Taysha Gene Therapies Reports Third Quarter 2021 Financial Results and Provides Corporate Update

Anticipate clinical safety and MFM32 functional data for TSHA-120 from the highest dose cohort of $3.5x10^{14}$ total vg in GAN in December 2021

Expect preliminary clinical safety data and Hex A enzyme activity in the plasma and cerebral spinal fluid for TSHA-101 in GM2 gangliosidosis in December 2021

Anticipate preliminary clinical data for the first-generation construct in CLN7 disease including safety data from first patient ever dosed intrathecally at $1.0x10^{15}$ total vg in December 2021

On track to initiate Phase 1/2 trials for TSHA-118 in CLN1 disease and TSHA-102 in Rett syndrome by year-end 2021

Completed five successful concurrent GMP campaigns for multiple programs to date, sufficient to support clinical-stage programs this year

Received Orphan Drug Designation from the European Commission for TSHA-101 for GM2 gangliosidosis, TSHA-102 for Rett syndrome and TSHA-105 for SLC13A5-related epilepsy

Successfully completed nine regulatory meetings with multiple agencies to support clinical trial initiations; submitted initial request for end-of-Phase meeting to align regulatory pathway for TSHA-120 in giant axonal neuropathy (GAN)

Recent publications of positive preclinical data from an AAV-mediated UBE3A gene replacement approach for Angelman syndrome and TSHA-104 for the treatment of SURF1-associated Leigh syndrome further support clinical development strategies

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

DALLAS--(BUSINESS WIRE)--Nov. 10, 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 reported financial results for the third quarter ended September 30, 2021 and provided a corporate update.

“We made significant advances in multiple aspects of our business, including nine productive regulatory meetings across several programs, a strategic addition of the clinical-stage CLN7 program and publication of positive preclinical data related to the Angelman syndrome and SURF1-associated Leigh syndrome programs,” noted RA Session II, President, Founder and CEO of Taysha. “In September, we submitted an end-of-Phase meeting request for TSHA-120 with a major ex-US regulatory agency and look forward to submitting additional requests to multiple regulatory agencies by the end of this year. In GAN, we have up to 6 years of longitudinal data in individual patients and collectively 55-patient years of clinical safety and efficacy data from our ongoing clinical study. We also have eight years of robust longitudinal data from a natural history study being conducted at the NIH by Dr. Carsten Bönnemann. There has been consistency in the strength of data across multiple functional and biomarker endpoints, including the MFM32 scale, ophthalmological assessments and nerve biopsies. We look forward to reporting clinical safety and functional MFM32 data for TSHA-120 from the high dose cohort of $3.5x10^{14}$ total vg in December, where we believe continued clinically meaningful slowing of disease progression similar to that achieved with the lower dose cohorts would be considered confirmation of disease modification. For TSHA-101 in GM2 gangliosidosis, we remain on track to report preliminary clinical safety data and Hex A enzyme activity in plasma and CSF in December. Based on natural history, 2% to 4% Hex A enzyme activity in plasma normalizes survival and significantly improves clinical phenotype of GM2 gangliosidosis. For the CLN7 program, we anticipate preliminary clinical data including safety data for the first patient in history to be dosed at $1.0x10^{15}$ total vg with the first-generation construct in December. In parallel, we expect to finalize the second-generation CLN7 construct by year-end and initiate a planned pivotal clinical trial in 2022 with reference to clinical data from the first-generation construct. For TSHA-102 in Rett syndrome, we intend to submit an IND/CTA filing in November followed by initiation of a clinical trial by the end of this year. We have recently obtained preclinical data showing improvement in survival, and respiratory and motor functions in relevant animal models. Notably, preliminary data from a GLP toxicology study in non-human primates demonstrated no adverse findings at the highest dose tested suggesting that the miRARE platform is successfully downregulating MECP2 expression to within normal physiological levels. On the manufacturing front, we have completed five concurrent GMP campaigns to support multiple clinical programs this year,” continued Mr. Session.

“We believe the combination of our experience in gene therapy drug development, clinical pipeline and a strong balance sheet provides us with the financial and operational flexibility to achieve numerous value-generating milestones across our programs, and importantly, a potential regulatory approval for TSHA-120 in GAN in the near term. We look forward to continued execution on our development and regulatory strategies, and will provide updates throughout the remainder of this year,” concluded Mr. Session.

Recent Corporate Highlights

- Publication of AAV-mediated *UBE3A* gene replacement approach for the treatment of Angelman syndrome in the *Journal of Clinical Investigation Insight* (*JCI Insight*)
- Sponsored genetic testing for giant axonal neuropathy (GAN) in partnership with GeneDx, Inc to support inclusion of the genetic marker for GAN in the GeneDx hereditary neuropathy panel at no cost to individuals at risk for or suspected of having GAN
- Announced collaboration with Hereditary Neuropathy Foundation and Charcot-Marie-Tooth Association Centers of Excellence to increase GAN disease awareness and access to testing

- Obtained an exclusive option from UT Southwestern (UTSW) to license worldwide rights to a clinical-stage AAV9 gene therapy replacement program for the treatment of CLN7 disease
- Entered into a research collaboration with UTSW to develop a next-generation construct for the treatment of CLN7 disease, which is expected to improve potency, safety profile, packaging efficiency and manufacturability over the first-generation construct
- Provided a grant to Batten Hope, the leading CLN7 patient advocacy group, to support patient education, disease awareness and newborn screening initiatives
- Announced publication of positive preclinical data for TSHA-104 demonstrating therapeutic potential in SURF-1-associated Leigh syndrome in *Molecular Therapy: Methods & Clinical Development*
- Completed five successful concurrent GMP campaigns for multiple programs to date, sufficient to support clinical-stage programs this year. 187,000 square foot internal manufacturing facility on track to be fully operational in 2023
- Received Orphan Drug Designation from the European Commission for TSHA-105 for SLC13A5-related epilepsy, TSHA-102 for Rett syndrome and TSHA-101 for GM2 gangliosidosis
- Hosted CLN1 Investor Day on August 30th highlighting the company's TSHA-118 program
    - TSHA-118-treated CLN1 knockout mice demonstrated persistent supraphysiological levels of active PPT1, improved survival rates and sustained preservation of motor function
    - Insights from Key Opinion Leaders on preclinical data, utility of natural history data and current clinical trial design
- Hosted Rett Syndrome Investor Day on September 22nd highlighting the company's TSHA-102 program
    - miRARE reduced overall expression of miniMeCP2 transgene expression and regulated genotype-dependent myc-tagged miniMECP2 expression across different brain regions on a cell-by-cell basis
    - Reviewed preclinical and natural history data that support an anticipated IND/CTA filing
- Hosted Angelman Syndrome Investor Day on October 26th highlighting the company's two-pronged approach to treating Angelman syndrome
    - Two therapeutic approaches target entire Angelman syndrome population using gene replacement strategy on *UBE3A* to mimic the maternal UBE3A allele expression and a vectorized knockdown of UBE3A-ATS to unsilence the paternal allele
    - AAV-mediated *UBE3A* gene replacement recapitulates endogenous isoform ratios by replacing both the short and long isoforms of UBE3A in key regions of the brain, leading to improvements in motor learning, behavior outcomes, and seizure phenotypes in Angelman mouse models

Anticipated Milestones by Program

TSHA-120 for GAN: an intrathecally dosed AAV9 gene therapy currently being evaluated in a clinical trial for the treatment of GAN, 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*

- Based on a longitudinal prospective natural history study conducted at the NIH by Dr. Carsten Bönnemann, there is a predictable decline in the MFM32 score of approximately 8-points per year across all patients regardless of age. A 4-point change in MFM32 is considered clinically meaningful. To date, we have up to eight years of robust data from this study.
- Currently in the GAN program, we have up to 6 years of longitudinal data in individual patients and collectively 55-patient years of clinical safety and efficacy data from our ongoing clinical study with no drug-related serious adverse events, no signs of acute or subacute inflammation, no sudden sensory changes and no drug-related or persistent elevation of transaminases
- In December, anticipate clinical safety and functional MFM32 data for TSHA-120 from the highest dose cohort of $3.5x10^{14}$ total vg in GAN, with continued clinically meaningful slowing of disease progression similar to that achieved with the lower dose cohorts would be considered confirmation of disease modification
- Request for end-of-Phase meeting with ex-US regulatory agency for TSHA-120 completed in September with a preliminary meeting date in January 2022. Additional submissions expected by the end of 2021
- Finalized plan for commercial grade material and initiated development of comparability protocol to support BLA/MAA filing

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

- Based on natural history data, 2% to 4% Hex A enzyme activity in plasma normalizes survival and significantly improves clinical phenotype of GM2 gangliosidosis
- Preclinical data demonstrated intrathecal delivery of TSHA-101 was safe and well-tolerated in GM2 knockout mice
- Expect preliminary clinical safety data and HEX A enzyme activity in plasma and CSF for TSHA-101 in GM2 gangliosidosis in December 2021 from ongoing Canadian study, where Hex A enzyme activity level of at least 5% in plasma would be considered disease modifying based on natural history data
- Due to severity of the disease and unmet medical need, currently assessing the need for US study to support regulatory filing

AAV9 Gene Replacement for CLN7 disease: an investigational AAV9 intrathecally dosed gene replacement therapy designed to deliver a full-length copy of the CLN7 gene to potentially treat CLN7 disease, a rapidly progressing rare lysosomal storage disease with no approved treatments. The first-generation construct is currently in clinical development with the next-generation construct anticipated to have improved potency, safety, packaging efficiency and manufacturability.

- Toxicology studies in wild type rodents demonstrated safety and tolerability of intrathecal administration of the first-generation construct across all dose levels and time points
- Preliminary clinical safety data for the first patient in history to be intrathecally dosed at $1.0x10^{15}$ total vg with the first-generation construct expected by December 2021
- Completion of next-generation construct by year-end 2021, with initiation of a planned pivotal trial in 2022 using next-generation construct with reference to human proof-of-concept clinical data generated from the first-generation construct
- Commercial-grade GMP material for next-generation construct expected in 2022

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

- Preclinical data demonstrated that TSHA-118 was safe and well tolerated following intrathecal administration in CLN1 knockout mice
- In preclinical models, TSHA-118-treated mice demonstrated supraphysiological levels of active PPT1 enzyme with no associated adverse effects, suggesting a wide therapeutic window for clinical dosing
- Currently open IND
- Additional CTA filing submitted
- Initiation of a Phase 1/2 clinical trial by year-end 2021
- Preliminary clinical safety and PPT1 enzyme activity data expected in first half of 2022

TSHA-102 in Rett syndrome: a self-complementary AAV9 gene therapy in development for a severe neurodevelopmental disorder, designed to deliver miniMECP2, as well as a novel miRARE platform that regulates transgene expression genotypically on a cell-by-cell basis

- In preclinical animal models, intrathecal myc-tagged TSHA-102 was not associated with early death and did not cause adverse behavioral side effects in wild type mice demonstrating appropriate downregulation of miniMECP2 protein expression as compared to unregulated MECP2 gene therapy constructs
- Preclinical data demonstrated that miRARE regulated transgene expression genotypically on a cell-by-cell basis and improved the safety of TSHA-102 without compromising efficacy in juvenile mice
- Recently obtained pharmacology data demonstrated improvement in survival, and respiratory and motor functions in disease relevant mouse models. Data to be shared at a later date
- Preliminary data from a GLP toxicology study in non-human primates demonstrated no adverse findings at the highest dose tested suggesting that the miRARE platform is successfully downregulating MECP2 expression to within normal physiological levels
- Submission of IND/CTA filing in November 2021
- Initiation of Phase 1/2 clinical trial by year-end 2021
- Preliminary clinical data expected by year-end 2022

Third Quarter 2021 Financial Highlights

Research and Development (R&D) Expenses: Research and development expenses were $39.5 million for the three months ended September 30, 2021, compared to $11.1 million for the three months ended September 30, 2020. The $28.4 million increase was primarily attributable to an increase of $14.5 million of expenses incurred in research and development manufacturing and other raw material purchases, which included cGMP batches produced by Catalent and UT Southwestern. There was an increase in employee compensation expenses of $10.7 million, which included $1.9 million of non-cash stock-based compensation, and $4.9 million in third-party research and development expenses, which includes clinical trial CRO activities, GLP toxicology studies, and consulting for regulatory and clinical studies. This was partially offset by a decrease in licensing fees of $1.7 million.

General and Administrative (G&A) Expenses: General and administrative expenses were $11.2 million for the three months ended September 30, 2021, compared to $4.0 million for the three months ended September 30, 2020. The increase of approximately $7.2 million was primarily attributable to $4.3 million of incremental compensation expense, which included $1.8 million of non-cash stock-based compensation. There was an increase of $2.9 million mainly in professional fees related to legal, insurance, investor relations/communications, accounting, personnel recruiting, market research, and patient advocacy activities.

Net loss: Net loss for the three months ended September 30, 2021 was $51.2 million or $1.35 per share, as compared to a net loss of $15.0 million, or $1.28 per share, for the three months ended September 30, 2020.

Cash and cash equivalents: As of September 30, 2021, Taysha had $188.8 million in cash and cash equivalents.

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 financial and operating results and to provide a corporate update. 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 13723855. 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 30 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," "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.

Taysha Gene Therapies, Inc.
Condensed Consolidated Statements of Operations
(in thousands, except share and per share data)
(Unaudited)

	For the Three Months Ended September 30,		For the Nine Months Ended September 30,	
	2021	2020	2021	2020
Operating expenses:				
Research and development	$ 39,528	$ 11,057	$ 94,025	$ 19,633
General and administrative	11,153	3,984	29,518	5,002
Total operating expenses	(50,681)	15,041	123,543	24,635
Loss from operations	(50,681)	(15,041)	(123,543)	(24,635)
Other income (expense):				
Change in fair value of preferred stock tranche liability	-	-	-	(17,030)
Interest income	37	-	143	-
Interest expense	(543)	(1)	(737)	(28)
Total other expense, net	(506)	(1)	(594)	(17,058)
Net loss	**$ (51,187)**	**$ (15,042)**	**$ (124,137)**	**$ (41,693)**
Net loss per common share, basic and diluted	$ (1.35)	$ (1.28)	$ (3.31)	$ (3.73)
Weighted average common shares outstanding, basic and diluted	38,003,954	11,733,170	37,495,537	11,176,429

Taysha Gene Therapies, Inc.
Condensed Consolidated Balance Sheet Data
(in thousands, except share and per share data)
(Unaudited)

	September 30, 2021	December 31, 2020
ASSETS		
Current assets:		
Cash and cash equivalents	$ 188,785	$ 251,253
Prepaid expenses and other current assets	8,385	6,626
Total current assets	197,170	257,879
Restricted cash	2,628	-

Deferred lease asset	691	715
Property, plant and equipment, net	40,553	287
Total assets	**$ 241,042**	**$ 258,881**
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities		
Accounts payable	$ 22,051	$ 1,994
Accrued expenses and other current liabilities	21,163	5,135
Total current liabilities	43,214	7,129
Build-to-suit lease liability	26,607	-
Term Loan, net	27,812	-
Other non-current liabilities	3,015	450
Total liabilities	100,648	7,579
Stockholders' equity		
Preferred stock, $0.00001 par value per share; 10,000,000 shares authorized and no shares issued and outstanding as of September 30, 2021 and December 31, 2020	-	-
Common stock, $0.00001 par value per share; 200,000,000 shares authorized and 38,473,945 and 37,761,435 issued and outstanding as of September 30, 2021 and December 31, 2020	-	-
Additional paid-in capital	325,657	312,428
Accumulated deficit	(185,263)	(61,126)
Total stockholders' equity	140,394	251,302
Total liabilities and stockholders' equity	**$ 241,042**	**$ 258,881**

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