TAYSHAGTX.COM
3000 Pegasus Park Drive, Suite 1430
Dallas, Texas 75247 USA

27 January 2022

Dear Tay-Sachs and Sandhoff disease communities,

Today, Taysha issued a press release related to the Queen's University ongoing Phase 1/2 TSHA-101 investigational clinical trial of GM2 gangliosidosis (Tay-Sachs disease and Sandhoff disease) evaluating the use of TSHA-101, an AAV9 gene therapy treatment of GM2 gangliosidosis. This press release discussed initial biomarker data from the first two patients dosed in the clinical trial.

We are sharing this information as part of our commitment to ongoing, open communication with the Tay-Sachs disease and Sandhoff disease patient communities.

Based on natural history data, patients with asymptomatic GM2 gangliosidosis have a Hex A enzyme level that are at least 5% of normal activity. The first patient, a Sandhoff infant, demonstrated a 190% increase in Hex A enzyme levels at the one-month timepoint, and a 288% increase at the 3-month timepoint to within the normal range. The second patient, a Tay-Sachs infant, demonstrated a 25% increase in Hex A enzyme levels at the one-month timepoint and had not reached the 3-month timepoint at the time of analysis.

These positive findings are tempered with some difficult news. We are deeply saddened that one of the participants in the Phase 1/2 clinical trial of TSHA-101, passed away on Friday, January 14, 2022. The cause of death was pneumonia with fluid build-up in the lungs, in addition to a secondary hospital-acquired methicillin-resistant staphylococcus aureus (MRSA) septic infection. The principal investigator has made the initial assessment that the death was unrelated to the study drug. Final determination from the independent data safety monitoring board is anticipated in the near term. We extend our deepest sympathies to the participant's family.

We recognize the need for clarity regarding some information as it becomes publicly available. Therefore, we want to answer some questions you may have and provide context to the recent press release.

What are the objectives of the Phase 1/2 TSHA-101 investigational gene therapy clinical trial?

- To learn about the safety of the investigational gene therapy product
- To learn whether the investigational gene therapy product improves Hex A enzyme activity

How many participants have been dosed in the clinical trial to date?

- Three participants have been dosed with the investigational gene therapy product

What are the early, preliminary findings that were shared?

- The data published included results from the first two participants, one with Tay-Sachs disease and one with Sandhoff disease
- The investigational gene therapy caused no significant drug-related events
- Based on one month of data, the investigational gene therapy appears to have increased Hex A enzyme levels in the blood in both the Tay-Sachs patient and the Sandhoff patient
- Importantly, preliminary data does not accurately predict the full risk/benefit profile of an investigational product

Once again, we offer our deepest condolences and respect the privacy of the family whose child passed away.

"This moment is sad, yet hopeful. The preliminary findings from the biomarker data are positive, however, the Tay-Sachs and Sandhoff communities lost a life. This child and family made a significant impact and are pioneers in the treatment of GM2 gangliosidosis. Perhaps more importantly, this child is a conduit to the many lives we hope may be helped, and this child's legacy will live on in the many children with Tay-Sachs and Sandhoff diseases who may someday be able to benefit from TSHA-101." - Suyash Prasad, MBBS, M.SC., MRCP, MRCPCH, FFPM, Chief Medical Officer and Head of Research and Development at Taysha Gene Therapies

We hope this information is helpful in answering some of the questions you may have.

- If your child is currently participating in the Queens University trial, please speak with the physician and his or her staff at your clinical trial site
- For general inquiries, please contact medinfo@tayshagtx.com

We are grateful for the support and partnership of the Tay-Sachs and Sandhoff communities and will share further information as it becomes available through the patient advocacy groups.

Sincerely,
The Taysha Team

The clinical trial is sponsored by the Kingston Health Sciences Centre at Queen's University in Ontario, Canada. The trial receives financial support from the Canadian Glycomics Network (GlycoNet) and Taysha Gene Therapies, Inc.