Taysha Gene Therapies Presents New Supplemental Data Analysis from Part A of the REVEAL Phase 1/2 Trials for TSHA-102 in Rett Syndrome at the 54th CNS Annual Meeting

Previously disclosed 100% response rate across all 10 patients in Part A for pivotal trial primary endpoint of gain/regain of ≥ one natural history defined developmental milestone assessed via video-evidenced review by independent central raters

New supplemental analysis of validated, structured efficacy scales provides supportive evidence of additional functional gains, with 100% of patients demonstrating multiple skill gains/improvements outside the natural history defined developmental milestones

Findings reinforce the broad and consistent functional gains seen across the core domains that impact activities of daily living, with 22 developmental milestones and 165 additional skills/improvements achieved across the 10 patients post-TSHA-102

DALLAS, Oct. 09, 2025 (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 results from a new supplemental data analysis from Part A of the REVEAL Phase 1/2 adult/adolescent and pediatric trials evaluating TSHA-102 in females with Rett syndrome at the 54th Child Neurology Society (CNS) Annual Meeting. The analysis provides supportive evidence of additional functional gains in skills and improvements across core disease characteristics that are outside of the natural history defined developmental milestones, further highlighting the consistent, multi-domain impact of TSHA-102 on activities of daily living.

"To assess the broad therapeutic impact of TSHA-102 on functional aspects of Rett syndrome, systematic evaluation criteria were applied to REVEAL Part A data," said Elsa Rossignol, M.D., FRCP, FAAP, Associate 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 trials. "This included the pivotal trial primary endpoint of developmental milestone achievements not expected without treatment based on natural history data, assessed by independent raters through video-evidenced evaluation. Importantly, this approach enabled the reliable and objective measure of TSHA-102's efficacy. The supplemental analysis of validated, structured efficacy scales was also conducted to capture supportive evidence of additional skill gains and improvements outside of the 28 natural history defined milestones."

Sukumar Nagendran, M.D., President and Head of R&D of Taysha added, "The new supplemental analysis of Part A data further underscores the potential consistency and breadth of TSHA-102's impact across the core domains of Rett syndrome, including communication, fine motor, gross motor and autonomic function. In addition to the developmental milestones achieved across the treatment cohort in Part A, patients consistently gained additional skills and improvements across core disease characteristics. We believe this reinforces the potential therapeutic impact of TSHA-102 on activities of daily living that are important to caregivers and clinicians."

Supplemental Analysis of Previously Disclosed Part A REVEAL Phase 1/2 Data Reinforces the Broad, Multi-domain Functional Gains/Improvements Consistently Demonstrated Post-TSHA-102

- **Pivotal trial primary endpoint of the gain/regain of ≥ one of the 28 developmental milestones defined in the natural history study assessed independently via video-evidenced evaluation by multiple independent central raters**
  - 100% of patients in Part A (N=10) gained/regained ≥ one defined developmental milestone across the core functional domains of communication, fine motor and gross motor post-TSHA-102, with 0% to <6.7% likelihood of being achieved without treatment based on natural history data
  - A total of 22 developmental milestones were achieved across the 10 patients, reflecting meaningful functional gains impacting activities of daily living

- **Additional skills and improvements outside of the 28 natural history defined developmental milestones demonstrated in supplemental data analysis derived from structured scales validated in Rett syndrome**
  - 100% of patients in Part A (N=10) gained multiple additional functional skills/improvements across the domains of communication, fine motor, gross motor and autonomic function
  - A total of 165 additional skills/improvements were achieved across the 10 patients, further supporting the potential broad and consistent therapeutic impact of TSHA-102 on functional abilities and activities of daily living

- **Poster presentation with additional details and accompanying figures are available through Taysha's website.**

Results reflect previously disclosed data from the REVEAL Phase 1/2 trials (N=10, 6-21 years; May 2025 data cutoff) treated with the high dose ($1x10^{15}$ total vg; N=6) or low dose ($5.7x10^{14}$ total vg; N=4) of TSHA-102. The new supplemental data analysis was based on additional skills and improvements achieved in core disease characteristics outside of the natural history defined developmental milestones that were derived from structured efficacy scales assessed in Part A that are validated in Rett syndrome. The scales include the Adapted Mullen Scales of Early Learning (MSEL-A) evaluating defined communication skills (N=5 patients with available data), the Revised Motor Behavior Assessment (R-MBA) evaluating specific Rett syndrome disease characteristics (N=10 patients with available data), and the Observer-Reported Communication Ability (ORCA) evaluating communication skills (N=5 patients with available data).

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 reproducibility and durability of any favorable results initially seen in patients dosed to date in clinical trials, including with respect to functional milestones; 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 including the timing of initiating additional trials, reporting data from its clinical trials and making regulatory submissions; 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 its 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 June 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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