August 12, 2025

Dear Rett Syndrome Community,

We are writing to share an update on Taysha's clinical development plans for TSHA-102, our investigational gene therapy for Rett syndrome. Below is a summary of the latest updates.

Key Updates

- Taysha has begun site activation for the REVEAL Pivotal Study after receiving a No Objection Letter from Health Canada and feedback from the U.S. FDA. Enrollment in the REVEAL Pivotal Study is expected to begin in the fourth quarter of 2025.
- Taysha is planning a separate safety-focused study for younger girls ages of 2 to under 6.
- Both doses of TSHA-102 continue to be generally well tolerated. As of August 2025, there were no treatment-related serious adverse events or dose-limiting toxicities in the 12 pediatric, adolescent and adult patients who received the treatment in Part A of the REVEAL Study.
- We plan to report new supplemental REVEAL Part A clinical data in the fourth quarter of 2025.

Frequently Asked Questions

What is the REVEAL Pivotal Study?

- This clinical trial will test the efficacy and safety of TSHA-102, which will be administered **once directly into the fluid around the spinal cord** (called intrathecal delivery).
- The dose will be $1x10^{15}$ total vector genomes (vg), which was the dose selected based on the clinical data from Part A of the REVEAL studies.
- The study will enroll **15 girls and young women** between the ages of **6 and under 22 years old** with typical Rett syndrome who are in the developmental plateau population.
- The study will be a **single-arm study**, which means all participants enrolled will receive gene therapy. Each participant will serve as their own control, which means that a participant's abilities following administration of TSHA-102 will be compared to their abilities before they received TSHA-102.
- The **primary endpoint** in the study will measure the percentage of participants who gain or regain at least one important developmental milestone in areas like hand use (fine motor), mobility (gross motor) and communication, following treatment.

Will younger girls be included in the study?

- Females aged 6 and older with Rett syndrome are typically in a **developmental plateau -** a stage where there is a **very low chance (0% to <6.7%) of gaining or regaining certain lost developmental milestones**. This is based on Taysha's analysis of the NIH-funded International Rett Syndrome Foundation (IRSF) natural history study data from approximately 1,100 females with up to 14 years of follow-up.
- Because gaining or regaining a milestone at this stage is rare, this age group is ideal for showing whether a treatment like TSHA-102 is having a real impact.
- Taysha is also planning a **separate safety study** for girls between the ages of **2 and under 6 years**, who are in earlier stages of development. The data collected from this study will be an important part of our overall submission to regulators.

Can I sign up my loved one for a trial?

- We will share more information about how to sign up for the REVEAL Pivotal Study, including who may be eligible and where the study will take place, in the fall of 2025.

What are your plans for a clinical trial outside of the U.S. and Canada?

- We are continuing to have discussions with regulatory agencies outside the U.S. and Canada to determine the best path forward for TSHA-102 into other countries.

If you have any questions, please email us at **patientaffairs@tayshagtx.com**.

We truly appreciate your continued partnership and look forward to sharing more news with you soon.

Sincerely,
The Taysha Patient Affairs Team
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