December 27, 2023

Dear Rett Patient Advocacy Leaders,

We are writing to provide an update on Taysha's Phase 1/2 clinical trial for female children with Rett syndrome in the United States (U.S.), the REVEAL Pediatric Study.

We are pleased to announce that the REVEAL Pediatric Study is open for enrollment in the U.S. Additional details about the study and contact details for the clinical trial sites are available at https://clinicaltrials.gov/study/NCT06152237.

We have received several questions about the REVEAL Pediatric Study, which we hope to address below.

What is the REVEAL Pediatric Study?

- The REVEAL Pediatric Study is a Phase 1/2 study designed to evaluate whether TSHA-102, the investigational gene therapy, is safe, whether it is tolerable, and whether there may be beneficial effects in females between 3 and 8 years old with Rett syndrome.

What is the dose, or amount, of investigational gene therapy that is being studied?

- The REVEAL Pediatric Study will test two different dose levels to determine the appropriate dose to test in future clinical trials.

How many participants will be included in the REVEAL Pediatric Study?

- There are two parts to the study – Part A and Part B.
    - In Part A, the study will assess the two different dose levels of the investigational gene therapy in **six participants** aged **5 to 8 years old** with Rett syndrome.
        - The first three participants in Part A will receive the first dose level.
        - The next three participants in Part A will receive the second dose level.
    - In Part B, the study will evaluate the dose that is selected from Part A of the study.
        - Part B will include **up to 21 additional participants** and will expand to enroll female children **3 to 8 years old** with Rett syndrome.
        - Additional information about Part B will be shared in the future.
- The REVEAL Pediatric Study is currently enrolling Part A of the study.

What is Taysha's investigational gene therapy for Rett syndrome (TSHA-102)?

- TSHA-102 consists of a miniature form of the *MECP2* gene (miniMECP2) that is paired with a control element called miRNA-Responsive Auto-Regulatory Element (miRARE).
- miRARE is designed to regulate, or control, the amount of MeCP2 protein that is made to avoid overexpression.
- TSHA-102 is administered as a **one-time injection into the spinal fluid in the lower back** (lumbar region).

What is the time commitment for participating in the REVEAL Pediatric Study?

- The overall study duration will be up to six years for most participants.
- Visits will be more frequent for the first three months, then eventually reduce to two times per year.
- It is important to note that, although participants will be monitored for six years in the study, this does not mean that Taysha must wait for the completion of the trial to initiate discussions with regulatory agencies about a potential path forward for TSHA-102.

Who may be eligible for the REVEAL Pediatric Study?

- It is important to note that ultimately the Principal Investigator (the lead physician at a clinical trial site) will decide the eligibility of an individual for the clinical trial, not Taysha.
- Participants must have a confirmed diagnosis of Rett syndrome with a documented *MECP2* gene mutation.
- For Part A of the study, participants must be girls aged 5 to 8 years old.
- Children who have taken DAYBUE™* (trofinetide) may be eligible to participate. The study team at the sites will review specific eligibility criteria related to trofinetide with families.
- There are several other criteria that will determine whether a child is eligible to participate, which the study team at the sites will review with families.

Will families who live outside the U.S. be eligible to participate in the REVEAL Pediatric Study?

- In the United Kingdom (UK), Taysha expects to receive feedback by year-end 2023 on a clinical trial application that was submitted to the Medicines and Healthcare products Regulatory Agency (MHRA) to study TSHA-102 in female children with Rett syndrome.
- In Canada, Taysha recently announced that Health Canada granted approval to expand the ongoing REVEAL Adult Study to include females with Rett syndrome age 12 years and older.

Who do I contact for more information about the REVEAL Pediatric Study?

- Families who are interested in learning more about the REVEAL Pediatric Study can contact one of the participating clinical trial sites.
- Contact information for each clinical trial site is available at https://clinicaltrials.gov/study/NCT06152237.

If you have any general questions or would like to connect with someone from the Taysha Patient Affairs team, please contact patientaffairs@tayshagtx.com. If your healthcare provider would like to connect with a member of our Taysha Medical Affairs team, please ask them to contact medinfo@tayshagtx.com.

We would like to thank the entire Rett community and the Rett patient advocacy groups for your continued partnership. We would also like to acknowledge the individuals and families who choose to participate in research to help better understand the potential of gene therapy for Rett syndrome.

We look forward to sharing more information as it is publicly available.

Sincerely,
The Taysha Patient Affairs Team

*DAYBUE™ is a registered trademark of Acadia Pharmaceuticals Inc.