Taysha Gene Therapies Regains Full Rights to Lead TSHA-102 Program in Clinical Evaluation for the Treatment of Rett Syndrome

The 2022 Option Agreement between Astellas and Taysha has expired

Regaining full rights to TSHA-102 Rett syndrome program enables Taysha to focus on driving its long-term value with full strategic flexibility and optionality

TSHA-102 has demonstrated compelling Part A REVEAL Phase 1/2 safety and efficacy data, received FDA Breakthrough Therapy designation and is advancing with a clear path to potential registration

Dosing of the first patient in the REVEAL pivotal trial is scheduled this quarter

DALLAS, Oct. 16, 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 that the Company has regained full rights to its lead TSHA-102 program in clinical evaluation for Rett syndrome. The 2022 Option Agreement between Astellas and Taysha, which had granted Astellas the exclusive option to enter a negotiation period to obtain an exclusive license to TSHA-102 in Rett syndrome and certain rights with respect to change in control transactions involving Taysha, has expired.

In accordance with the 2022 Option Agreement, Taysha delivered a TSHA-102 data package to Astellas in mid-2025 that contained the previously disclosed Part A REVEAL clinical data (May 2025 data cutoff), initiating a 90-day review period for Astellas to elect to exercise an option to trigger exclusive negotiations for a transaction. These data were shared with the U.S. Food and Drug Administration (FDA) as part of the application for, and subsequent receipt of, Breakthrough Therapy designation for TSHA-102. Following the expiration of the Option Agreement, Taysha now holds unencumbered rights to the TSHA-102 program.

These previously disclosed Part A REVEAL clinical data (May 2025 data cutoff) demonstrated a generally well-tolerated safety profile and a 100% response rate post-TSHA-102 for the pivotal trial primary endpoint of the gain/regain of ≥ one defined developmental milestone, with <6.7% likelihood of being achieved without treatment based on natural history data. These findings were corroborated by dose-dependent improvements in multiple outcome measures, including Revised Motor Behavior Assessment (R-MBA) and Clinician Global Impression – Improvement (CGI-I).

“We greatly appreciate the collaborative relationship we’ve had with Astellas, and the progress made to date across our TSHA-102 program, including recent clinical data further highlighting the therapy’s broad and consistent impact and the receipt of Breakthrough Therapy designation from the FDA,” said Sean P. Nolan, Chairman and Chief Executive Officer of Taysha. “We are thrilled to regain full global rights to our lead TSHA-102 Rett syndrome program, which enables full strategic flexibility and optionality as we continue to advance the program and focus on driving long-term value.”

Mr. Nolan continued, “With an estimated 15,000 to 20,000 patients across the U.S., EU and U.K. suffering from Rett syndrome, we believe the profound unmet medical need paired with the robust clinical data observed in Part A of our REVEAL trials highlight the significant market opportunity for TSHA-102. We believe our strong balance sheet, team with proven gene therapy expertise and clear path to registration position us well to advance TSHA-102 toward late-stage development and potential commercialization, if approved. We remain focused on execution, with dosing of the first patient in the REVEAL pivotal trial scheduled this quarter.”

Taysha has finalized FDA alignment on the REVEAL pivotal trial protocol and statistical analysis plan**,** which includes a 6-month interim analysis that may serve as the basis for BLA submission. The REVEAL pivotal trial is a single-arm, open-label trial with each patient serving as their own control. A single intrathecal administration of high dose TSHA-102 ($1x10^{15}$ total vector genomes) will be evaluated in 15 females between the ages of 6 and less than 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 or more defined developmental milestone from a list of 28 across the core functional domains of communication, fine motor and gross motor, following dosing with TSHA-102. Selected milestones have a 0% to <6.7% likelihood of spontaneous gain/regain in the untreated Rett syndrome population aged ≥ 6 years based on natural history data. Standardized milestone assessments will be administered and captured on video at pre- and post-treatment timepoints, with determination of milestone gain/regain by video-evidence review by independent, blinded central raters based on prespecified definitions of achievement for each milestone. Dosing of the first patient in the REVEAL pivotal trial has been scheduled for the current quarter.

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, 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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Source: Taysha Gene Therapies, Inc.