Taysha Gene Therapies to Present New Preclinical Data Supporting Construct Design of TSHA-102 for Rett Syndrome at the ASGCT 2026 Annual Meeting

In vitro data demonstrated self-complementary AAV9 (scAAV9) enabled ~30-fold higher MeCP2 protein expression compared to single-stranded AAV9 (ssAAV9), supporting the ability to effectively deliver TSHA-102 to the CNS by lumbar IT administration

MiniMeCP2 is functionally comparable to full-length MeCP2 across molecular and biochemical functions, with both proteins exhibiting comparable, stable expression in neuronal cells

Data further validate the selection of scAAV9 and miniMeCP2 in the TSHA-102 construct and provide translational support for the Part A REVEAL Phase 1/2 clinical data in patients with Rett syndrome

DALLAS, April 27, 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 that it will present new preclinical in vitro data from a head-to-head evaluation of TSHA-102 (scAAV9-mini*MeCP2*) compared to an analogous ssAAV9 construct with the full-length *MECP2* in neuronal cell models. The data will be presented during a poster presentation at the upcoming American Society of Gene and Cell Therapy (ASGCT) Annual Meeting, taking place in Boston from May 11-15, 2026.

TSHA-102 is a scAAV9 gene therapy in clinical evaluation for Rett syndrome that encodes a functional, miniaturized *MECP2* transgene, a key design feature that supports enhanced transduction efficiency and stability. Data to be presented are consistent with previously published vector comparisons demonstrating that scAAV9 drives significantly higher MeCP2 protein expression than ssAAV9, which support Taysha's ability to effectively deliver TSHA-102 to the CNS using a minimally invasive lumbar intrathecal (IT) administration. In addition, the data show that the miniMeCP2 protein is functionally comparable to full-length MeCP2 protein across molecular and biochemical functions and exhibits comparable, stable expression in neuronal cells.

"These findings demonstrate that miniMeCP2 protein is functionally comparable to full-length MeCP2 and that the scAAV9 vector enables significantly higher protein expression, delivering up to 30-fold higher MeCP2 than a comparable ssAAV9 construct in neuronal cell models," said Sukumar Nagendran, M.D., President and Head of Research & Development at Taysha. "The enhanced transduction efficiency and improved genomic stability of scAAV9 supports our ability to effectively deliver TSHA-102 to the CNS using a minimally invasive lumbar intrathecal administration. Importantly, the data provide direct mechanistic validation of TSHA-102's differentiated construct design and offer translational support for the early, sustained and deepening functional gains demonstrated following treatment with TSHA-102 in Part A of our REVEAL Phase 1/2 trials. We look forward to reporting longer-term safety and efficacy data from our Part A of REVEAL Phase 1/2 trials later this quarter."

Poster presentation details are as follows:

Title: Superior expression of self-complementary AAV and comparable functionality of mini and full-length *MECP2* support the design of TSHA-102 gene therapy for Rett syndrome

Presenter: Ryan Chaparian, Principal Scientist, Bioanalytics, at Taysha Gene Therapies

Poster Session Date and Time: Thursday, May 14 from 5:00-6:30 PM ET

Session: Poster Reception

Poster Number: 3481

Additional details on the meeting can be found at the ASGCT Annual Meeting 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, the expected timing of reporting longer-term safety and efficacy data from Part A of the REVEAL Phase 1/2 trials, and the ability of scAAV9 to effectively deliver TSHA-102 to the CNS using lumbar intrathecal administration. 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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