Taysha Gene Therapies Announces Initiation of Clinical Development of TSHA-118 for the Treatment of CLN1 Disease

CTA approved by Health Canada in November 2021; IND approved and open in 2019

Queen's University selected as initial clinical site under the direction of Dr. Jagdeep Walia, principal investigator

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Preliminary clinical safety and PPT1 enzyme activity data expected in the first half of 2022

Dallas – December 16, 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 initiation of clinical development of TSHA-118 for the treatment of CLN1 disease under a recently approved Clinical Trial Application (CTA). Queen's University in Ontario, Canada has been selected as the initial clinical site under the direction of Dr. Jagdeep Walia. There is also an open investigational new drug application (IND) in the United States for TSHA-118 in CLN1 disease.

"CLN1 disease is caused by mutations in the *CLN1* gene, which encodes the soluble lysosomal enzyme palmitoyl-protein thioesterase-1, or PPT1," said Suyash Prasad, MBBS, M.SC., MRCP, MRCPCH, FFPM, Chief Medical Officer and Head of Research and Development of Taysha. "Introduction of a functional *CLN1* gene with TSHA-118 treatment offers a potentially effective therapeutic approach that addresses the root cause of the disease. In preclinical models of CLN1, TSHA-118 significantly extended survival and improved behavior. We are highly encouraged by the therapeutic potential of TSHA-118 and expect PPT1 activity of 5% or greater to normalize survival and significantly improve clinical phenotype based on natural history data."

TSHA-118 is a self-complementary AAV9 gene replacement therapy designed to express a human codon-optimized CLN1 transgene for the treatment of CLN1 disease. The global trial is a single arm, open-label Phase 1/2 trial evaluating TSHA-118 for the treatment of CLN1 disease utilizing commercial grade material. The initial clinical site is Queen's University under the direction of principal investigator, Jagdeep S. Walia, MBBS, FRCPC, FCCMG, Clinical Geneticist and Associate Professor Head, Division of Medical Genetics (Department of Pediatrics) at Queen's, and Director of Research (Department of Pediatrics) at the Kingston Health Sciences Centre. Preliminary clinical safety and PPT1 enzyme activity data in the serum and CSF are expected in the first half of 2022. TSHA-118 has been granted orphan drug designation, rare pediatric disease designation and fast track designation from the U.S. Food and Drug Administration and orphan drug designation from the European Commission for the treatment of CLN1 disease.

"Currently, there are no approved treatments for this severe and rapidly progressive neurodegenerative lysosomal storage disease," said RA Session II, President, Founder and CEO of Taysha. "Initiation of clinical development is a formative moment and, based on its compelling profile and the promising preclinical data generated to date, we believe TSHA-118 offers the potential for a disease-modifying therapeutic approach for patients affected by this disease. We look forward to working in collaboration with Queen's University and expect the availability of preliminary clinical safety and PPT1 enzyme activity data in the first half of 2022."

Encouraging preclinical data have demonstrated that intrathecal treatment with TSHA-118 significantly extended survival of CLN1 knockout mice and improved behavior. TSHA-118-treated mice showed persistent supraphysiological levels of active PPT1 and sustained preservation of motor function. In CLN1 knockout mice, TSHA-118 was safe and well-tolerated with no associated adverse events, suggesting a wide therapeutic window for clinical dosing.

Two ongoing natural history studies include an observational study in Hamburg to assess the natural history of CLN1 and other CLN diseases as part of the international DEM-CHILD database, as well as a combined retrospective and prospective study at the University of Rochester to characterize the age-at-onset of major symptoms and the relationship between age and severity. Disease severity and different forms of CLN1 disease have been shown to correlate with PPT1 enzyme activity. Adult-onset patients have 5% to 8% PPT1 enzyme activity and delayed symptom onset, indicating that an increase in PPT1 activity from 0.1% to 5% with therapeutic approaches has the potential to be disease modifying.

About CLN1 Disease

CLN1 disease, also known as Infantile Neuronal Ceroid Lipofuscinosis or infantile Batten disease, is a lysosomal storage disorder that is a progressive, fatal neurodegenerative disease with early childhood onset impacting approximately 1 in 138,000 live births worldwide. The estimated prevalence of CLN1 disease is 1,000 patients in the United States and European Union. CLN1 disease is caused by loss-of-function mutations in the CLN1 gene that encodes the enzyme palmitoyl-protein thioesterase-1, or PPT1 involved in the degradation of lipid-modified proteins. Loss of function mutations in the CLN1 gene causes accumulation of lipid-modified proteins that eventually leads to neuronal cell dysfunction and death. CLN1 typically manifests during the first year of life with progressive vision impairment, motor and cognitive decline, seizures and ultimately early death. Some patients have late-infantile, juvenile, or adult-onset CLN1 disease and develop symptoms later in childhood or in adulthood. There are no approved disease-modifying therapies for the treatment of CLN1 disease.

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 goa 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, 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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