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

The Phase 1/2 REVEAL trial is a first-in-human, randomized, dose-escalation and dose-expansion study evaluating the safety and preliminary efficacy of TSHA-102 in adults with Rett syndrome

TSHA-102 utilizes novel miRARE technology, designed to regulate cellular MECP2 levels

Initial available clinical safety data from Phase 1/2 REVEAL trial will be reported at Taysha's upcoming R&D Day on June 28, 2023, at 10:00 AM Eastern Time

DALLAS, June 05, 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 first patient has been dosed with TSHA-102 in the Phase 1/2 REVEAL trial evaluating the safety and preliminary efficacy of TSHA-102 in adult patients with Rett syndrome. TSHA-102 is a self-complementary intrathecally delivered AAV9 investigational gene transfer therapy that utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) platform designed to regulate cellular *MECP2* expression. The study is being conducted at CHU Sainte-Justine, the Université de Montréal mother and child university hospital centre in Montreal, Canada.

"Dosing of the first adult patient marks the beginning of clinical evaluation of TSHA-102 in the Phase 1/2 REVEAL trial, and, to our knowledge, the first time a gene therapy has ever been evaluated in a clinical setting for the treatment of Rett syndrome," said Sukumar Nagendran, M.D., President, and Head of R&D. "By targeting the regulation of gene expression on a cell-by-cell basis, we believe our miRARE technology has the ability to enable safe expression of *MECP2*, which may help address the risks associated with both under and overexpression resulting from the mosaic pattern of *MECP2* silencing. This is a significant milestone that furthers our quest to bring a potentially transformational gene therapy to patients and families living with Rett syndrome. We look forward to sharing initial available clinical safety data from the Phase 1/2 REVEAL trial at our R&D Day on June 28, 2023."

The Phase 1/2 REVEAL trial is 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. Participants will receive a single lumbar intrathecal injection of TSHA-102. Dose escalation will evaluate two dose levels of TSHA-102 sequentially, with an initial dose of $5x10^{14}$ total vector genomes (vg) and the second dose of $1x10^{15}$ vg. The maximum tolerated dose (MTD) or maximum administered dose (MAD) established will then be administered during dose expansion. Per the protocol, an independent data monitoring committee will review available safety data from the first patient at approximately six weeks post-dosing to determine if the Company can proceed with dosing the second patient. Initial available clinical safety data will be reported at Taysha's upcoming R&D Day on June 28, 2023. To register for the event, please click here.

Elsa Rossignol, M.D., FRCP, FAAP, Associate Professor Neuroscience and Pediatrics, and Principal Investigator of the REVEAL study added, "Based on its unique and compelling technology targeting the genetic root cause of Rett syndrome, TSHA-102 has the potential to transform care by addressing a significant unmet medical need for patients with this devastating and currently incurable disease. The dosing of the first patient in this important clinical trial represents a critical advancement in evaluating the potential of gene therapy for Rett syndrome. It is a privilege to be part of this important endeavor. In the name of all affected families, I thank Taysha for bringing this potentially transformative therapy from the bench to the bedside."

Sabrina Millson, President of Ontario Rett Syndrome Association further added, "This is a momentous day for the Rett syndrome community. As a mom to a daughter living with Rett syndrome and the president of the Ontario Rett Syndrome Association here in Canada, I know first-hand how this disease leads to debilitating symptoms, including difficulties in communication, mobility and breathing. The potential for a treatment that addresses the underlying cause of disease and slows progression or potentially prevents the onset of disease with early intervention is truly remarkable. We're pleased to collaborate with Taysha Gene Therapies in an effort to bring a gene therapy treatment that could meaningfully change the lives of patients and their caregivers."

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 regulate cellular *MECP2* expression. TSHA-102 has received Orphan Drug and Rare Pediatric Disease designations from the United States (U.S.) Food and Drug Administration (FDA) and has been granted Orphan Drug designation from the European Commission. We are advancing TSHA-102 in the REVEAL Phase 1/2 clinical trial under a CTA approved by Health Canada. A CTA submission to United Kingdom (UK) MHRA in pediatric patients with Rett syndrome is expected in mid-2023, and an Investigational New Drug (IND) application to the FDA is anticipated in the second half of 2023.

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.

About the CHU Sainte-Justine

The Centre hospitalier universitaire Sainte-Justine is the largest mother-child hospital in Canada. A member of the Université de Montréal extended network of excellence in health (RUIS), CHU Sainte-Justine has 6759 employees, including 1770 nurses and nursing assistants; 1131 other healthcare professionals; 531 physicians, dentists and pharmacists; 931 residents and over 280 researchers; 170 volunteers; and 3 406 interns and students in a wide range of disciplines. CHU Sainte-Justine has 484 beds, including 67 at the Centre de réadaptation Marie Enfant (CRME), the only exclusively pediatric rehabilitation centre in Québec. The World Health Organization has recognized CHU Sainte-Justine as a "health-promoting hospital." chusj.org

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 our product candidates, including TSHA-102, 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, and whether, if approved, these product candidates will be successfully distributed and marketed and the potential market opportunity for these 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 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, which is 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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