# Taysha Gene Therapies Announces Progress Across TSHA-102 Pivotal Gene Therapy Program in Rett Syndrome

*First patient dosed in REVEAL pivotal trial evaluating TSHA-102 (N=15, aged 6 to <22 years) in Q4 2025, with enrollment advancing across multiple sites*

*Reached written alignment with FDA on inclusion of ≥3 months of safety data from ASPIRE trial evaluating TSHA-102 (N=3, aged 2 to <4 years) in planned BLA submission to support a broad label in patients aged ≥2 years with Rett syndrome*

*Completion of dosing in REVEAL pivotal trial and ASPIRE trial expected in Q2 2026*

*Longer-term safety and efficacy data update from Part A of REVEAL Phase 1/2 trials expected in H1 2026*

DALLAS, Jan. 06, 2026 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA) (Taysha or the Company), a clinical-stage biotechnology company focused on advancing adeno-associated virus (AAV)-based gene therapies for severe monogenic diseases of the central nervous system (CNS), today announced progress across the TSHA-102 pivotal program, an intrathecally (IT) delivered AAV9 gene therapy with disease modifying potential, in clinical evaluation for the treatment of Rett syndrome.

"Dosing the first patient in our REVEAL pivotal trial last quarter represents a significant milestone in the development of TSHA-102 for Rett syndrome, and enrollment is further advancing across multiple sites. As we progress pivotal development, we continue to maintain consistent and productive dialogue with the FDA," said Sean P. Nolan, Chairman and Chief Executive Officer of Taysha. "Importantly, we recently reached written alignment with the FDA that our planned BLA submission will include at least three months of safety data from three patients aged two to under four years in the ASPIRE trial to support a broad label for patients aged two years and older with Rett syndrome. We believe this recent alignment on ASPIRE, together with the alignment on a six-month interim analysis for our REVEAL pivotal trial, streamlines our path toward BLA submission for TSHA-102. We expect to complete dosing across our REVEAL and ASPIRE trials in the second quarter of 2026. With an estimated 15,000 to 20,000 patients affected by Rett syndrome across the U.S., EU and U.K. and compelling REVEAL Part A clinical data, we see a significant opportunity to redefine the treatment paradigm for this devastating disease with high unmet need."

**TSHA-102 Program Updates and Overview**

- **Dosed First Patient in REVEAL Pivotal Trial in the Fourth Quarter of 2025.** Additional enrollment continues to advance across multiple clinical trial sites. The single-arm, open-label trial is evaluating a single IT administration of high dose TSHA-102 ($1x10^{15}$ total vector genomes (vg)) in 15 females between the ages of 6 and <22 years in the developmental plateau population of Rett syndrome. The primary endpoint will assess response rate, defined as the percentage of patients who gain or regain ≥one of the 28 natural history-defined developmental milestones, with each patient serving as their own control. The study includes a six-month interim analysis that may serve as the basis for Biologics License Application (BLA) submission.
- **Reached Written FDA Alignment on ASPIRE Trial and Data for Inclusion in BLA Submission to Enable Broad Label Following Type D Meeting.** The Company confirmed prior alignment and obtained further written alignment with the U.S. Food and Drug Administration (FDA) on the ASPIRE safety-focused trial and the data for inclusion in the planned BLA submission to enable broad labeling of TSHA-102 for patients aged ≥2 years with Rett syndrome, including:
    - ASPIRE will enroll three females aged 2 to <4 years with Rett syndrome to evaluate the safety and preliminary efficacy of a single IT administration of high dose TSHA-102 ($1x10^{15}$ total vg), scaled to account for the lower brain volume in 2 to <4-year-olds
    - A minimum of three months of ASPIRE safety data will be included in the planned BLA submission, while efficacy in the 2 to <6-year-old population will be extrapolated from data collected in the REVEAL pivotal trial, to support a broad label for TSHA-102 in patients aged ≥2 years with Rett syndrome

**Anticipated Milestones**

- Completion of dosing in the REVEAL pivotal trial is expected in the second quarter of 2026
- Completion of dosing in the ASPIRE trial is expected in the second quarter of 2026
- Update on longer-term safety and efficacy data from Part A of the REVEAL Phase 1/2 trials is expected in the first half of 2026

**About TSHA-102**

TSHA-102 is a self-complementary intrathecally delivered AAV9 investigational gene transfer therapy in clinical evaluation for Rett syndrome. Designed as a one-time treatment, TSHA-102 aims to address the genetic root cause of the disease by delivering a functional form of *MECP2* to cells in the CNS. TSHA-102 utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) technology designed to mediate levels of *MECP2* in

the CNS on a cell-by-cell basis without risk of overexpression. TSHA-102 has received Breakthrough Therapy, Regenerative Medicine Advanced Therapy, Fast Track and Orphan Drug and Rare Pediatric Disease designations from the FDA, Orphan Drug designation from the European Commission and Innovative Licensing and Access Pathway designation from the Medicines and Healthcare products Regulatory Agency.

**About Rett Syndrome**
Rett syndrome is a rare neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene encoding methyl CpG-binding protein 2 (MeCP2), which is essential for regulating neuronal and synaptic function in the brain. The disorder is characterized by loss of communication and hand function, slowing and/or regression of development, motor and respiratory impairment, seizures, intellectual disabilities and shortened life expectancy. Rett syndrome progression is divided into four key stages, beginning with early onset stagnation at 6 to 18 months of age followed by rapid regression, plateau and late motor deterioration. Rett syndrome primarily occurs in females and is one of the most common genetic causes of severe intellectual disability. Currently, there are no approved disease-modifying therapies that treat the genetic root cause of the disease. Rett syndrome caused by a pathogenic/likely pathogenic *MECP2* mutation is estimated to affect between 15,000 and 20,000 patients in the U.S., EU, and U.K.

**About Taysha Gene Therapies**
Taysha Gene Therapies (Nasdaq: TSHA) is a clinical-stage biotechnology company focused on advancing adeno-associated virus (AAV)-based gene therapies for severe monogenic diseases of the central nervous system. Its lead clinical program TSHA-102 is in development for Rett syndrome, a rare neurodevelopmental disorder with no approved disease-modifying therapies that address the genetic root cause of the disease. With a singular focus on developing transformative medicines, Taysha aims to address severe unmet medical needs and dramatically improve the lives of patients and their caregivers. The Company's management team has proven experience in gene therapy development and commercialization. Taysha leverages this experience, its manufacturing process and a clinically and commercially proven AAV9 capsid in an effort to rapidly translate treatments from bench to bedside. For more information, please visit www.tayshagtx.com.

**Forward-Looking Statements**
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "anticipates," "believes," "expects," "intends," "projects," "plans," and "future" or similar expressions are intended to identify forward-looking statements. Forward-looking statements include, but are not limited to, statements concerning the potential of TSHA-102 and Taysha's other product candidates to positively impact quality of life and alter the course of disease in the patients Taysha seeks to treat, its research, development and regulatory plans for its product candidates, communications with the FDA, including with respect to the BLA for TSHA-102, the potential for these product candidates to receive regulatory approval from the FDA or equivalent foreign regulatory agencies, and whether, if approved, these product candidates will be successfully distributed and marketed and the potential market opportunity for Taysha's product candidates. Forward-looking statements are based on management's current expectations and are subject to various risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. Risks regarding Taysha's business are described in detail in Taysha's Securities and Exchange Commission ("SEC") filings, including in Taysha's Annual Report on Form 10-K for the full-year ended December 31, 2024 and Quarterly Report on Form 10-Q for the quarter ended September 30, 2025, which are available on the SEC's website at www.sec.gov. Additional information will be made available in other filings that Taysha makes from time to time with the SEC. These forward-looking statements speak only as of the date hereof, and Taysha disclaims any obligation to update these statements except as may be required by law.

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