Taysha Gene Therapies Announces Completion of Dosing in REVEAL Pivotal Trial and Reports Longer-Term Clinical Data from Part A of REVEAL Phase 1/2 Trials Evaluating TSHA-102 for Rett Syndrome

Completed dosing of 17 patients in REVEAL pivotal trial; topline data from 6-month interim analysis and FDA feedback on next steps toward BLA submission pathway expected 1H 2027

TSHA-102 was generally well-tolerated with no treatment-related SAEs or DLTs reported as of the June 2026 data cutoff across REVEAL Phase 1/2 and pivotal trials (N=29)

100% of REVEAL Part A patients (N=12, 6-21 years) gained/regained ≥one developmental milestone by 12 months post-TSHA-102, with consistent responses across ages and disease severity

Longer-term follow-up showed a durable and deepening treatment effect ≥12 months post-TSHA-102, with functional gains accumulating over time across core disease domains

310 total functional gains demonstrated ≥12 months post-TSHA-102 (~26 per patient), comprising 31 developmental milestones and 279 additional skill gains/improvements

Robust and clinically meaningful responses at both 6 and ≥12 months in REVEAL Part A further support potential for BLA submission based on REVEAL pivotal trial 6-month interim analysis

Conference call and webcast today at 8:30 AM ET

DALLAS, June 22, 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 the completion of dosing in the REVEAL pivotal trial and reported positive longer-term clinical data from Part A of the REVEAL Phase 1/2 trials evaluating TSHA-102 for the treatment of Rett syndrome.

“As we advance toward a potential BLA submission for TSHA-102, we remain committed to developing a comprehensive, scientifically rigorous data package informed by our ongoing discussions with the FDA. We are pleased to report the completion of dosing in our REVEAL pivotal trial and positive longer-term follow-up data from our REVEAL Phase 1/2 trials. The data demonstrated early, durable treatment effect across all 12 pediatric, adolescent and adult patients, with responses continuing to deepen over time. On average, patients achieved 26 functional gains across core disease domains that impact activities of daily living at ≥12 months post-treatment, with consistent benefits observed regardless of age or disease severity,” said Sean P. Nolan, Chairman and Chief Executive Officer of Taysha.

Mr. Nolan continued, “We believe the robust, clinically meaningful responses observed at both 6 and ≥12 months post-treatment continue to demonstrate the potential for TSHA-102 to transform the treatment paradigm for this devastating disease and further support the potential for a BLA submission based on the six-month interim analysis from our pivotal trial. In early 2027, we plan to engage with the FDA to review the interim data and discuss next steps toward submitting the BLA, with topline results and regulatory feedback expected in the first half of 2027.”

REVEAL Pivotal Trial and ASPIRE Trial Updates:

Completed dosing in the overenrolled REVEAL pivotal trial, with a total of 17 females in the developmental plateau population of Rett syndrome dosed with TSHA-102

- The single-arm, open-label trial is evaluating a single intrathecal (IT) administration of high dose TSHA-102 ($1x10^{15}$ total vector genomes (vg)) in females with Rett syndrome between the ages of 6 to <22 years. 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. A response rate of 33% is the minimum threshold for success sufficient to reject the natural history established null hypothesis of 6.7%
- TSHA-102 continues to be generally well tolerated, with no treatment-related serious adverse events (SAEs) or dose-limiting toxicities (DLTs) reported as of the June 2026 data cutoff
- The interim analysis to support the planned Biologics License Application (BLA) submission is expected to occur after all 17 patients complete six months of post-treatment follow-up. Subsequently, Taysha plans to discuss data from the 6-month interim analysis and next steps toward the BLA submission pathway with the FDA in early 2027, with topline data and regulatory feedback anticipated in 1H 2027

ASPIRE trial ongoing with enrollment exceeding the initial target of (N=3); on track to complete dosing of the three patients in Q2 2026 and expect to dose one additional patient in July 2026, further strengthening potential BLA submission for TSHA-102

- The ASPIRE safety-focused trial is designed to enable a broad label of TSHA-102 for patients aged ≥2 years with Rett syndrome
- Taysha has elected to overenroll the trial to include one additional screened and eligible patient and will now dose a total of four females with Rett syndrome, aged 2 to <4 years, 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

Longer-Term Clinical Data from Part A of the REVEAL Phase 1/2 Adolescent/Adult and Pediatric Trials

REVEAL Part A efficacy data based on the May 2026 data cutoff included 12 females with Rett syndrome aged 6-21 years (high dose, n=8; low dose, n=4) treated with the high dose ($1x10^{15}$ total vg) or low dose ($5.7x10^{14}$ total vg) of TSHA-102, each with ≥12 months of follow-up

- 100% of patients gained/regained ≥one developmental milestone across the core functional domains of fine motor, gross motor and communication post-TSHA-102 (i.e., spoke in phrases with meaning, used utensils to eat without assistance, walked with support), as assessed by multiple independent raters through video-evidenced evaluation
- Longer-term follow-up demonstrated a durable, deepening treatment effect across all patients, with additional functional gains continuing to accumulate over time through ≥12 months
    - Developmental milestone gains increased by 69% from 6 to 12 months and by 94% from 6 to ≥12 months post-TSHA-102
    - Patients with longest follow-up at 30 months continued to demonstrate functional gains
- Broad functional impact consistently demonstrated across core disease domains post-TSHA-102 regardless of age, disease severity or genotype
    - ≥12 months post-TSHA-102, a total of 310 functional gains were observed (~26 per patient), comprising 31 developmental milestones and 279 additional skill gains/improvements
- Robust and clinically meaningful responses at 6 and ≥12 months exceed the FDA-aligned minimum threshold for efficacy and support potential for a BLA submission based on the REVEAL pivotal trial 6-month interim analysis
- Improvements observed across multiple clinician-assessed outcome measures, including Revised Motor Behavior Assessment (R-MBA), Clinician Global Impression–Improvement (CGI-I) and Clinical Global Impression–Severity (CGI-S) corroborated the functional gains demonstrated

REVEAL Part A safety data based on the May 2026 data cutoff included 12 females with Rett syndrome aged 6-21 years treated with TSHA-102 (high dose, n=8; low dose, n=4), each with ≥12 months of follow-up

- TSHA-102 has been generally well tolerated with no treatment-related SAEs or DLTs
- All treatment-emergent adverse events related to TSHA-102 were mild to moderate in severity

“Longer-term data from the REVEAL Phase 1/2 trials demonstrate remarkable responses following treatment with TSHA-102, far exceeding what would be expected based on the natural history of patients aged six years and older in the developmental plateau population,” said Elsa Rossignol, M.D., FRCP, FAAP, Professor in Neuroscience and Pediatrics at the Université de Montréal, Director of the Rett Multidisciplinary Clinic of the CHU Sainte-Justine and a Principal Investigator of the REVEAL trial. “TSHA-102 consistently drove early, durable functional gains across the core domains of the disease, including communicating with words or phrases, eating with utensils without assistance and walking with support, which continue to accumulate over time. These outcomes support greater independence, reduce caregiver burden and enhance social engagement. I believe this sustained trajectory, combined with a favorable tolerability profile and minimally invasive intrathecal delivery approach, reinforces the potential of TSHA-102 to deliver meaningful improvements for patients and families who continue to face profound unmet need.”

Anticipated Milestones

- Completion of dosing in the ASPIRE trial (N=4) is expected in July 2026
- Completion of BLA-enabling Process Performance Qualification (PPQ) campaign for TSHA-102 is expected in the fourth quarter of 2026
- Topline data from the REVEAL pivotal trial 6-month interim analysis and FDA feedback on the BLA submission pathway for TSHA-102 is expected in the first half of 2027

Conference Call and Webcast Information
Taysha management will host a live conference call and webcast today at 8:30 a.m. ET to discuss the longer-term data from the REVEAL Phase 1/2 trials. Participants may access the live webcast of the conference call by visiting Taysha’s website.

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, Taysha's 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 Taysha's 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, including anticipated clinician and caregiver demand. 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 our Annual Report on Form 10-K for the full-year ended December 31, 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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