Taysha Gene Therapies Receives Orphan Drug Designation from the European Commission for TSHA-101 for the Treatment of Infantile GM2 Gangliosidosis

TSHA-101 is the first and only bicistronic vector being developed in a Phase 1/2 clinical study to date

Preliminary clinical safety and biomarker data from the Queen's University study expected by year-end

No approved treatments for the disease

DALLAS--(BUSINESS WIRE)--Sep. 29, 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 that it has been granted orphan drug designation from the European Commission for TSHA-101, an AAV9-based bicistronic gene replacement therapy in development for GM2 gangliosidosis, also called Tay-Sachs or Sandhoff disease.

"GM2 gangliosidosis is a fatal neurodegenerative disease caused by deficiency in the lysosomal enzyme β-hexosaminidase A, also known as Hex A. The prognosis is devastating, with infantile forms often leading to death within the first four years of life and juvenile onset patients rarely surviving beyond mid-teens," said Suyash Prasad, MBBS, M.Sc., MRCP, MRCPCH, FFPM, Chief Medical Officer and Head of Research and Development of Taysha. "Residual Hex A activity correlates with the severity of GM2, and based on our understanding of this correlation, small increases in Hex A activity are likely to lead to significant improvements in clinical outcomes and quality of life. Based on dose-dependent improvements in survival in preclinical models, we are highly encouraged that our novel bicistronic gene therapy approach with TSHA-101 has the potential to be a life changing therapy for patients suffering from this rapidly progressive disorder with no current treatment options."

GM2 gangliosidosis is a rare and fatal monogenic lysosomal storage disorder that is part of a family of neurodegenerative genetic diseases that includes Tay-Sachs and Sandhoff diseases. The disease is caused by defects in the *HEXA* or *HEXB* genes that encode the two subunits of the β-hexosaminidase A (Hex A) enzyme. These genetic defects result in progressive dysfunction of the central nervous system. Residual Hex A enzyme activity determines the severity of the disease. The infantile form of the disease has an onset of symptoms usually before six months of age with residual Hex A enzyme activity of less than 0.1%. Juvenile onset occurs between 1.5 and five years of age with residual Hex A enzyme activity of approximately 0.5%. Early adult onset of the disease has residual Hex A enzyme activity of between 2% to 4%. There are no approved therapies for the treatment of the disease, and current treatment is limited to supportive care.

TSHA-101 is an investigational gene therapy that delivers the *HEXA* and *HEXB* genes that make up the β-hexosaminidase A enzyme. The two genes are driven by a single promoter within the AAV9 bicistronic vector ensuring that the 2 sub-units of Hex A are produced in a one-to-one ratio within each cell, which is important to ensure efficient production of the transgene. TSHA-101 is the first and only bicistronic vector currently in clinical development and has been granted Orphan Drug and Rare Pediatric Disease designations by the U.S. Food and Drug Administration (FDA). TSHA-101 is administered intrathecally and is currently being evaluated in a single arm, open-label Phase 1/2 clinical trial for the treatment of infants with GM2 gangliosidosis sponsored by Queen's University. Preliminary clinical safety and biomarker data are expected by year-end 2021.

The European Commission grants orphan drug designation for medicines being developed for the diagnosis, prevention or treatment of treat life-threatening or chronically debilitating conditions that affect fewer than five in 10,000 people in the European Union. Orphan designation in the European Union includes benefits such as protocol assistance, reduced regulatory fees and market exclusivity.

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," 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-101, 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-101'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, and our Quarterly Report on Form 10-Q for the quarter ended June 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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