February 26, 2025

Dear Rett Patient Advocacy Leaders,

We are writing to share the latest updates on Taysha's ongoing **Phase 1/2 clinical trials for TSHA-102**, our investigational gene therapy for Rett syndrome. Below is a summary of the key updates.

Clinical Trial Updates

- **Completed dosing of 10 participants** in Part A of both the REVEAL Adolescent/Adult and Pediatric trials:
  - **4 participants** received the **low dose** ($5.7x10^{14}$ vg).
  - **6 participants** received the **high dose** ($1x10^{15}$ vg).
- Both doses were generally **well tolerated**. As of February 17, 2025, there have been **no treatment-related serious adverse effects (SAEs) or dose-limiting toxicities (DLTs)** in the 10 participants treated across the two REVEAL trials (pediatric and adolescent/adult).
- We expect to share **clinical data** from both REVEAL trials (including results from the low and high-dose groups) in the **first half of 2025**.
- We are in ongoing **discussions with the FDA** to review Part A results and solidify the plan for the pivotal phase of our trial (Part B), in which we will dose additional participants and gather more data to support potential regulatory approval. We plan to share an update on the trial design for Part B in the **first half of 2025**.

Frequently Asked Questions

What is TSHA-102?

- TSHA-102 is an investigational gene therapy designed as a potential one-time treatment for Rett syndrome. It is designed to **replace the faulty MECP2 gene** with a working version to help the body make the MeCP2 protein, which is important for brain function. TSHA-102 includes:
  - **A smaller but fully working MECP2 gene (miniMECP2):** This version of the gene was carefully designed to produce functional MeCP2 protein and make room for other important features of our gene therapy.
  - **A built-in MeCP2 regulator (miRARE technology):** This helps the body make just the right amount of MeCP2 protein—not too much and not too little.
  - **An efficient delivery system (self-complementary AAV vector):** Self-complementary design allows the therapy to start working faster.
- TSHA-102 is given through an **intrathecal injection in the lumbar region of the spine (spinal tap)**, a well-known minimally invasive medical procedure that delivers the therapy directly into cerebrospinal fluid (CSF). CSF naturally flows through the brain and spinal cord, ensuring widespread biodistribution across the central nervous system.

What are the goals of the REVEAL studies?

In **Part A,** the REVEAL studies aim to:

- Evaluate if TSHA-102 is **safe and well tolerated**.
- See if it has **potential benefits** for people with Rett syndrome.
- Test **two dose levels** ($5.7x10^{14}$ vg and $1x10^{15}$ vg) to determine the highest tolerable dose.

Once the dose has been selected in Part A, more participants will be enrolled in **Part B** of the REVEAL studies to collect additional safety and efficacy data to support a potential regulatory approval.

Where are the REVEAL Phase 1/2 studies being conducted?

REVEAL Adolescent & Adult Study (females ages 12+)

- U.S. & Canada study sites: San Diego, CA | Chicago, IL | Boston, MA | Saint Paul, MN | Dallas, TX | Montreal, QC
- For additional information, a list of clinical trial sites and contact information please visit https://clinicaltrials.gov/study/NCT05606614.

REVEAL Pediatric Study (females ages 5-8)

- U.S. & Canada study sites: San Diego, CA | Chicago, IL | Boston, MA | Saint Paul, MN | Saint Louis, MO | Philadelphia, PA | Nashville, TN | Dallas, TX | Montreal, QC
- The U.K. site in London is expected to open during Part B of the study.
- For additional information, a list of clinical trial sites and contact information please visit https://clinicaltrials.gov/study/NCT06152237.

Thank You

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
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