February 29, 2024

Dear Rett Patient Advocacy Leaders,

We are writing to provide a series of updates that Taysha provided in a press release today. Please find a summary of these updates below, as well as a list of answers to some frequently asked questions.

- The REVEAL Adolescent & Adult Study (females age 12+) will expand into the United States (U.S.) following submission of an investigational new drug application to the Food and Drug Administration (FDA).
- The REVEAL Adolescent & Adult Study will proceed to the next dose cohort (or "group") following approval from the study's Independent Data Monitoring Committee to move to the next dose level. Dosing of the first participant in cohort two (high dose) is expected in Q2 2024.
- The IDMC also approved the dosing of the second participant in cohort one (low dose) of the REVEAL Pediatric Study, which is expected to take place in Q1 2024.

What is the REVEAL Adolescent & Adult Study?

- The REVEAL Adolescent & Adult 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 12 years and older** with Rett syndrome. The study is designed to evaluate two different dose levels to determine the highest tolerable dose of TSHA-102.
- The study is being conducted in **Canada and the U.S.** Additional information and clinical trial sites will be posted at https://clinicaltrials.gov/study/NCT05606614 once available.

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 5-8 years old**, with plans to expand to females 3-8 years old in future phases of the study. The study is designed to evaluate two different dose levels to determine the highest tolerable dose of TSHA-102.
- The study is being conducted in the **U.S. and the United Kingdom**. Additional information and clinical trial sites will be posted at https://clinicaltrials.gov/study/NCT06152237 once available.

What is the Independent Data Monitoring Committee (IDMC)?

- The IDMC is an independent group of experts who monitor patient safety, potential efficacy, and study conduct while a clinical trial is ongoing. Taysha confers with the IDMC to make decisions related to key clinical activities, such as proceeding with dose escalation (or moving to the next planned dose level).
- As announced today, the IDMC reviewed initial data from the ongoing clinical trials and recommended to proceed with moving to the next dose level (high dose) for the third participant in the REVEAL Adolescent & Adult Study and to proceed with dosing a second participant at the first dose level (low dose) as planned in the REVEAL Pediatric Study.

Will families who live outside of the country where a study is taking place be eligible to participate?

- 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 patient for the clinical trial. Though this varies

site to site, participants are typically selected for enrollment using several considerations, including proximity to the clinical site, which can limit cross-border participation.
- Rett families and/or their treating physician may contact a participating site directly to ask about potential trial participation.

Who can families contact for more information about the REVEAL Adolescent & Adult Study?

- Families who are interested in learning more about the REVEAL Adolescent & Adult Study can contact one of the participating clinical trial sites. Contact information for each clinical trial site is available at https://clinicaltrials.gov/study/NCT05606614.

Who can families 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.

Does Taysha have plans for an investigational gene therapy clinical trial for males with Rett syndrome?

- Currently, Taysha is focused primarily on running preliminary clinical trials in adult, adolescent, and pediatric females with Rett syndrome.

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.

Sincerely,
The Taysha Patient Affairs Team