Sio Gene Therapies Announces Positive Interim Safety and Biomarker Data from Ongoing Phase 1/2 Clinical Study of AXO-AAV-GM1 Gene Therapy in GM1 Gangliosidosis

October 21, 2021

- *Consistent dose-dependent improvements across biomarker measures*
- *Normalization of serum beta-galactosidase activity and GM1 ganglioside in CSF in the high-dose cohort*
- *No overt disease progression in six out of seven patients treated across low- and high-dose cohorts*
- *Total of ten patients have received gene therapy to date without SAEs attributable to AXO-AAV-GM1*
- *Management to host conference call and webcast today, October 21, at 8:30 a.m. EDT*

NEW YORK and DURHAM, N.C., Oct. 21, 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, today presented positive interim data from the Company's ongoing Phase 1/2 study of AXO-AAV-GM1, its adeno-associated viral vector (AAV)9-based gene therapy candidate for the treatment of GM1 gangliosidosis, in an oral presentation at the European Society of Gene & Cell Therapy (ESGCT) Virtual Congress 2021, held from October 19-22, 2021. These follow-up data from five Type II (late-infantile to juvenile) patients in the low-dose cohort and the initial two Type II patients in the high-dose cohort demonstrate an encouraging safety profile and a consistent dose-response in disease biomarkers across the evaluation period.

"Our team continues to lead the industry in the development of a new, potentially disease-modifying therapeutic option for GM1 gangliosidosis. We are extremely proud of these data, representing our broadest dataset generated thus far, which support a dose response and a favorable safety and tolerability profile at both low and high doses," said Gavin Corcoran, M.D., Chief R&D Officer of Sio Gene Therapies. "We observed dose-dependent responses in two key biomarkers, serum β-galactosidase and cerebrospinal fluid (CSF) GM1 ganglioside, including normalization of both biomarkers in the high-dose cohort. Taken together, six out of seven patients show no evidence of overt disease progression at the latest timepoint assessed, and we now have a better understanding of the clinical measures that may serve as important indicators of efficacy. Based on the results of this ongoing study, we are working on the continued development of AXO-AAV-GM1 and plan to engage the FDA to discuss further development, recognizing that there is currently no approved therapy available for GM1 patients."

Dr. Cynthia Tifft, Deputy Clinical Director of the National Human Genome Research Institute (NHGRI) and study Principal Investigator added, "I have dedicated my career to the care of patients with GM1 gangliosidosis and to research efforts in the search for a functional cure. The biomarker dose response and favorable safety profile is a remarkable finding for the gene therapy field. I am excited about the potential impact that AXO-AAV-GM1 may have on the lives of these children and their families. I look forward to seeing the longer-term data, where we may have a chance to see not only durable disease stabilization, but possibly even improvement."

Key findings:

- Generally well-tolerated at both low and high doses with the majority of adverse events considered mild to moderate
  - To date, there have been no reported serious adverse events attributed to gene therapy in any patients
  - To date, there have been no adverse events leading to study withdrawal in any patients
    - No liver-related adverse events required clinical intervention or had associated clinical sequelae
    - No clinically relevant changes were observed in complement factors, platelet count or other liver function tests
- Data demonstrate a dose-dependent improvement in key biomarkers of disease activity: β-galactosidase enzyme activity in the serum and GM1 ganglioside activity in the CSF
  - Serum β-galactosidase activity achieved a normal range, increasing by 12x and 17x pre-treatment levels, respectively, in both patients in the high-dose cohort at six months
    - All five patients in the low-dose cohort saw a 1.3-2.3x increase in the same timeframe
  - Levels of CSF GM1 ganglioside, the toxic substrate which accumulates in patients with GM1 gangliosidosis and which is associated with disease activity, were normalized in both patients in the high-dose cohort with 42% and 72% reductions, respectively, at six months
    - In the low-dose cohort, a 18-49% decrease was seen in four out of five patients, and a 19% increase in a single patient was seen in the same timeframe
    - GM1 ganglioside levels were below baseline in all five low-dose patients at 12 months
- MRI assessment of total brain volume and ventricular volume, which decrease and increase respectively in the natural history of the disease, showed the following in the low-dose cohort at 12 months:
  - Total brain volume (excluding ventricles) was maintained within ± 5% in all five patients
  - Ventricular volume remained within ± 15% in four patients and increased by 104% in one patient
- There was no clinical evidence of overt disease progression in four of five low-dose patients at 12 months and both

high-dose patients at six months as assessed by measures of development including the Vineland-3 Adaptive Behavior and Upright and Floor Mobility scales

Upcoming Milestones:

- **1H 2022:** Expect to provide data update from Stage 1 of the study, including both Type I (early-infantile) and Type II patients, at future scientific conferences
- **1H 2022:** Expect to engage with the FDA to review Stage 1 data and discuss next steps for clinical development

Phase 1/2 Clinical Trial in GM1 Gangliosidosis:
The Phase 1/2 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 a dose of $1.5x10^{13}$ vg/kg and the high-dose cohort is evaluating a dose of $4.5x10^{13}$ vg/kg in both disease sub-types.

Ten patients have been dosed to date in Stage 1 of the clinical study (including eight Type II patients and two Type I patients)

- Longer-term evaluation of eight Type II patients in the low- and high-dose cohort is ongoing
- Two Type I patients have received the low dose of AXO-AAV-GM1, and screening for enrollment of Type I patients in the high dose ($4.5x10^{13}$ vg/kg) cohort is ongoing

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.

Conference Call and Webcast Details:
Sio will host a conference call and webcast today, October 21, 2021, at 8:30 a.m. EDT to review the data, with participation from Sio management and Guangping Gao, Ph.D., Co-Director of the Li Weibo Institute for Rare Disease Research, Director of the Horae Gene Therapy Center and Viral Vector Core, Professor of Microbiology and Physiological Systems and Penelope Booth Rockwell Professor in Biomedical Research at UMass Chan Medical School, and Chief AAV Scientific Advisor at Sio.

Thursday, October 21, 2021, at 8:30 a.m. EDT

Toll Free:	877-407-0792
International:	201-689-8263
Conference ID:	13723622
Webcast:	http://public.viavid.com/index.php?id=146710

A replay will be archived on the Company's website at www.siogtx.com after the conference call.

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 achieve a broad central and peripheral biodistribution. Preclinical studies in murine and a naturally-occurring feline model of GM1 gangliosidosis have supported AXO-AAV-GM1's ability to increase 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 UMass Chan 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 "expect," "estimate," "may" 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 and outcome of its upcoming clinical and manufacturing 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 occurrence of adverse safety events during our current and future trials; the development of a suspension-based manufacturing process for AXO-Lenti-PD; the scaling up of manufacturing; the outcome of interactions with regulatory agencies and 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 August 12, 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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