Taysha Receives Orphan Drug Designation from the European Commission for TSHA-102 for the Treatment of Rett Syndrome

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Preclinical data provide quantitative evidence of TSHA-102's ability to exhibit genotype-dependent regulation of MECP2 gene expression across different brain regions on a cell-by-cell basis

Significant survival benefit demonstrated in 4-5 week-old myc-tagged TSHA-102-treated knockout Rett mice with meaningful accumulated disease, a more translatable model of the disorder in humans

IND/CTA filing expected in second half of 2021, with Phase 1/2 trial initiation anticipated by year-end

Estimated 25,000 patients in U.S. and Europe represent multi-billion-dollar commercial opportunity

DALLAS--(BUSINESS WIRE)--Sept. 22, 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-102, an AAV9-based gene replacement therapy in development for Rett syndrome.

"The receipt of orphan drug designation from the European Commission represents an important regulatory milestone that has the potential to expedite the global clinical development of TSHA-102, a one-time gene therapy with disease modifying potential," said RA Session II, President, Founder and Chief Executive Officer of Taysha. "Promising preclinical data demonstrate that TSHA-102's novel self-regulatory feedback mechanism, miRARE, has the ability to regulate *MECP2* expression in a genotype-dependent manner on a cell-by-cell basis. We are highly encouraged that this novel treatment approach can help effectively address a disease that has historically been difficult to treat, and we look forward to submitting an IND/CTA in the second half of this year and initiating a Phase 1/2 clinical trial by year-end."

Rett syndrome is a severe genetic neurodevelopmental disorder caused by a mutation in the X-linked *MECP2* gene essential for neuronal and synaptic function in the brain. Primarily occurring in females, Rett syndrome is one of the most common genetic causes of severe intellectual disability worldwide, with a prevalence of over 25,000 in the United States and European Union. Patients have normal early development, with symptom onset typically beginning between six to 18 months of age. Rett syndrome is characterized by rapid developmental regression that leads to intellectual disabilities, loss of speech, loss of purposeful use of hands, loss of mobility, seizures, cardiac impairments and breathing issues. Currently, there are no approved therapies.

TSHA-102 is a self-complementary intrathecally delivered AAV9 gene replacement therapy under development for the treatment of Rett syndrome. TSHA-102 delivers the *MECP2* gene, which includes the novel miRNA-Responsive Auto-Regulatory Element (miRARE), to regulate MECP2 expression in a genotypic-dependent manner on a cell-by-cell basis. The miRARE technology is designed to prevent toxicity associated with overexpression of MECP2.

Positive preclinical data for myc-tagged TSHA-102 in Rett syndrome recently published in *Brain* provide quantitative evidence of miRARE's ability to exhibit genotype-dependent regulation of *MECP2* gene expression on a cell-by-cell basis across different regions of the brain in both wild type and knockout mouse models of Rett syndrome. TSHA-102 has previously received rare pediatric disease designation and orphan drug designation from the U.S. Food and Drug Administration (FDA). Submission of an IND/CTA filing for TSHA-102 is expected in the second half of 2021, with initiation of a Phase 1/2 clinical trial 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-102, 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-102'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.

Company Contact:
Kimberly Lee, D.O.
SVP, Corporate Communications and Investor Relations

Taysha Gene Therapies
klee@tayshagtx.com

Media Contact:
Carolyn Hawley

Canale Communications
carolyn.hawley@canalecomm.com