Taysha Gene Therapies Acquires Exclusive Worldwide Rights to Clinical-Stage AAV9 Gene Therapy Program, Now Known as TSHA-120, for the Treatment of Giant Axonal Neuropathy, a Rare and Severe Neurodegenerative Disease

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Program invented in the lab of Dr. Steven Gray, Taysha's Chief Scientific Advisor, immediately transforms Taysha into a sustainable pivotal-stage gene therapy company

Clinical and preclinical data package validates the scientific approach of Dr. Steven Gray, UT Southwestern, and Taysha, with readthrough to existing portfolio

Groundbreaking clinical trial run by the NIH is the first intrathecally dosed gene therapy program in history

Human proof-of-concept data for TSHA-120 demonstrated clear arrest of disease progression and long-term durability at therapeutic dose levels in patients with giant axonal neuropathy

Plans to engage with regulatory agencies in the United States, Europe and Japan as soon as possible

Estimated 2,400 patients in U.S. and Europe represent potentially greater than $2 billion near-term commercial opportunity

Program provides basis for accelerating build-out of commercial infrastructure to support patient identification, payor engagement and product distribution

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

DALLAS--(BUSINESS WIRE)--Apr. 12, 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 acquisition of exclusive worldwide rights to a clinical-stage AAV9 gene therapy program, now known as TSHA-120, for the treatment of giant axonal neuropathy (GAN). TSHA-120 is an intrathecally dosed AAV9 gene therapy currently being evaluated in a clinical trial for the treatment of GAN. The trial is being conducted by the National Institutes of Health (NIH) in close collaboration with a leading patient advocacy group focused on finding treatments and cures for GAN. TSHA-120 has received rare pediatric disease and orphan drug designations from the U.S. Food and Drug Administration (FDA) for the treatment of GAN.

GAN is a rare inherited genetic disorder that affects both the central and peripheral nervous systems and is caused by loss-of-function mutations in the gene coding for *gigaxonin*. Many children with GAN show symptoms and features before the age of five, including progressive scoliosis, contractures, atrophy of the spinal cord, giant axons – also known as nerve fibers – and abnormalities of the white matter in the brain. Currently, there are no approved treatments for GAN, which often results in death for patients in their late teens or early twenties. TSHA-120 was originally developed in the laboratory of Taysha's Chief Scientific Advisor, Dr. Steven Gray, and advanced in a historic ongoing clinical trial by the NIH as the first intrathecally dosed gene therapy study.

"Dr. Steven Gray's work on the GAN program was the catalyst for all the other translational research initiatives in his lab and we are very pleased to continue this important and meaningful work that has had a significant impact across the entire gene therapy landscape. As the program that laid the foundation for our robust pipeline, we believe that TSHA-120 is a seamless strategic fit and will be immediately value-accretive for Taysha. TSHA-120 clinical data generated to date is a clear validation of our scientific approach with read-through to our existing product development pipeline. Consistent with all of our gene therapy candidates, TSHA-120 targets a monogenic CNS disease, is delivered intrathecally using a proven AAV9 vector, and utilizes a highly scalable HEK293 suspension manufacturing process. Collectively, these key parallels enable Taysha to leverage synergies across its core competencies to efficiently develop and commercialize TSHA-120," said RA Session II, President, Founder and Chief Executive Officer of Taysha. "The efficacy data in preclinical studies with the GAN knockout rodent model were extremely compelling, and TSHA-120 demonstrated significant improvement in pathology across a range of tissues, and notably improved the pathological appearance of the dorsal root ganglia, which is a key component of disease progression. We look forward to quickly working with the regulatory agencies on a path forward to approval of TSHA-120, and in parallel, accelerating the build-out of our commercial infrastructure to support patient identification, payor engagement and product distribution. TSHA-120 has the potential to address a significant unmet need for an estimated 2,400 patients with GAN across the United States and in Europe, potentially representing a near-term commercial opportunity of greater than $2 billion."

The National Institute of Neurological Disorders and Stroke (NINDS) division of the NIH is conducting the ongoing open-label, non-randomized, dose-escalation clinical trial of TSHA-120 for the treatment of GAN. The primary endpoint is safety, with secondary endpoints measuring efficacy using pathologic, physiologic, functional, and clinical markers. A primary measure of clinical efficacy is the Motor Function Measure 32 (MFM32) score, a quantitative scale designed to assess the severity and progression of motor function abilities. There is precedent for its use in multiple clinical studies for neuromuscular diseases, including spinal muscular atrophy amongst others. To date, 14 patients have been dosed with one of four dose levels of TSHA-120. TSHA-120 has demonstrated a dose-response relationship with arrest of disease progression at the second-highest dose level ($1.8x10^{14}$

total vector genomes [vg]) at one-year post-treatment, affecting a statistically significant 8-point improvement on the MFM32 score. A 4-point change on the MFM32 score is considered clinically meaningful. Six of these patients treated at therapeutic dose levels have shown sustained dose-dependent improvements in MFM32 scores for more than three years. Long-term results demonstrated that treatment with TSHA-120 at multiple dose levels was well-tolerated with no severe drug-related adverse events. Additional data are expected later this year, including results from the highest dose cohort ($3.5x10^{14}$ total vg).

“TSHA-120 is the first successful in-human intrathecal gene transfer in the history of gene therapy and, as such, has had a significant impact across the field. This program further supports our approach to treating monogenic diseases of the CNS and may enable us to pursue proof-of-concept for our redosing platform,” said Suyash Prasad, MBBS, M.SC., MRCP, MRCPCH, FFPM, Chief Medical Officer and Head of Research and Development of Taysha. “We are very encouraged by TSHA-120’s halting effect on disease progression at therapeutic dose levels and long-term durability of effect in patients living with GAN, and we look forward to highlighting the initial clinical data in an R&D Day in June 2021. In the meantime, we plan to engage regulatory agencies in the United States, Europe and Japan as soon as possible.”

Before the end of the year, Taysha intends to request an End-of-Phase meeting with the FDA and engage with the European Medicines Agency (EMA) and the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan to discuss the regulatory pathway for TSHA-120. Taysha expects to provide a regulatory and clinical update on TSHA-120, including data from the $3.5x10^{14}$ total vg cohort by year-end.

Under the terms of the agreement, in exchange for granting Taysha the exclusive worldwide rights to TSHA-120, the leading GAN patient advocacy group will receive an upfront payment of $5.5 million and will be eligible to receive clinical, regulatory and commercial milestones totaling up to $19.3 million, as well as a low, single-digit royalty on net sales upon commercialization of the product.

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 review its acquisition of 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 13718632. 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 60 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,” 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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