Dear Tay Sachs and Sandhoff patient communities,

On behalf of Sio Gene Therapies, it is our privilege to share an exciting update. Today, we are delighted to announce that the first patient has been dosed in a Phase 1/2 trial evaluating AXO-AAV-GM2, an investigational gene therapy for the treatment of GM2 gangliosidosis, also known as Tay-Sachs or Sandhoff Disease.

The two-part AXO-AAV-GM2 study consists of (1) a dose ranging cohort evaluating the safety and efficacy of various doses of the gene therapy, followed by (2) a confirmatory cohort treated with the optimal dose identified from the dose ranging cohort. Both infantile and juvenile patients with GM2 gangliosidosis will be enrolled in the study which is being conducted in partnership between the University of Massachusetts Medical School and Massachusetts General Hospital (MGH)under the direction of Dr. Terence Flotte and Dr. Florian Eichler respectively, who work together to provide the treatment and follow-up of the patients enrolled in the study.

Information about the study, including inclusion/exclusion criteria, are posted on clinicaltrials.gov (NCT04669535): A Dose-escalation and Safety & Efficacy Study of AXO-AAV-GM2 in Tay-Sachs or Sandhoff Disease - Full Text View - ClinicalTrials.gov. As with all clinical trials, enrollment is dependent upon the study investigator's medical assessment of the patient meeting the inclusion criteria for the study, and as such, Sio will play no role in the selection of patients for the trial. A few of the criteria are listed below:

- Must have a genetically confirmed diagnosis of Tay Sachs Disease or Sandhoff disease
- Age at the time of gene transfer is 2-12 years for juvenile-onset patients and 6-20 months for infantile-onset patients
- There are also factors assessed by the study investigator that will impact whether your child is eligible for the trial such as disease severity, surgical readiness for the gene transfer route of administration, and medical conditions that could interfere with conduct of the study or assessments

As always, your treating physician will serve as the best source of information for ongoing medical treatment and management of your child's disease. To learn more about this study, you or your doctor may contact the Clinical Research Coordinator at MGH, Haley Andonian (handonian@partners.org).

This is an important milestone for the entire GM2 community made possible by the many families, researchers and patient organizations committed to finding new treatments for Tay-Sachs and Sandhoff disease, and we look forward to enrollment of additional patients in this program. If you would like to reach out directly with any questions or feedback, you can contact us at patients@siogtx.com.

Sincerely,

Gavin Corcoran
Chief R&D Officer

Erika De Boever
VP, Clinical Development