Taysha Gene Therapies Announces Second Patient Dosed with TSHA-102 in the REVEAL Phase 1/2 Adult Trial for the Treatment of Rett Syndrome

Available clinical data from the two adult patients dosed with TSHA-102 in the first cohort (low dose) to be discussed during upcoming quarterly earnings call following Independent Data Monitoring Committee (IDMC) review

Dosing of third adult patient and completion of enrollment in the low-dose cohort expected in the fourth quarter of 2023

Dosing of first pediatric Rett syndrome patient expected in the first quarter of 2024

DALLAS, Sept. 26, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today announced that the second Rett syndrome patient has been dosed with TSHA-102 in the REVEAL Phase 1/2 adult trial in Canada.

"Dosing the second adult patient in the REVEAL Phase 1/2 adult trial in Canada marks important progress in the ongoing clinical evaluation of TSHA-102 for Rett syndrome," said Sukumar Nagendran, M.D., President, and Head of R&D of Taysha. "The enthusiasm for a potential disease-modifying therapy among the Rett syndrome community is encouraging, and we remain focused on further evaluating the therapeutic potential of TSHA-102 in adults and expanding the clinical evaluation to pediatric patients with this devastating disease. We look forward to reporting initial clinical data on the second adult patient and providing an update on the first adult patient in the low-dose cohort at our quarterly earnings conference call in mid-November, following the pre-specified IDMC review."

TSHA-102 is being evaluated in the REVEAL Phase 1/2 adult trial in Canada, a first-in-human, open-label, randomized, dose-escalation and dose-expansion study evaluating the safety and preliminary efficacy of TSHA-102 in adult females with Rett syndrome due to *MECP2* loss-of-function mutation. TSHA-102 is administered as a single lumbar intrathecal injection. Dose escalation will evaluate two dose levels of TSHA-102 sequentially. The maximum tolerated dose (MTD) or maximum administered dose (MAD) established will then be administered during dose expansion. Enrollment in the low-dose cohort is expected to be complete in the fourth quarter of 2023 with the dosing of the third patient.

The REVEAL adult trial is being conducted at CHU Sainte-Justine, the Université de Montréal mother and child university hospital centre in Montreal, Canada, under Principal Investigator Dr. Elsa Rossignol, M.D., FRCP, FAAP, Associate Professor Neuroscience and Pediatrics at CHU Sainte-Justine.

The United States Food and Drug Administration (FDA) cleared the Investigational New Drug (IND) application for TSHA-102 in pediatric patients with Rett syndrome, and the Company expects to dose the first pediatric patient in the first quarter of 2024. Additionally, the Company submitted a Clinical Trial Application to the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) for TSHA-102 in pediatric patients with Rett syndrome and expects to receive MHRA feedback in the second half of 2023.

About TSHA-102
TSHA-102 is a self-complementary intrathecally delivered AAV9 investigational gene transfer therapy in clinical evaluation for Rett syndrome. TSHA-102 utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) platform designed to mediate levels of *MECP2* in the CNS on a cell-by-cell basis without risk of overexpression. TSHA-102 has received Fast Track designation and Orphan Drug and Rare Pediatric Disease designations from the FDA and has been granted Orphan Drug designation from the European Commission.

About Rett Syndrome
Rett syndrome is a rare neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene, which is a gene that's essential for neuronal and synaptic function in the brain. The disorder is characterized by intellectual disabilities, loss of communication, seizures, slowing and/or regression of development, motor and respiratory impairment, and shortened life expectancy. 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 UK.

About Taysha Gene Therapies
Taysha Gene Therapies (Nasdaq: TSHA) is on a mission to eradicate monogenic CNS disease. With a singular focus on developing curative medicines, we aim to rapidly translate our treatments from bench to bedside. We have combined our team's proven experience in gene therapy drug development and commercialization with the world-class UT Southwestern Gene Therapy Program. Together, we leverage our fully integrated platform with a goal of dramatically improving patients' lives. More information is available at 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 statements concerning the potential of TSHA-102, including the reproducibility and durability of any favorable results initially seen in our first patient dosed in the REVEAL trial, and our other product candidates, including our preclinical product candidates, to positively impact quality of life and alter the course of disease in the patients we seek to treat, our research, development and regulatory plans for our product candidates, the potential for these product candidates to receive regulatory approval from the FDA or equivalent foreign regulatory agencies, whether, if approved, these product candidates will be successfully distributed and marketed and the potential market opportunity for these product candidates and the potential benefits of Fast Track, Orphan Drug and Rare Pediatric Disease designations for TSHA-102. 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 our business are described in detail in our Securities and Exchange Commission ("SEC") filings, including in our Annual Report on Form 10-K for the

full-year ended December 31, 2022, and our Quarterly Report on Form 10-Q for the quarter ended June 30, 2023, both of which are available on the SEC's website at www.sec.gov. Additional information will be made available in other filings that we make from time to time with the SEC. Such risks may be amplified by the impacts of the COVID-19 pandemic. These forward-looking statements speak only as of the date hereof, and we disclaim any obligation to update these statements except as may be required by law.

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