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

Positive pre-IND/CTA feedback obtained from several key regulatory agencies for TSHA-102 in Rett syndrome, TSHA-101 in GM2 gangliosidosis and TSHA-118 in CLN1 disease, paving the way for multiple anticipated IND/CTA filings in the second half of 2021

Entered into a non-dilutive term loan agreement with Silicon Valley Bank that provides up to $100 million in tranches at an attractive interest rate that lowers overall cost of capital, strengthens the balance sheet and offers additional financial and operational flexibility; assuming full drawdown, cash runway expected to be sufficient to achieve potential regulatory approval for TSHA-120 in GAN without the need for additional financing

Reiterate guidance for clinical, regulatory and preclinical milestones in second half of 2021, including Phase 1/2 data from the highest dose cohort of TSHA-120 study in GAN, regulatory update for GAN program, preliminary Phase 1/2 safety and biomarker data for TSHA-101 in GM2 gangliosidosis, and initiation of Phase 1/2 trials in CLN1 disease, Rett syndrome and SURF1-associated Leigh syndrome

Numerous successful GMP runs provided sufficient drug products to support five planned Phase 1/2 trials and multiple programs in IND/CTA-enabling studies in the second half of 2021

Recent publications of GAN natural history data for TSHA-120 and positive preclinical data for TSHA-102 in Rett syndrome in the journal Brain provide further support of clinical development strategies

Completed first R&D and manufacturing investor days highlighting preclinical and clinical data from multiple programs, the company's unique three-pillar approach to manufacturing and its capabilities, the regulatory environment for gene therapy manufacturing, and the immunology of gene therapy

Upcoming virtual investor mini-series for CLN1, Rett and Angelman syndrome programs to feature Key Opinion Leaders and highlight progress across these programs

Conference call and live webcast today at 8:00 a.m. Eastern Time

DALLAS--(BUSINESS WIRE)--Aug. 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 reported financial results for the second quarter ended June 30, 2021 and provided a corporate update.

"We continue to make significant progress on several key clinical, manufacturing and strategic corporate initiatives which were highlighted in our R&D and Manufacturing investor days and in our recent press release announcing our non-dilutive financing with SVB," noted RA Session II, President, Founder and CEO of Taysha. "We have received positive pre-IND/CTA feedback from several key regulatory agencies for our Rett syndrome, GM2 gangliosidosis and CLN1 disease programs, which pave the way for multiple expected IND/CTA filings and clinical trial initiations in the second half of the year. Our success relies on robust, sustainable and high-quality manufacturing to support our portfolio, and we have completed numerous successful GMP runs to support five planned Phase 1/2 trials and several programs in IND/CTA-enabling studies. With ambitious corporate objectives planned over the next 12 to 18 months, we are pleased to have recently entered into a loan agreement for up to $100 million at an attractive interest rate which lowers overall cost of capital and contains no financial covenants or warrants. The initial draw bolsters our cash position and provides financial and operational flexibility. We believe full drawdown of this non-dilutive financing will extend our cash runway to support key value-creating milestones, including the release of Phase 1/2 data from the highest dose cohort in GAN, and Phase 1/2 data in GM2 gangliosidosis, Rett syndrome, CLN1 disease and SURF1-associated Leigh syndrome and, importantly, a potential regulatory approval for TSHA-120 in GAN without the need for additional financing. We look forward to updating you on our continued progress throughout the year."

Recent Corporate Highlights

- Positive pre-IND/CTA feedback obtained from multiple key regulatory agencies for TSHA-102 in Rett syndrome, TSHA-101 in GM2 gangliosidosis and TSHA-118 in CLN1 disease, paving the way for multiple expected IND/CTA filings in the second half of 2021
- Secured up to $100 million non-dilutive term loan financing, with $40 million available at closing from Silicon Valley Bank (SVB), of which Taysha has drawn $30 million. The company has the option to draw down the remaining tranches, subject to certain conditions. The interest rate is the greater of 7.0% or the WSJ Prime Rate plus 3.75% and there are no financial covenants or warrants
- Multiple successful GMP runs provided drug products to support five planned Phase 1/2 trials and multiple programs in IND/CTA-enabling studies in the second half of 2021
- Publication of GAN natural history data for TSHA-120 in peer-reviewed journal, *Brain*, that included robust assessment across clinical outcomes for GAN, including motor, sensory, respiratory, neurophysiologic, MRI and biopsy data. All GAN natural history data was generated and supported by the Intramural Program of the National Institute of Neurological Disorders and Stroke (NINDS), U.S. National Institutes of Health (NIH) under umbrella protocol NCT01568658 and under the leadership of the Principal Investigator, Carsten Bönneman
- Publication of positive preclinical data for TSHA-102 in Rett syndrome in *Brain* that provided 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
- Announcement of positive data from multiple programs at R&D Day on June 28-29
    - Phase 1/2 visual acuity data for TSHA-120 in patients with GAN demonstrated a dose-dependent trend towards stabilization of visual acuity, one of the most challenging symptoms to treat. Recently obtained preclinical data demonstrated no impact on dorsal root ganglia in non-human primates when TSHA-120 was delivered intrathecally
    - Preclinical data for TSHA-102 in Rett syndrome demonstrated that miRARE reduced overall expression of MECP2 transgene expression compared to unregulated *MECP2* in wild type mice. miRARE regulated genotype-dependent *MECP2* expression across different brain regions in wild type and Rett knockout mouse models on a cell-by-cell basis
    - An in-depth look into natural history provided incremental data on disease progression and motor development delays in patients with GM2 gangliosidosis
    - Preclinical data for TSHA-118 demonstrated sustained preservation of motor function and rescue of survival with higher doses of TSHA-118 and earlier intervention in CLN1 knockout mice
    - Positive findings indicated a small increase in COX1 activity can significantly improve the clinical phenotype of patients with SURF1-associated Leigh syndrome; similarly, reduction in COX activity correlated with disease worsening in patient fibroblast data
    - In SLC13A5 knockout mice, TSHA-105 decreased plasma citrate levels and reduced seizures and associated deaths
    - In SLC6A1 knockout and heterozygous mouse models, CNS administration of TSHA-103 rescued abnormal seizure activity. Recently obtained data demonstrated rescue of functional measures such as nesting, open field activity, hind limb clasping and latency to fall from the rotarod
    - TSHA-112 reduced *GYS1* expression in the APBD knockout model which resulted in decreased polyglucosan body formation in mice brain
    - TSHA-111-LAFORIN and TSHA-111-MALIN reduced GYS1 expression in the laforin and malin knockout models which resulted in decreased Lafora body formation in mice brain
    - Preclinical data for TSHA-113 demonstrated significant reduction of tau mRNA and protein levels, validating the potential of using AAV-mediated gene silencing to achieve life-long reduction of tau protein levels and warranting further preclinical development
    - Two novel approaches to treat Angelman syndrome disclosed, including knockdown of *UBE3A-ATS* to unsilenced the paternal allele and a gene replacement strategy on UBE3A to mimic maternal UBE3A allele expression
- Manufacturing Day on July 27th highlighted the company's unique three-pillar approach to the manufacturing process, its manufacturing capabilities, the regulatory environment for gene therapy manufacturing, and the immunology of gene therapy with a focus on the practical aspects of initiating and monitoring immunosuppressive regimes
- Appointment of Chief Development Officer, Mary Newman, who previously served as Senior Vice President of Regulatory Affairs at Astellas Gene Therapies, formerly Audentes, and brings over 30 years of experience in translational development, program management and regulatory affairs in the biotech industry
- Founding member of the newly formed Rare Disease Company Coalition, a first-of-its-kind alignment of life sciences companies committed to discovering, developing and delivering rare disease treatments for the patients they collectively serve
- Continued progress on internal manufacturing facility with completion of the demolition phase
- Opened the Dallas headquarters in May 2021
- Expansion of employee base to 150 across all areas of the organization

Anticipated Milestones by Program

TSHA-120 for giant axonal neuropathy (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*

- Report clinical data for TSHA-120 from the high dose cohort of $3.5x10^{14}$ total vg in second half of 2021
- Engage with key regulatory agencies to discuss the approval pathway and provide a regulatory update by year-end 2021

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 Beta Hexoseaminidase A, intrathecally for the treatment of GM2 gangliosidosis, also called Tay-Sachs or Sandhoff disease

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

- CLN1 Investor Day on August 30, 2021
- Maintain current open IND
- Initiate a Phase 1/2 clinical trial in second half of 2021
- Report biomarker data 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 MECP2, as well as a novel miRARE platform that regulates transgene expression on a cell-by-cell basis

- Rett syndrome Investor Day in September 2021
- Submit IND/CTA filing in second half of 2021
- Initiate Phase 1/2 clinical trial by year-end 2021
- Report clinical data by year-end 2022

TSHA-104 in SURF1-associated Leigh syndrome: a self-complementary AAV9 viral vector with a 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 second half of 2021
- Initiate Phase 1/2 trial by year-end 2021
- Report biomarker data in first half of 2022

Pipeline programs in IND/CTA-enabling studies

- Submit an IND/CTA filing for one of six programs in 2021: TSHA-105 in SLC13A5 deficiency, TSHA-111-LAFORIN and TSHA-111-MALIN in two forms of Lafora disease, TSHA-112 in APBD, TSHA-119 in GM2 AB variant and TSHA-103 in SLC6A1 haploinsufficiency disorder

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 focused on regulated transgene expression with expansion of miRARE platform into additional CNS diseases
- Initiate confirmatory preclinical studies for the vagus nerve redosing platform in canines
- Advance mini-gene discovery program in genetic forms of epilepsy and neurodevelopmental disorders
- Continue discovery and development efforts around next-generation capsids

Second Quarter 2021 Financial Highlights

Research and Development (R&D) Expenses: Research and development expenses were $30.6 million for the three months ended June 30, 2021, compared to $3.1 million for the three months ended June 30, 2020. The $27.5 million increase was primarily attributable to an increase of $10.3 million of expenses incurred in research and development manufacturing and other raw material purchases, which included cGMP batches produced by Catalent and UT Southwestern. We incurred an increase in employee compensation expenses of $8.5 million, which included $2.2 million of non-cash stock-based compensation, and $8.7 million in third-party research and development expenses, which includes clinical trial CRO activities, GLP toxicology studies, and consulting for regulatory and clinical studies.

General and Administrative (G&A) Expenses: General and administrative expenses were $10.1 million for the three months ended June 30, 2021, compared to $0.9 million for the three months ended June 30, 2020. The increase was primarily attributable to incremental compensation expense, which included non-cash stock-based compensation, and additional consulting and professional fees.

Net loss: Net loss for the second quarter ended June 30, 2021 was $40.9 million or $1.09 per share, as compared to a net loss of $21.2 million, or $1.95 per share, for the second quarter ended June 30, 2020.

Cash and cash equivalents: As of June 30, 2021, Taysha had $197.4 million in cash and cash equivalents.

Conference Call and Webcast Information

Taysha management will hold a conference call and webcast today at 8:00 a.m. ET / 7:00 a.m. 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 13722197. 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 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, our corporate growth plans and our plans to establish a commercial-scale cGMP manufacturing facility to provide preclinical, clinical and commercial supply and our anticipated cash runway assuming full access to the $100 million potentially available under the loan and security agreement. 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.

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

	For the Three Months Ended June 30,		For the Six Months Ended June 30,	
	2021	2020	2021	2020
Operating expenses:				
Research and development	$ 30,643	$ 3,062	$ 54,497	$ 8,576
General and administrative	10,129	948	18,365	1,018
Total operating expenses	40,772	4,010	72,862	9,594
Loss from operations	(40,772)	(4,010)	(72,862)	(9,594)
Other income (expense):				
Change in fair value of preferred stock tranche liability	-	(17,210)	-	(17,030)
Interest income	40	-	106	-
Interest expense	(194)	-	(194)	(27)
Total other expense, net	(154)	(17,210)	(88)	(17,057)
Net loss	**$ (40,926)**	**$ (21,220)**	**$ (72,950)**	**$ (26,651)**
Net loss per common share, basic and diluted	$ (1.09)	$ (1.95)	$ (1.96)	$ (2.45)
Weighted average common shares outstanding, basic and diluted	37,479,164	10,894,999	37,237,115	10,894,999

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

	June 30, 2021	December 31, 2020
ASSETS		
Current assets:		
Cash and cash equivalents	$ 197,370	$ 251,253
Prepaid expenses and other current assets	9,932	6,626
Total current assets	207,302	257,879
Deferred lease asset	691	715
Property, plant and equipment, net	33,867	287
Total assets	**$ 241,860**	**$ 258,881**
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities		
Accounts payable	$ 6,355	$ 1,994
Accrued expenses and other current liabilities	22,036	5,135
Total current liabilities	28,391	7,129

Build-to-suit lease liability	26,209	-
Other non-current liabilities	765	450
Total liabilities	55,365	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 June 30, 2021 and December 31, 2020	-	-
Common stock, $0.00001 par value per share; 200,000,000 shares authorized and 38,391,165 and 37,761,435 issued and outstanding as of June 30, 2021 and December 31, 2020, respectively	-	-
Additional paid-in capital	320,571	312,428
Accumulated deficit	(134,076)	(61,126)
Total stockholders' equity	186,495	251,302
Total liabilities and stockholders' equity	**$ 241,860**	**$ 258,881**

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