Taysha Gene Therapies Highlights Strategic Priorities and Provides 2021 Business Outlook

February 1, 2021

Expects Phase 1/2 biomarker and preliminary clinical data for TSHA-101 in GM2 gangliosidosis in second half of 2021 and by year-end 2021, respectively

Plans to initiate a U.S. Phase 1/2 trial for TSHA-101 in GM2 gangliosidosis in second half of 2021 as well as Phase 1/2 trials for TSHA-118 in CLN1, TSHA-102 in Rett syndrome and TSHA-104 in SURF1-associated Leigh syndrome by year-end 2021

Anticipates advancement of four programs into IND/CTA-enabling studies: SLC13A5 deficiency, Adult Polyglycosan Body Deficiency (APBD), Lafora disease and GM2 AB variant

Expects IND/CTA submission from one of the following programs: SLC13A5 deficiency, APBD, Lafora disease, GM2 AB variant and SLC6A1 haploinsufficiency

Anticipates advancement of four new undisclosed programs into preclinical development focused on neurodevelopmental disorders, genetic epilepsies and neurodegenerative diseases

Intends to advance the development of next-generation technologies including miRARE platform, redosing strategy, mini-gene payloads and novel capsids, to optimize key components of the company's AAV-based gene therapies

Continues to make progress on internal 187,000 square-foot, 2,000-liter capacity, multi-product cGMP facility located in Durham, NC

Dallas – February 1, 2021 – Taysha Gene Therapies, Inc. (Nasdaq: TSHA) ("Taysha"), a patient-centric, clinical-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 highlighted its strategic priorities and provided a business outlook for 2021.

"We enter 2021 having built a strong foundation on which to execute our corporate and pipeline objectives. Notably, we expanded our seasoned leadership team and esteemed board of directors steeped in gene therapy development and commercialization expertise, successfully raised funds in our initial public offering, transitioned from a preclinical- to a clinical-stage company, and achieved important progress on R&D initiatives and our three-pillar manufacturing strategy," said RA Session II, President, Founder and CEO of Taysha. "2021 will be a transformational year as we intend to rapidly advance multiple drug candidates to clinical proof-of-concept, further expand our platform-enabled pipeline and advance next-generation technologies. Specifically, we expect to report clinical data for our GM2 gangliosidosis program in the second half of this year and have multiple ongoing clinical studies by year end. We also anticipate several IND/CTA submissions across three CNS franchises and have multiple therapies in IND/CTA-enabling studies while advancing four new programs into preclinical development. In addition, we are excited to advance our next-generation platform technologies and further our efforts in redosing, transgene regulation and capsid development. We believe that our platform will drive future sustained innovation and value creation and look forward to highlighting the productivity of our platform in an R&D day later this year. Lastly, we continue to make progress on cGMP facility and process development capabilities with the completion of the design phase and initiation of procurement of long lead equipment."

Anticipated Milestones by Program

TSHA-101 for infantile GM2 gangliosidosis: the first bicistronic gene therapy in clinical development designed to deliver two genes – *HEXA* and *HEXB* – intrathecally for the treatment of infantile GM2 gangliosidosis, also called Tay-Sachs or Sandhoff disease

- Report Phase 1/2 safety and biomarker data (Queen's University trial) in the second half of 2021
- Submit an Investigational New Drug (IND) application in the U.S. in the second half of 2021
- Initiate Phase 1/2 clinical trial in the U.S. in the second half of 2021
- Report preliminary Phase 1/2 clinical data (Queen's University trial) by year-end 2021

TSHA-118 in CLN1: a self-complementary AAV9 viral vector designed to express a human codon-optimized CLN1 transgene to potentially treat CLN1, a rapidly progressing rare lysosomal storage disease with no approved treatments

- Maintain current open IND
- Initiate a Phase 1/2 clinical trial in the second half of 2021 with commercial-grade GMP material

TSHA-102 in Rett syndrome: a self-complementary AAV9 gene therapy in development for a severe neurodevelopmental disorder, designed to deliver MECP2 as well as a novel miRARE platform that regulates transgene expression on a cell-by-cell basis

- Submit IND/Clinical Trial Application (CTA) filing in the second half of 2021
- Initiate Phase 1/2 clinical trial by year-end 2021 with commercial-grade GMP material

TSHA-104 in SURF1-associated Leigh syndrome: a self-complementary AAV9 viral vector with a codon optimized transgene encoding the human SURF1 protein to potentially treat SURF1-associated Leigh syndrome, a monogenic mitochondrial disorder with no approved treatments

- Submit IND/CTA filing in the second half of 2021
- Initiate Phase 1/2 trial by year-end 2021 with commercial-grade GMP material

Pipeline programs advancing into IND/CTA-enabling studies

- Advance four programs into IND/CTA-enabling studies including TSHA-105 in SLC13A5 deficiency, TSHA-111 in Lafora, TSHA-112 in APBD and TSHA-119 in GM2 AB variant, and continue IND/CTA-enabling work on TSHA-103 in SLC6A1 haploinsufficiency in 2021
- Submit an IND/CTA filing for one of the five above-named programs in 2021

Discovery programs

- Advance four new undisclosed programs focused on neurodevelopmental disorders, genetic epilepsies and neurodegenerative diseases into preclinical development in 2021

Next-generation technology platform

- Continue development efforts on regulated transgene expression with expansion of miRARE platform into additional CNS diseases
- Explore vagus nerve redosing platform in large animal models
- Advance mini-gene discovery program in genetic forms of epilepsy and neurodevelopmental disorders
- Continue discovery and development efforts on next-generation capsids

Anticipated Corporate Milestones in 2021

- Complete technical development of, and initiate construction on, internal cGMP facility in 2021
- Complete buildout of Dallas headquarters by mid-year
- Expand employee base from nearly 40 to approximately 150 by year-end 2021

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 or implying the potential of our 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 and early-stage programs, 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, our corporate growth plans and our plans to establish a commercial-scale cGMP manufacturing facility to provide preclinical, clinical and commercial supply. 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 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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