today at 6:15 PM EDT
- On-track to report safety and efficacy data at 12 months follow-up in 2H 2021

NEW YORK and RESEARCH TRIANGLE PARK, N.C., May 13, 2021 (GLOBE NEWSWIRE) -- Sio Gene Therapies Inc. (NASDAQ: SIOX), a clinical-stage company focused on developing gene therapies to radically transform the lives of patients with neurodegenerative diseases, will present new biomarker data from the Company's study of AXO-AAV-GM1, its adeno-associated viral vector (AAV)9-based gene therapy candidate for the treatment of GM1 gangliosidosis, at the 24th Annual Meeting of the American Society of Gene & Cell Therapy (ASGCT), today, May 13, 2021 at 6:15 PM EDT.

Dr. Cynthia Tifft, Deputy Clinical Director of the National Human Genome Research Institute (NHGRI) and Principal Investigator in the study, will review patient-level data on safety and efficacy at six-months follow-up from the low-dose cohort of the Company's ongoing Phase 1/2 clinical study, with a focus on new six-month biomarker data from cerebrospinal fluid (CSF).

Previously reported data from the clinical study demonstrated that AXO-AAV-GM1 was well-tolerated with a favorable safety profile and provided early indications of clinical disease stability. In the low-dose cohort, five patients with late-infantile and juvenile GM1 gangliosidosis received a $1.5x10^{13}$ vg/kg intravenous (IV) infusion of AXO-AAV-GM1. At 6 months following gene transfer, serum beta-galactosidase enzyme activity approximately doubled and was restored to 23-57% of the lower limit of the normal reference range in the low-dose cohort. All five children demonstrated signs of clinical stabilization as assessed by measures of development including the Vineland-3 Adaptive Behavior, Upright and Floor Mobility, and Clinical Global Impression scales. To date, there have been no serious adverse events attributed to gene therapy in any patients receiving either the low-dose or the high-dose of AXO-AAV-GM1.

"AAV9 is one of the best-studied vector systems currently in development. These new 6-month CSF biomarker data are an important update to the growing body of evidence for AXO-AAV-GM1 where we now provide direct evidence of biodistribution and biochemical effect in the CNS at the lowest dose, similar to what we saw in prior translational studies with naturally occurring animal models," said Gavin Corcoran, M.D., Chief R&D Officer of Sio Gene Therapies. "Intravenous administration is likely to impact the disease in the periphery, where the disease burden is substantial. Today's CSF data, indicating a biomarker response in the CNS, provides the first indication that intravenous administration of AXO-AAV-GM1 may be able to treat both the systemic and neurological manifestations of this progressive, multisystem disease. We are proud to continue to lead the way in the development of a potentially transformative treatment for patients and families affected by GM1 gangliosidosis and look forward to the upcoming 12-month data readout later this year to provide further evidence regarding the durability of our AAV9 gene therapy and its potential to slow or halt the progression of GM1 gangliosidosis."

Key findings from the new biomarker analysis:

- 18-49% reductions from baseline in accumulated substrate, GM1 ganglioside, were observed in CSF of 4 out of 5 children in the low-dose cohort at 6 months
  - 3 out of 5 children demonstrated CSF GM1 ganglioside levels less than 100 ng/mL at the 6-month follow-up visit
  - One child, whose disease was the most advanced at baseline and who worsened on certain clinical parameters, exhibited an increase in CSF GM1 ganglioside of 19% from baseline at 6 months
  - Literature reported mean levels of normal GM1 ganglioside in CSF range from 29.7- 52.3 ng/ml in healthy children 1 month to 18 years of age (Izumi 1993, Kaye 1992, Ginns 1980)
- These data represent the first direct evidence in humans that intravenously administered AXO-AAV-GM1 gene therapy exerts a measurable biochemical effect on GM1 ganglioside accumulation within the central nervous system (CNS)
  - Builds upon previous findings of widespread CNS transfection, disease modification, and improved survival in naturally occurring feline models. These preclinical studies suggest progressive normalization of GM1 ganglioside content in brain regions beginning at 4 months after intravenous gene therapy (when animals were 5 months of age) and continuing until 42 months of age
  - Additional evidence from a murine model of GM1 gangliosidosis suggests that the blood-brain barrier is more permeable than healthy controls due to local neuroinflammation (Jeyakumar 2003), supporting the view that intravenous (systemic) administration of AAV9 may enable widespread CNS distribution in GM1 gangliosidosis

Dr. Tifft said, "These data are highly encouraging and underscore the potential of Sio's gene therapy program for GM1 gangliosidosis. I have been involved in the clinical and research aspects of this disease for more than 10 years and have seen first-hand a disease that only gets worse, so I am

proud to share this clinical update for a trial where we have seen kids remain stable and most children have shown some overall improvement."

Upcoming Milestones

- 12-month data from the low-dose cohort in the second half of 2021;
- 12-month data from the first two children dosed in the high-dose cohort in Q1 2022; and
- In the first half of 2022, meeting with the U.S. Food and Drug Administration to discuss the registrational pathway for AXO-AAV-GM1

The clinical study (NCT03952637) is designed to evaluate the safety, tolerability, and potential efficacy of AXO-AAV-GM1 delivered intravenously in children with Type I and Type II GM1 gangliosidosis. Stage 1 is a dose-escalation study in which the low-dose cohort is evaluating $1.5x10^{13}$ vg/kg and the high-dose cohort is evaluating a dose of $4.5x10^{13}$ vg/kg in early infantile, late infantile, and juvenile children.

GM1 gangliosidosis is a progressive and fatal pediatric lysosomal storage disorder caused by mutations in the *GLB1* gene that cause impaired production of the β-galactosidase enzyme. Currently, there are no FDA-approved treatment options for GM1 gangliosidosis.

About AXO-AAV-GM1

AXO-AAV-GM1 delivers a functional copy of the *GLB1* gene via an adeno-associated viral (AAV) vector, with the goal of restoring β-galactosidase enzyme activity for the treatment of GM1 gangliosidosis. The gene therapy is delivered intravenously, which has the potential to broadly transduce the central nervous system and treat peripheral manifestations of the disease as well. Preclinical studies in murine and a naturally-occurring feline model of GM1 gangliosidosis have supported AXO-AAV-GM1's ability to improve β-galactosidase enzyme activity, reduce GM1 ganglioside accumulation, improve neuromuscular function, and extend survival.

AXO-AAV-GM1 has received both Orphan Drug Designation and Rare Pediatric Disease Designation from the Food and Drug Administration and is the only gene therapy in clinical development for all pediatric forms of GM1 gangliosidosis.

In 2018, Sio licensed exclusive worldwide rights from the University of Massachusetts Medical School for the development and commercialization of gene therapy programs for GM1 gangliosidosis and GM2 gangliosidosis, including Tay-Sachs and Sandhoff diseases.

About Sio Gene Therapies
Sio Gene Therapies combines cutting-edge science with bold imagination to develop genetic medicines that aim to radically improve the lives of patients. Our current pipeline of clinical-stage candidates includes the first potentially curative AAV-based gene therapies for GM1 gangliosidosis and Tay-Sachs/Sandhoff diseases, which are rare and uniformly fatal pediatric conditions caused by single gene deficiencies. We are also expanding the reach of gene therapy to highly prevalent conditions such as Parkinson's disease, which affects millions of patients globally. Led by an experienced team of gene therapy development experts, and supported by collaborations with premier academic, industry and patient advocacy organizations, Sio is focused on accelerating its candidates through clinical trials to liberate patients with debilitating diseases through the transformational power of gene therapies. For more information, visit www.siogtx.com.

Forward-Looking Statements

This press release contains forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995 and other federal securities laws. The use of words such as "believe," "estimate, " "may be," and other similar expressions are intended to identify forward-looking statements. For example, all statements Sio makes regarding costs associated with its operating activities, funding requirements and/or runway to meet its upcoming clinical milestones, and timing of its upcoming clinical milestones are forward-looking. All forward-looking statements are based on estimates and assumptions by Sio's management that, although Sio believes to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that Sio expected. Such risks and uncertainties include, among others, the impact of the Covid-19 pandemic on our operations; the actual funds and/or runway required for our clinical and product development activities and anticipated upcoming milestones; actual costs related to our clinical and product development activities and our need to access additional capital resources prior to achieving any upcoming milestones; the initiation and conduct of preclinical studies and clinical trials; the availability of data from clinical trials; the development of a suspension-based manufacturing process for Axo-Lenti-PD; the scaling up of manufacturing, the expectations for regulatory submissions and approvals; the continued development of our gene therapy product candidates and platforms; Sio's scientific approach and general development progress; and the availability or commercial potential of Sio's product candidates. These statements are also subject to a number of material risks and uncertainties that are described in Sio's most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on February 9, 2021, as updated by its subsequent filings with the Securities and Exchange Commission. Any forward-looking statement speaks only as of the date on which it was made. Sio undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

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