Taysha Gene Therapies Announces Publication of Natural History Data for TSHA-120 in Giant Axonal Neuropathy in the Journal, Brain

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Largest cohort of genetically confirmed patients with GAN, including patients with the classic (early-onset) and milder (late-onset) forms of GAN

Largest cross-sectional analysis highlighted clinical differences in patients with early-onset GAN versus late-onset GAN based on MFM32 performance as well as other functional motor scales and disease markers

Robust assessment across clinical outcomes for GAN, including motor, sensory, respiratory, neurophysiologic, MRI and biopsy data

First clinical study to evaluate a cohort of individuals with GAN for autonomic impairment

On track to report clinical data for TSHA-120 from the $3.5x10^{14}$ total vg dose cohort in the second half of 2021

Planning to engage with major regulatory agencies to discuss the approval pathway and expect to provide a regulatory update by year-end 2021

DALLAS--(BUSINESS WIRE)--Jun. 21, 2021-- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a patient-centric, pivotal-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) in both rare and large patient populations, today announced the publication of new analyses of natural history data for TSHA-120 in giant axonal neuropathy, or GAN. The data were published online and will be included in the June edition of *Brain*, a highly esteemed neurological science peer-reviewed journal.

GAN is a progressive neurodegenerative disease that affects both the central and peripheral nervous systems. The disease is caused by loss-of-function mutations in the gene coding for gigaxonin, which results in dysregulation of intermediate filament turnover, an important structural component of the cell. Although no symptoms are present in the first few months of life, many children with GAN do show early symptoms and features before the age of five, including unsteady gait, frequent falls, and motor weakness. Symptoms worsen over time and children develop scoliosis, contractures, atrophy of the spinal cord and abnormalities of the white matter in the brain. Currently, there are no approved treatments for GAN, which results in death for patients in their late teens or early twenties.

In this natural history study, 45 patients, age 3 years to 21 years old, with genetically confirmed GAN were enrolled at NIH and evaluated at their first enrollment visit. The objective of the cross-sectional analysis was to identify genetic variants, explore correlations between genotype and phenotype, identify reliable markers of disease severity and assess how these markers correlate with ambulatory function and the impact of the early- and late-onset phenotypes on these markers.

The two sub cohorts of GAN patients in the study included thirty-five patients with early-onset GAN and 10 patients with late-onset GAN. In the early-onset cohort, the mean age of onset of gait or motor impairment was 2.3 years old whereas the mean age of onset of symptoms in the late-onset cohort was 5.4 years old. Motor Function Measure 32 (MFM32), a validated and well-known scale to measure strength and motor function had the strongest correlation across outcome measures and age in patients with GAN. Patients with late-onset GAN had better functional performance compared to similarly aged patients with early-onset GAN. Ambulatory ability between the two phenotypes also differed. Disease progression in early-onset GAN patients occurred in a uniform and homogenous manner. Autonomic manifestations of the disease did not correlate with age or motor function.

“The recent publication in *Brain* serves as the baseline data for a longitudinal natural history assessment and adds important context to results from three dose cohorts in the ongoing clinical GAN trial,” said Suyash Prasad, MBBS, M.Sc., MRCP, MRCPCH, FFPM, Chief Medical Officer and Head of Research and Development of Taysha. “These results also confirm our findings that there is a clinical difference between early-onset GAN, a relentlessly progressive and fatal neuropathy, and late-onset GAN, which has significant disease morbidity, and underscores the importance for GAN to be included in genetic screens for hereditary neuropathies. The estimated prevalence for GAN is 2,400 patients but the GAN population may be larger than previously appreciated. We view genetic testing as an important aspect of patient identification and look forward to leveraging our key collaborations with companies to increase patient diagnostic efforts and allow for earlier intervention. Of note, data from today’s publication provide further support and confidence in the overall clinical program design for TSHA-120 which include this ongoing, prospective, natural history and outcomes assessment study, and an interventional dose selection safety and efficacy study. Building on the previously presented and favorable interventional study data, we remain on track to report clinical data from the highest dose cohort in the interventional clinical trial for TSHA-120 in the second half of this year. We look forward to engaging with major regulatory agencies to discuss the approval pathway for TSHA-120 and to provide a regulatory update by year-end.”

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 to build an extensive, AAV gene therapy pipeline

focused on both rare and large-market indications. Together, we leverage our fully integrated platform—an engine for potential new cures—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," 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-120, 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, TSHA-120's eligibility for accelerated approval in the United States and Europe, 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, 2020, 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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