June 22, 2026

Dear Rett Syndrome Community,

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

Key Updates

- **Dosing in the REVEAL Pivotal Study is complete** (17 participants aged 6 to 21 years). Once all participants have completed 6 months of follow-up, Taysha plans to review interim results with the U.S. Food & Drug Administration (FDA) to discuss next steps needed to seek potential approval of TSHA-102. **Initial pivotal study results and feedback from the FDA are expected in the first half of 2027.**
- **TSHA-102 was generally well-tolerated with no treatment related serious adverse events in all 29 participants** in the REVEAL Part A & Part B (Pivotal) Studies as of the June 2026 data cutoff.
- **Longer-term interim data from REVEAL Part A** (12 participants aged 6-21 years) **was shared earlier today** (see below).

Overview of Clinical Trials Evaluating TSHA-102

Dosing in the REVEAL Studies is complete and dosing in the ASPIRE Study is expected to be complete in July 2026.

- **REVEAL Part A** (REVEAL Pediatric Study and REVEAL Adolescent & Adult Study)[*]
  - **12 participants (ages 6-21) received TSHA-102** across two dose levels ($5.7x10^{14}$ vg or $1x10^{15}$ vg).
- **REVEAL Part B** (REVEAL Pivotal Study) [*]
  - **17 participants (ages 6-21) received TSHA-102** at the selected dose level ($1x10^{15}$ vg).
- **ASPIRE Study**[†] (on track to complete dosing in July 2026)
  - **4 participants (ages 2 to under 4)** to receive TSHA-102 at the selected dose level ($1x10^{15}$ vg), scaled to account for lower brain volume in younger children

Clinical Trial Follow-up and Regulatory Engagement

- **Follow-up and data collection:** Clinical trial participants are followed and information is collected to track potential benefits and safety of TSHA-102. Initial 6-month data from the REVEAL Pivotal Study is expected in the first half of 2027.
- **Regulatory discussions:** Taysha intends to review the 6-month interim data with the FDA to discuss plans for a Biologics License Application (BLA), the application a company submits to the FDA to ask for approval of a treatment.

Longer-Term Interim Data from REVEAL Part A (Phase 1/2 Adolescent/Adult and Pediatric Studies)[‡]

It is important to note that data is interim, and conclusions cannot be made until all data have been fully evaluated.

- All 12 participants (ages 6-21 years) in Part A have now been followed for at least 12 months. Interim results from the May 2026 data cutoff were reported while longer-term follow-up continues.
- No treatment-related serious adverse events or dose-limiting toxicities were seen at the low or high dose.
  - Side effects were generally mild to moderate, with the most common being elevated liver enzymes (in 4 participants), an increase in protein in spinal fluid (in 3 participants) and fever (in 3 participants).
- Longer-term follow-up shows that the early improvements demonstrated across participants have been sustained, with additional functional gains achieved over time at ≥12 months post-TSHA-102.
- Functional gains were seen across the core domains of communication, hand use and mobility regardless of the participant's age, severity or genotype.

[*]Please visit ClinicalTrials.gov and search NCT05606614 for more information about the REVEAL Study.
[†]Please visit ClinicalTrials.gov and search NCTNCT07480564 for more information about the ASPIRE Study.
[‡]Interim data presented by Taysha on June 22, 2026.

- At ≥12 months post-TSHA-102, a total of 310 functional gains were observed across the 12 participants (an average of ~26 per patient). These functional gains included:
    - 31 developmental milestones across the core functional domains of communication, hand use and mobility.
        - 100% of participants gained or regained at least one developmental milestone, as assessed by multiple independent experts using video evidence.
        - Examples included spoke in phrases with meaning, used utensils to eat without assistance and walked with support.
    - 279 additional skill gains and improvements across the functional domains of communication, hand use, mobility, autonomic function and other Rett-related symptoms.
        - Skill gains and improvements were based on clinician- and caregiver-reported assessments.
        - Examples included improved motor skills and hand use, understood and responded to questions, reduced/no hand stereotypies and decreased/no breath-holding.

Looking Ahead

- Taysha's goal is to ensure TSHA-102 will be available to the broad Rett community, regardless of age, sex or clinical presentation. Final approval and labeling will be determined by regulatory authorities.
- If approved, Taysha intends to work with payors and other stakeholders to support patient access to TSHA-102 for patients within the approved indication. However, the ultimate decision for gene therapy coverage will be up to the specific payor or insurer.

Overview of TSHA-102[§]

- TSHA-102 is an investigational gene therapy designed to address the root cause of Rett syndrome by delivering a functional copy of the *MECP2* gene to cells in the brain and central nervous system.
- TSHA-102 is made up of:
    - **A version of the *MECP2* gene** that includes the essential parts of the MECP2 gene required to make functional MeCP2 protein.
    - **Double-stranded DNA**, which helps cells make theMeCP2 protein more quickly and reliably – about 10 to 100 times better than single-stranded approaches.
    - **A built-in control sensor (miRARE)**, which makes sure that each cell gets the right amount of protein, not too much and not too little.
    - **An AAV9 delivery vehicle**, a non-disease-causing virus that carries the gene to target cells.
- TSHA-102 is designed to be given as a one-time treatment, administered through an **intrathecal (IT) injection** in the lower back.
    - IT delivery is a common, minimally invasive procedure that allows the therapy to get **directly into the fluid that circulates around the brain and spinal cord**—called cerebrospinal fluid (CSF).
    - Delivering TSHA-102 to the CSF allows it to **target the areas of the brain affected by Rett syndrome**, including those involved in movement, communication, social interaction, body functions, and seizures.

Thank You

We would like to extend our sincere gratitude to the individuals and families participating in our clinical studies, as well as to the broader Rett syndrome community, whose support has helped make this progress possible. We recognize that not every interested family was able to participate in our studies, and we remain committed to advancing TSHA-102 with urgency and care on behalf of all individuals and families affected by Rett syndrome.

If you have additional questions, please contact us at patientaffairs@tayshagtx.com.

Sincerely,
The Taysha Patient Affairs Team

[§]Please visit tayshagtx.com/patients-caregivers/ for more information about TSHA-102.