Taysha Gene Therapies Reports Positive Clinical Efficacy and Safety Data for High Dose Cohort and Long-term Durability Data for TSHA-120 in Giant Axonal Neuropathy

January 31, 2022

Efficacy data for high dose cohort demonstrated clinically meaningful and statistically significant improvement in MFM32 by Year 1 compared to natural history (n=3)

Long-term durability data across all therapeutic dose cohorts demonstrated a 10-point improvement in mean change in MFM32 by Year 3 compared to estimated natural history decline of 24 points (n=5)

Biopsy data in five of six patient samples analyzed to date confirmed active regeneration of nerve fibers following treatment with TSHA-120 (n=6)

TSHA-120 was safe and well-tolerated supported by 53 patient-years of clinical data

Conference call and live webcast today at 8:00 AM Eastern Time

DALLAS--(BUSINESS WIRE)--Jan. 31, 2022-- 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 reported positive clinical efficacy and safety data for the high dose cohort of $3.5x10^{14}$ total vg, as well as long-term durability data across all therapeutic doses of TSHA-120 in giant axonal neuropathy (GAN).

“The totality of data generated by TSHA-120 to date support our plans to engage with major regulatory agencies in order to discuss pathways for registration and we look forward to providing a regulatory update later this year,” noted RA Session II, President, Founder and CEO of Taysha. “In the interim, we are finalizing our commercial strategy with a focus on patient identification, disease awareness and payor engagement for the estimated 5,000 affected patients in addressable markets.”

Key Clinical Data Support Durable, Clinically Meaningful and Statistically Significant Slowing of Disease Progression Across All Therapeutic Cohorts ($1.2x10^{14}$ total vg, $1.8x10^{14}$ total vg and $3.5x10^{14}$ total vg)

- **High Dose Cohort Data ($3.5x10^{14}$ total vg) by Year 1:** 5-point improvement in the change in rate of decline in MFM32 score for the high dose cohort compared to natural history decline of 8 points by Year 1 (n=3, p = 0.04)
- **Analysis of All Therapeutic Dose Cohorts by Year 1:** 7-point improvement in the change in rate of decline in MFM32 score across all therapeutic dose cohorts compared to natural history decline of 8 points by Year 1 (n=12, p<0.001)
- **Analysis of All Therapeutic Dose Cohorts over 3 Years:** 10-point improvement in the mean change from baseline in MFM32 score across all therapeutic dose cohorts compared to estimated natural history decline of 24 points by Year 3 (n=5, statistical analysis not performed)
- **Disease Stabilization Demonstrated in the Single Patient to Reach Year 5 Visit:** 26-point improvement in the change from baseline in MFM32 score for the single patient treated with TSHA-120 compared to estimated natural history by Year 5 (n=1, statistical analysis not performed)
- **Bayesian Analysis:** Confirmed 97% probability of clinically meaningful slowing of 50% or more in disease progression across all therapeutic dose cohorts

Secondary Endpoints for Pathologic, Physiologic and Clinical Markers Demonstrate Preservation of Visual Acuity, Stabilization of Retinal Nerve Fiber Layer Thickness and Regeneration of Nerve Fibers

- Biopsies obtained pre- and post-gene transfer in five of six patient samples analyzed confirmed active regeneration of axons with increased number of regenerative nerve clusters (n=6; remaining samples being analyzed)
- Preservation of visual acuity across all therapeutic doses compared to progressive loss of visual acuity observed in natural history (n=12)
- Stabilization of retinal nerve fiber layer (RNFL) thickness and prevention of axonal nerve degeneration compared to diffuse thinning of RNFL observed in natural history (n=12)

Key Long-Term Safety and Tolerability Findings

- 53 patient-years of clinical data support favorable safety and tolerability profile

Suyash Prasad, MBBS, M.Sc., MRCP, MRCPCH, FFPM, Chief Medical Officer and Head of Research and Development at Taysha added, “These results are consistent, clinically meaningful and statistically significant. Notably, analysis across all therapeutic dose cohorts confirms the sustained long-term durability of effect for TSHA-120-treated patients. These data also provide new evidence of TSHA-120’s ability to regenerate nerve fibers, demonstrating an improvement in disease pathology, and to preserve visual acuity, which should significantly benefit patients’ and families’ quality-of-life.”

TSHA-120 is an intrathecally dosed AAV9 gene replacement therapy delivering the gene *gigaxonin* for the treatment of GAN. TSHA-120 is currently being evaluated in an ongoing clinical trial conducted by the National Institute of Neurological Disorders and Stroke (NINDS) division of the National Institutes of Health (NIH) under the leadership of principal investigator, Carsten Bönneman, M.D. Taysha has partnered with GeneDx to support inclusion of the genetic marker for GAN in the GeneDx hereditary neuropathy panel at no cost to individuals at risk for or suspected of having GAN, and with the Hereditary Neuropathy Foundation and Charcot-Marie-Tooth Association Centers of Excellence to increase GAN disease awareness and access to testing.

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. Children with GAN present before the age of five with symptoms including unsteady gait, frequent falls, motor weakness. Currently, there are no approved treatments for GAN, which results in death for patients in their late teens or early twenties.

Conference Call and Webcast Information

Taysha management will hold a conference call and webcast today at 8:00 am ET / 7:00 am CT to provide an update on the GAN program. The dial-in number for the conference call is 877-407-0792 (U.S./Canada) or 201-689-8263 (international). The conference ID for all callers is 13726815. The live webcast and replay may be accessed by visiting Taysha’s website at https://ir.tayshagtx.com/news-events/events-presentations. An archived version of the webcast will be available on the website for 30 days.

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,” “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, such as TSHA-120 and 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, and whether, if approved, these product candidates will be successfully distributed and marketed, the potential market opportunity for these product candidates, and our corporate growth plans. 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 and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, 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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