Longer-Term Data From the REVEAL Phase 1/2 Studies

Taysha GENE THERAPIES

TSHA-102 is an investigational gene therapy designed to treat the root cause of Rett syndrome[1]

Overview of the REVEAL Phase 1/2 Studies (Part A)

Goals of the Studies[2]

- Evaluate the safety, tolerability and potential benefits of **TSHA-102**
- Assess 2 different dose levels of **TSHA-102**

Study Designs[2,3]

Total of 12 females, aged 6+ with typical Rett syndrome across 2 groups

Pediatric **Adolescent/Adult**

Current Status

- The $1x10^{15}$ total vg dose was selected for the REVEAL Pivotal Study (Part B)[4]
- All participants who received **TSHA-102** have now been followed for at least 12 months. Results are being reported while longer-term follow-up continues[2]

Longer-Term Results Following Treatment With TSHA-102*

Functional Gains

At ≥12 months post-**TSHA-102**, a total of **310 functional gains** were observed across the 12 participants (~26 gains each). This number reflects a combination of developmental milestones (**31**) and skill gains and improvements (**279**).[5]

Developmental Milestones[6]

100% of all 12 participants gained or regained at least 1 developmental milestone after receiving TSHA-102, achieving a total of **31 milestones** across communication, fine motor, and gross motor skills—progress that would have had around a 0% chance of occurring without treatment based on natural history.[2,5]

Communication

- ✓ Spoke in phrases (2 words or more) with meaning
- ✓ Used word(s) with meaning
- ✓ Followed a command without a gesture
- ✓ Followed a command with a gesture
- ✓ Pointed for something they wanted
- ✓ Identified body parts

Fine Motor

- ✓ Used utensils to eat without assistance
- ✓ Finger fed
- ✓ Held a bottle unpropped
- ✓ Used a pincer grasp
- ✓ Reached for a toy
- ✓ Transferred an object from one hand to another

Gross Motor

- ✓ Walked with support
- ✓ Climbed down stairs with support
- ✓ Stood while holding on
- ✓ Pulled to standing
- ✓ Sat without support

Developmental milestones defined in the natural history study are assessed using rigorous video evidence taken before and after treatment. Multiple independent experts using prespecified definitions of achievement reviewed the videos to determine if a milestone had been achieved.[6,7]

Skill Gains and Improvements[6]

279 skill gains and improvements were achieved beyond developmental milestones, highlighting the broad impact of **TSHA-102.**[5]

Communication

- ✓ Followed directions related to daily routine(s)
- ✓ Understood and responded to questions
- ✓ Engaged in play with others

Fine Motor

- ✓ Improved hand use
- ✓ Reduced/absent hand stereotypies
- ✓ Improved frequency of reaching for objects/people

Gross Motor

- ✓ Improved dystonia/hypertonia
- ✓ Improved motor skills
- ✓ Improved speed and ease of movement

Autonomic/ Other

- ✓ Reduced/absent seizure episodes
- ✓ Reduced/absent breath holding/hyperventilation
- ✓ Reduced/absent teeth grinding

Skill gains and improvements are based on validated clinician- and caregiver-reported assessments that measure communication, fine and gross motor, autonomic function and other characteristics of Rett syndrome that are not already classified as developmental milestones in our studies.[6]

The developmental milestones and skill gains and improvements listed are not inclusive of all that were observed in the study.[6]

*Results reflect a 12-month data cut and may change as more data become available. Based on May 2026 data cutoff (N=12).[5]

Longer-Term Results Following Treatment With TSHA-102* (continued)

Examples of Functional Gains (Developmental Milestones, Skill Gains and Improvements) Observed Among Participants in the Study Following Treatment With TSHA-102[6,†]

Communication Improvements

Pre-TSHA-102	Post-TSHA-102
Non-verbal	**Spoke in phrases/ sentences with meaning**
Understood simple words	**Engages in conversations and play/activity with others**
Made choices less than 10% of time using eye gaze	**Consistently makes choices by pointing**
Rarely responds to spoken words	**Follows directions and responds to questions**

Fine Motor Improvements

Pre-TSHA-102	Post-TSHA-102
Required caregiver-assisted feeding	**Finger feeds and uses utensils to eat independently**
No purposeful hand use	**Plays with toys and self-feeds**
Stereotypies 76-100% of time	**Stereotypies 1-25% of time**
Limited hand function	**Holds a bottle unpropped**

Gross Motor Improvements

Pre-TSHA-102	Post-TSHA-102
Non-ambulatory	**Walked with support**
Unable to use stairs	**Climbs down stairs with support**
Required caregiver support for positional transfers and to stand	**Pulls self to standing position and stands while holding on**
Most severe dystonia (fixed positional deformity)	**No dystonia**

Autonomic/Other Improvements

Pre-TSHA-102	Post-TSHA-102
Unable to eat by mouth and required a g-tube	**Eats/drinks by mouth**
Weekly to monthly seizure episodes	**Seizure-free for at least 6 months**
Hyperventilating/breath holding 26-50% of time	**Absent or reduced hyperventilating/breath holding**
Feeding took more than 30 minutes	**No feeding difficulties**

The examples shown were seen across different participants, but not everyone experienced the same results. Individual results may vary.

- 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**[5]
- Functional gains were seen across the core domains of communication, hand use, mobility and autonomic function regardless of the participant's age, severity or genotype[5,6]

Safety Results*

- No treatment-related serious adverse events or dose-limiting toxicities were seen at any dose level[5]
- The most common treatment-related adverse events were elevated liver enzymes (4 participants), an increase in protein in spinal fluid (3 participants) and fever (3 participants). All treatment-emergent adverse events were mild to moderate in severity[5,6]

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Additional TSHA-102 Clinical Trials Are Underway

The REVEAL Pivotal Study (Part B) is studying potential benefits and safety of **TSHA-102** at the selected dose in 17 girls and young women (aged 6 to 21) with Rett syndrome.[4]

The ASPIRE Study is evaluating the safety and potential benefits of **TSHA-102** in 4 young girls (aged 2 to 3) with Rett syndrome.[8]

Data from the REVEAL and ASPIRE Studies are intended to support the potential approval of TSHA-102 for a broad population of individuals living with Rett syndrome, across age, sex and clinical presentation.[9]

References: 1. Samanta D, et al. *Front Neurol.* 2026;17:1766679. **2.** Rossignol E, et al. 54th CNS Annual Meeting: October 8–11, 2025, Charlotte, NC, USA. **3.** Healthcare Professionals. Taysha Gene Therapies. Accessed June 15, 2026. https://tayshagtx.com/healthcare-professionals/ **4.** A Phase 1/2/3 Study of TSHA-102 Gene Therapy in Females With Rett Syndrome (REVEAL Pivotal Study). Clinicaltrials.gov identifier: NCT05606614. https://clinicaltrials.gov/study/NCT05606614 **5.** Taysha Gene Therapies. Press Release, June 22, 2026. https://ir.tayshagtx.com/news-releases/news-release-details/taysha-gene-therapies-announces-completion-dosing-reveal-pivotal **6.** Data on file. Taysha Gene Therapies, 2026. **7.** Data on file. Taysha Gene Therapies, 2026. **8.** Safety and Preliminary Efficacy of TSHA-102 Gene Therapy in Pediatric Females Aged >2 to <4 Years With Rett Syndrome (ASPIRE). Clinicaltrials.gov identifier: NCT07480564. https://clinicaltrials.gov/study/NCT07480564 **9.** Taysha Gene Therapies. Press Release, January 6, 2026. https://ir.tayshagtx.com/news-releases/news-release-details/taysha-gene-therapies-announces-progress-across-tsha-102-pivotal