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

May 11, 2021

TSHA-120 program demonstrated clear arrest of disease progression and long-term durability at therapeutic dose levels in patients with giant axonal neuropathy (GAN); Expects clinical data from highest dose cohort in second half of 2021 and regulatory feedback from agencies by year-end 2021

Expects to have five programs in Phase 1/2 trials in the second half of 2021, including GAN, GM2 gangliosidosis, CLN1 disease, Rett syndrome and SURF1-associated Leigh syndrome

Positive preclinical data for TSHA-102 in Rett syndrome provided quantitative evidence of miRARE's ability to exhibit genotype-dependent regulation of MECP2 gene expression across different brain regions in both wild type and knockout mouse models of Rett syndrome; Results published in Brain

Treatment with TSHA-102 resulted in a statistically significant survival extension by 56% in 4-5 week-old knockout Rett mice with meaningful accumulated disease, a more translatable model of the disorder in humans

New data for multiple preclinical programs, including tauopathies, SLC13A5 deficiency, SLC6A1 haploinsufficiency, Angelman disease, Adult Polyglucosan Body Disease (APBD), Lafora disease, and GM2 AB variant, highlighted Taysha's next wave of novel gene therapies that have the potential to impact meaningful patient populations

Plans for IND/CTA submission from one of the following programs by year-end 2021: SLC13A5 deficiency, APBD, Lafora disease, GM2 AB variant and SLC6A1 haploinsufficiency

Advancing development of multiple preclinical programs, including tauopathies and Angelman syndrome

Virtual Research and Development Day on June 28-29, 2021 to feature Key Opinion Leaders and highlight progress across pipeline

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

DALLAS--(BUSINESS WIRE)--May 11, 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 first quarter ended March 31, 2021 and provided a corporate update.

"Our team has ushered in the new year with a continued focus on achieving our corporate objectives and creating value for patients and shareholders," said RA Session II, President, Founder and CEO of Taysha. "Our recent acquisition of TSHA-120 for GAN immediately transformed Taysha into a pivotal-stage gene therapy company. Based on the compelling clinical and preclinical data package generated to date for this promising product candidate, we intend to engage with regulatory agencies to discuss a pathway to approval and look forward to providing clinical and regulatory updates in the second half of 2021 and by year-end 2021, respectively. We are also extremely pleased to share newly published preclinical data for TSHA-102 in Rett syndrome that provided, for the first time, quantitative evidence of miRARE's ability to show genotype-dependent regulation of *MECP2* gene expression across different regions of the brain in wild type and knockout mouse models. Rett syndrome is an incredibly difficult disease to treat with gene replacement therapy given the challenges of safely regulating the degree of MECP2 expression from the *MECP2* gene and we are encouraged that miRARE has achieved this regulation on a cell-by-cell basis without associated toxicities. The built-in self-regulatory feedback loop mechanism is a culmination of approximately 14 years of research and holds great potential for the treatment of what we now consider a reversible disease. Importantly, TSHA-102-treated knockout Rett mice with meaningful disease accumulation experienced a statistically significant survival extension by 56%, which we believe is a more translatable model of the disorder in humans. We believe these data validate our novel approach to treating Rett syndrome, help de-risk the clinical program and support advancement of TSHA-102 into a Phase 1/2 trial by year-end. With these and other recent value-creating achievements, we are even more confident in our outlook for the full year."

Suyash Prasad, MBBS, M.Sc., MRCP, MRCPCH, FFPM, Chief Medical Officer and Head of Research and Development of Taysha, said, "We expect a steady flow of near-term clinical, regulatory and preclinical catalysts for the remainder of 2021. We anticipate having five programs in Phase 1/2 trials and an additional six programs in IND/CTA-enabling studies by year-end 2021. For the remainder of 2021, we expect data from the highest dose cohort from the ongoing TSHA-120 trial for GAN, a regulatory update on the GAN program, first-in-human Phase 1/2 clinical data from the Queen's University trial of TSHA-101 in GM2 gangliosidosis and the initiation of Phase 1/2 trials in GM2 gangliosidosis in the U.S., CLN1 disease, Rett syndrome and SURF1-associated Leigh syndrome. For our preclinical programs, we expect to submit an IND/CTA for one of six programs in IND/CTA-enabling studies by year-end 2021. Moreover, we will continue to make advancements on payload design and on the miRARE, mini-gene and vagus nerve redosing platforms, which are expected to drive further innovation. We look forward to providing additional updates at our two-day R&D Day event in June and throughout the year."

Recent Corporate Highlights

- Published new preclinical data for TSHA-102 in Rett syndrome in *Brain* journal

- Preclinical data provided quantitative evidence of miRARE's ability to exhibit genotype-dependent regulation of *MECP2* gene expression across different brain regions in both wild type and knockout mouse models of Rett syndrome
- TSHA-102 resulted in a statistically significant survival extension by 56%, whereas unregulated constructs did not extend survival significantly in the validated *MECP2* knockout Rett mouse model
- Benefit in 4-5 week-old TSHA-102-treated knockout Rett mice with meaningful accumulated disease should be a more translatable model to humans
- In the pons and midbrain, miRARE inhibited mean expression in a genotype-dependent manner, as indicated by significantly fewer myc(+) cells observed in wild type mice than knockout mice ($p<0.05$), thereby demonstrating MECP2 levels within normal physiological parameters
- These quantitative data, for the first time, demonstrated miRARE's ability to regulate gene expression on a cell-by-cell basis, highlighting its potential application in numerous diseases that require controlled gene expression

- Acquired exclusive worldwide rights to TSHA-120, a clinical-stage AAV9 gene therapy program for the treatment of GAN
  - Human proof-of-concept data for TSHA-120 demonstrated clear arrest of disease progression and long-term durability at therapeutic dose levels in patients with GAN
  - To date, 14 patients have been dosed with one of four dose levels of TSHA-120. TSHA-120 has demonstrated a dose-response relationship with arrest of disease progression at the second-highest dose level ($1.8x10^{14}$ total vector genomes [vg]) at one-year post-treatment, affecting a statistically significant 8-point improvement on the MFM32 score
  - Six of these patients treated at therapeutic dose levels have shown sustained dose-dependent improvements in MFM32 scores for more than three years
  - Bayesian analyses confirmed nearly 100% probability of clinically meaningful slowing of disease in patients dosed at $1.8x10^{14}$ total vg compared to natural history
  - Long-term results demonstrated that treatment with TSHA-120 at multiple dose levels was well-tolerated with no severe drug-related adverse events

- Reported new preclinical data for TSHA-113 for tauopathies, TSHA-105 for SLC13A5 deficiency, TSHA-103 for SLC6A1 haploinsufficiency, TSHA-106 for Angelman syndrome, TSHA-112 for APBD, TSHA-111-LAFORIN and TSHA-111-MALIN for Lafora disease, and TSHA-119 for GM2 AB variant that support advancement into clinical testing
  - TSHA-113 significantly reduced tau mRNA and protein levels in mouse models of human tauopathies via cerebral spinal fluid (CSF) delivery
  - TSHA-105 significantly reduced plasma citrate levels, normalized EEG brain activity, and reduced the number of seizures and seizure susceptibility in SLC13A5 knockout mice
  - TSHA-103 improved nesting and EEG activity in the SLC6A1 knockout mouse model and reduced spike train activity in SLC6A1 knockout and heterozygous mouse models
  - TSHA-106 increased UBE3A expression through shRNA-mediated knockdown of UBE3A-ATS in in vitro cell lines across 26 distinct shRNA candidates for the treatment of Angelman disease
  - TSHA-112 generated significant reductions in GYS1 protein, abnormal glycogen accumulation and polyglucosan bodies in the APBD knockout mouse model
  - TSHA-111-LAFORIN and TSHA-111-MALIN achieved effective knockdown of GYS1 expression and insoluble glycogen and decreased Lafora body formation in laforin and malin mouse models
  - TSHA-119 caused a dose-dependent reduction of GM2 accumulation at 20 weeks in GM2A knockout mice

- Announced presentations of preclinical data for TSHA-104 in SURF1-associated Leigh syndrome and TSHA-105 in SLC13A5 deficiency at the 24th Annual Meeting of the American Society of Gene & Cell Therapy (ASGCT)
  - TSHA-104 increased COX1 activity in brain and muscle and restored elevation of blood lactate on exhaustive exercise in a dose-dependent manner in SURF1 knockout mice
  - TSHA-105 significantly reduced plasma citrate levels, normalized EEG brain activity, and reduced the number of seizures and seizure susceptibility in SLC13A5 knockout mice

- Initiated construction of its internal 187,000-square-foot current Good Manufacturing Practices (cGMP) manufacturing facility in Durham, North Carolina, that will include multiple production suites designed to have a total capacity of 2,000 liters for preclinical, clinical, and commercial production of Taysha's gene therapy pipeline; facility will include development, analytical, manufacturing and quality control testing capability for its broad portfolio of gene therapies

- Established collaboration with Yale University, a key addition to partnerships with Cleveland Clinic and UTSW, to advance next-generation mini-gene payloads for AAV gene therapies for the treatment of genetic epilepsies and neurodevelopmental disorders

- Grew company from 80 to approximately 120 employees between February and April 2021

- Announced a two-day virtual R&D Day on June 28th and June 29th to feature Key Opinion Leaders and highlight progress across the pipeline

First Quarter 2021 Financial Highlights

Research and Development (R&D) Expenses: R&D expenses were $23.9 million for the first quarter ended March 31, 2021, compared to $5.5 million for the first quarter ended March 31, 2020. The increase was primarily related to the company's development programs, as a result of increased manufacturing-related spend, clinical and preclinical activities, and headcount.

General and Administrative (G&A) Expenses: G&A expenses were $8.2 million for the first quarter ended March 31, 2021, compared to less than $0.1 million for the first quarter ended March 31, 2020. The increase was primarily due to an increase in personnel costs resulting from increased headcount, professional services fees, and other corporate-related expenses.

Net loss: Net loss for the first quarter ended March 31, 2021 was $32.0 million, or $0.87 per share, as compared to a net loss of $5.4 million, or $0.50 per share, for the first quarter ended March 31, 2020.

Cash and cash equivalents: As of March 31, 2021, Taysha had $228.7 million in cash and cash equivalents, which is expected to support planned operations into 2023.

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 $3.5x10^{14}$ total vg dose cohort in the second half of 2021
- Engage with major 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 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

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
- Report biomarker data in the 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

- Submit IND/CTA filing in the 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 the second half of 2021
- Initiate Phase 1/2 trial by year-end 2021
- Report biomarker data in the 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

Anticipated Corporate Milestones in 2021

- Continue construction of internal cGMP facility in 2021
- Complete buildout of Dallas headquarters in Q2 2021
- Expand employee base from approximately 120 (as of April 30, 2021) to approximately 150 by year-end 2021

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 855-327-6837 (U.S./Canada) or 631-891-4304 (international). The conference ID for all callers is 10014460. 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," 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. 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, 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.

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

	For the Three Months Ended March 31, 2021	For the Three Months Ended March 31, 2020
Operating expenses:		
Research and development	$ 23,854	$ 5,514
General and administrative	8,236	70
Total operating expenses	32,090	5,584
Loss from operations	(32,090)	(5,584)
Other income (expense):		
Change in fair value of preferred stock tranche liability	-	180
Interest income	66	-
Interest expense	-	(27)
Total other income, net	66	153
Net loss	**$ (32,024)**	**$ (5,431)**
Net loss per common share, basic and diluted	$ (0.87)	$ (0.50)
Weighted average common shares outstanding, basic and diluted	36,992,377	10,894,999

Taysha Gene Therapies, Inc.

Consolidated Balance Sheet Data
(in thousands)
(Unaudited)

	March 31, 2021	December 31, 2020
Cash and cash equivalents	$ 228,684	$ 251,253
Total assets	$ 242,829	$ 258,881
Total liabilities	$ 19,957	$ 7,579
Total stockholders' equity	$ 222,872	$ 251,302

View source version on businesswire.com: https://www.businesswire.com/news/home/20210511005453/en/

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