Taysha Gene Therapies Provides Clinical Updates for Investigational Programs TSHA-120 in Giant Axonal Neuropathy (GAN) and TSHA-102 in Rett Syndrome at R&D Day

Company views that results of comprehensive data analysis of TSHA-120 and development of disease progression model (DPM) address U.S. Food and Drug Administration (FDA) feedback regarding the effort-dependent nature of MFM32 as primary endpoint in an unblinded study and heterogeneity of GAN; Taysha plans to review potential regulatory pathway for TSHA-120 at a formal meeting with the FDA expected in Q3 2023

New GAN analysis identified multiple functional, electrophysiological and biological measurements that demonstrate a clinically meaningful and objective measurement of TSHA-120 treatment effect on disease progression

Encouraging initial clinical observations seen in the first adult patient with Rett syndrome recently dosed with TSHA-102 in REVEAL Phase 1/2 trial; safety and efficacy update and Independent Data Monitoring Committee (IDMC) approval to dose second patient expected in early Q3 2023

Detailed updates will be presented at virtual R&D Day today at 10:00 AM ET

DALLAS, June 28, 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), announced new data analyses for TSHA-120 in GAN and initial clinical observations for TSHA-102 in Rett syndrome. Taysha will host a virtual R&D Day today at 10:00 AM ET to discuss these updates. The webcast link can be accessed on the Events and Presentations section of Taysha's website.

"Late last year, the company submitted and discussed with the FDA a subset of available evidence supporting the potential therapeutic benefit and safety profile for TSHA-120 in patients with GAN, an ultra-rare disease with currently no approved treatments. FDA feedback included the need to address the heterogeneity of disease progression in GAN and the effort-dependent nature of MFM32 as a primary endpoint, considering the unblinded study design," said Sean P. Nolan, Chairman and Chief Executive Officer of Taysha. "Given the FDA also indicated it is open to regulatory flexibility in a controlled trial setting and willing to consider alternative study designs, we undertook an extensive analysis of the totality of data available to determine a feasible regulatory path forward for TSHA-120."

Mr. Nolan continued, "We believe the new analyses may help support an approval pathway for TSHA-120 for the treatment of GAN. Our newly developed disease progression model demonstrates predictable and homogenous disease progression in classic GAN, which in our view supports the use of natural history data as an external control. Additionally, we identified objective functional, electrophysiological and biological measurements that demonstrated a clinically meaningful treatment effect, which is also accompanied by over seven years of clinical data supporting the safety profile. We've requested a formal FDA meeting to discuss these new developments to support a potential regulatory path forward for TSHA-120. We expect the meeting to take place in the third quarter of this year."

"For our TSHA-102 program in Rett syndrome, we are encouraged by the initial clinical observations of the first adult patient recently dosed in the REVEAL Phase 1/2 trial," said Sukumar Nagendran, M.D., President, and Head of R&D. "We look forward to providing further clinical updates on the safety and efficacy observations for the first patient early in the third quarter of this year, following the required IDMC adjudication of the initial clinical data. Subsequent REVEAL trial updates will be provided quarterly, thereafter. We remain on track to submit a CTA to the UK MHRA in pediatric patients in mid-2023 and to submit an IND application to the FDA in the second half of 2023."

Key R&D Day Highlights

TSHA-120: a self-complimentary intrathecally delivered AAV9 gene therapy being evaluated in an open-label, dose-escalation, non-randomized Phase 1/2 trial for GAN, an ultra-rare inherited genetic neurodegenerative disorder with no approved treatments.

- New comprehensive data analysis enabled the development of a DPM using all available data from the largest existing GAN natural history database; DPM demonstrates a predictable and homogenous disease progression in classic GAN, which supports the potential for natural history data to serve as a suitable external control
- Given patient age and the extensive and wide-spread damage to the central nervous system as well as a length-dependent progression in the peripheral nervous system, a more positive treatment impact is expected in outcomes related to the arms compared to the legs; the longer the disease progresses, the greater the degeneration with decreasing likelihood of impacting the disease
- Relatively stable to improved sensory response amplitudes observed on nerve conduction studies, in conjunction with increased regenerative clusters on nerve biopsy, suggest sensory nerve or neuron regeneration in a progressive neurodegenerative disease
- Using natural history data as an external control, Bayesian analysis demonstrated a clinically meaningful treatment effect of TSHA-120 as measured through the slowing of disease progression observed across multiple

functional, electrophysiological and biological measures:

- **Functional endpoints:**
  - Modified Friedreich's Ataxia Rating Scale (mFARS) demonstrated a 99% probability of positive treatment effect on slowing disease progression, with an estimated average treatment effect of 31%
  - Motor Function Measure 32 (MFM32) Domain 3 (distal motor function – hands) demonstrated a 99% probability of positive treatment effect on slowing disease progression, with an estimated treatment effect of 28%
  - Visual Acuity, as measured by Logarithm of the Minimum Angle of Resolution (LogMAR), demonstrated 100% probability of positive treatment effect on slowing disease progression, with an estimated treatment effect of 70% in the right eye and 51% in the left eye
- **Electrophysiological endpoints:**
  - Analysis demonstrated a 100% probability of positive treatment effect on slowing disease progression, with an estimated treatment effect of 189% and 152% for Ulnar Sensory Nerve Action Potential (SNAP) and median SNAP amplitude, respectively, indicating disease improvement
  - Compound Muscle Action Potential (CMAP) demonstrated a 94% probability of positive treatment effect on slowing disease progression, with an estimated 29% treatment effect
- **Biological Endpoints:**
  - 4 out of the 5 patients that had stabilization or improvements in SNAPs had increased regenerative clusters on nerve biopsy
  - Skin biopsy-nerve fiber density: 5 patients saw stabilization or increases in nerve fiber density of the skin in at least one location of the proximal or distal leg at month 12, including 3/3 in the high-dose and one in the medium-high dose

- Over seven years of long-term clinical data support the safety and tolerability profile of TSHA-120
- New data analysis will help inform discussion with the FDA regarding a regulatory path forward for TSHA-120; formal meeting with FDA expected in the third quarter of 2023

TSHA-102: a self-complementary intrathecally delivered AAV9 gene transfer therapy being evaluated in the first-in-human, open labeled, randomized dose escalation and expansion REVEAL Phase 1/2 trial for Rett syndrome, a rare genetic neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene. TSHA-102 utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) platform designed to regulate cellular *MECP2* expression.

- First patient has been dosed in the REVEAL Phase 1/2 trial in adult patients with Rett syndrome being conducted at CHU Sainte-Justine, the Université de Montréal mother and child university hospital centre in Montreal, Canada
  - The patient was discharged from the hospital and has completed multiple follow-up visits, per the study protocol. Additional safety and efficacy updates on the first patient are expected in the early third quarter of 2023, following initial review of available safety data by the IDMC
  - Second potential patient has been identified and will undergo screening if all protocol defined criteria are met; dosing expected to proceed pending IDMC review of available clinical data from the first patient
- CTA submission to UK MHRA in pediatric patients anticipated in mid-2023
- IND application submission to U.S. FDA expected in the second half of 2023

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 timing, progress and results of our preclinical studies and clinical trials of our product candidates, including TSHA-102 and TSHA-120, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work and the period during which the results of the trials will become available, the potential of our product candidates, including TSHA-120 and 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.

Company Contact:
Hayleigh Collins
Director, Head of Corporate Communications
Taysha Gene Therapies, Inc.
hcollins@tayshagtx.com

Media Contact:
Carolyn Hawley
Canale Communications
carolyn.hawley@canalecomm.com

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