Taysha Gene Therapies Reports Fourth Quarter and Full Year 2021 Financial Results and Provides Corporate Update

Strategic pipeline prioritization initiatives focused on giant axonal neuropathy (GAN), with feedback on registration pathway by mid-2022, and Rett syndrome, with preliminary clinical data expected by year-end 2022 under recently approved Clinical Trial Application (CTA)

Rett syndrome affects over 350,000 patients worldwide; GAN has an estimated addressable patient population of 5,000 worldwide

Activities for other ongoing clinical programs will be minimized and all additional research and development will be paused to increase operational focus and efficiency

Pipeline prioritization initiatives, existing cash and financing under current debt facility expected to extend cash runway into Q4 2023

DALLAS--(BUSINESS WIRE)--Mar. 31, 2022-- 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 fourth quarter and full-year ended December 31, 2021 and provided a corporate update.

“2021 was a year of accomplishment that included positive data from three clinical programs, including GAN, GM2 gangliosidosis and CLN7 disease. We are sharpening our strategic focus to prioritize key value-driving registration-directed programs in GAN, which has an estimated addressable patient population of 5,000 worldwide, and Rett syndrome, which affects over 350,000 patients worldwide,” noted RA Session II, President, Founder and CEO of Taysha. “To increase operational efficiency, activities for other ongoing clinical programs will be minimized and all additional research and development will be paused. As a result, we have reduced our workforce by approximately 35 percent. Our strategic pipeline prioritization, along with existing cash and financing under our current debt facility is expected to extend cash runway into the fourth quarter of 2023.”

Recent Corporate Highlights

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.* TSHA-120 is designed to deliver a functional copy of the GAN gene to the CNS and PNS. The addressable patient population for GAN is estimated at 5,000 worldwide. TSHA-120 has received Orphan Drug and Rare Pediatric Disease designations from the U.S. Food and Drug Administration (FDA).

- Reported positive clinical efficacy and safety data for high dose cohort and long-term durability data across all therapeutic dose cohorts for TSHA-120 in GAN
    - Efficacy data for high dose cohort demonstrated clinically meaningful and statistically significant improvement in MFM32 by Year 1 compared to natural history (n=3)
    - Long-term durability data across all therapeutic dose cohorts demonstrated a 10-point improvement in mean change in MFM32 by Year 3 compared to estimated natural history decline of 24 points (n=5)
    - Biopsy data in five of six patient samples analyzed to date confirmed active regeneration of nerve fibers following treatment with TSHA-120 (n=6)
    - TSHA-120 was safe and well-tolerated supported by 53 patient-years of clinical data

TSHA-102 in Rett syndrome: a self-complementary intrathecally delivered AAV9 gene replacement therapy under development for the treatment of Rett syndrome. TSHA-102 utilizes the novel miRNA-Responsive Auto-Regulatory Element (miRARE) platform to regulate transgene expression genotypically on a cell-by-cell basis. TSHA-102 is the first-and-only gene therapy in clinical development for Rett syndrome. Rett syndrome affects an estimated 350,000 patients worldwide. TSHA-102 has received Orphan Drug and Rare Pediatric Disease designations from the FDA and has been granted Orphan Drug designation from the European Commission.

- Clinical Trial Application (CTA) approved by Health Canada in March 2022
- Positive preclinical data for TSHA-102 in mouse models of Rett syndrome
    - One-time IT injection of TSHA-102 significantly increased survival at all dose levels, with the mid to high doses improving survival across all age groups compared to vehicle-treated controls
    - Treatment with TSHA-102 significantly improved body weight, motor function and respiratory assessments in MECP2 knockout mice
    - Additional study in neonatal mice ongoing, with preliminary data suggesting normalization of survival
- Positive IND/CTA-enabling 6-month GLP toxicology data
    - Biodistribution, as reflected by DNA copy number, was observed in multiple areas of the brain, sections of spinal

cord and the dorsal root ganglion (DRG)
    - mRNA levels across multiple tissues were low, indicating miRARE regulation is minimizing transgene expression from the construct in the presence of endogenous MECP2 as expected, despite the high levels of DNA that were delivered
    - No toxicity from transgene overexpression was observed, confirmed by functional and histopathologic evaluations demonstrating no detrimental change in neurobehavioral assessments and no adverse tissue findings on necropsy

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. TSHA-101 has been granted Orphan Drug and Rare Pediatric Disease designations by the FDA and Orphan Drug designation from the European Commission.

- Positive initial biomarker data for TSHA-101 demonstrating normalization of β-hexosaminidase A enzyme activity in patients with GM2 gangliosidosis
    - Patient 1 with Sandhoff disease achieved Hex A enzyme activity of 190% of normal at Month 1 and 288% of normal at Month 3, representing 38-fold and 58-fold above the presumed asymptomatic level of 5% of normal identified by natural history at Month 1 and Month 3 respectively
    - Patient 2 with Tay-Sachs disease achieved Hex A enzyme activity of 25% of normal at Month 1, representing 5-fold above the presumed asymptomatic level of 5% of normal identified by natural history. This patient was only eligible for the Month 1 analysis at the time of data release
- TSHA-101 was well-tolerated with no significant drug-related events
    - Patient 1 succumbed to pneumonia and pleural effusion with a concomitant hospital-acquired MRSA infection.
    - The independent data safety monitoring board (DSMB) concluded the patient death was unrelated to study drug
- We do not intend to pursue further enrollment in the Phase 1/2 trial but will continue to follow patients who were previously dosed

AAV9 Gene Replacement for CLN7 Batten 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 clinical development of the CLN7 program is in collaboration with UT Southwestern (UTSW) and Children's Health and funded by Children's Medical Center Foundation.

- Reported positive preliminary clinical safety data for first-generation construct in CLN7 Batten disease from UTSW-sponsored clinical trial
    - Data on the initial three patients dosed were presented at the 18th Annual WORLDSymposium in February 2022 by Dr. Saima Kayani, MD of UTSW
- Fourth patient with CLN7 disease recently dosed at 1.0×10^{15} total vg
- Future CLN7 development will focus solely on the first-generation construct

2022 Prioritization Initiatives

- Prioritize key value-driving registration-directed programs, GAN and Rett syndrome
- Initial clinical studies in CLN1 and SLC13A5 will limit patient enrollment to focus on proof-of-concept
- Continued CLN7 clinical development in collaboration with existing partners
- All additional research and development activities will be paused to increase operational efficiency
- Reduction in workforce by approximately 35 percent with a focus on strategic prioritization

Anticipated 2022 Milestones

- Regulatory update for TSHA-120 in GAN by mid-2022
- First-in-human preliminary Phase 1/2 data for TSHA-102 in Rett syndrome by year-end 2022
- Initiation of clinical development for TSHA-105 in SLC13A5 deficiency in 2022
- Continued clinical development for TSHA-118 in CLN1 disease in 2022
- Continued clinical development of the first-generation construct for CLN7 disease in 2022

Fourth Quarter and Full-Year 2021 Financial Highlights

Research and Development (R&D) Expenses: Research and development expenses were $37.9 million for the three months ended December 31, 2021, compared to $12.3 million for the three months ended December 31, 2020. Research and development expenses were $131.9 million for the full year ended December 31, 2021, compared to $31.9 million for the full year ended December 31, 2020. The $100.0 million increase was primarily attributable to an increase of $38.3 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 also incurred an increase in employee compensation and expenses of $32.7 million, which included $7.1 million of non-cash stock-based compensation, due to an increase in employee headcount in the research and development function. We also incurred an increase of $29.0 million of third-party research and development consulting fees, primarily related to GLP toxicology studies, clinical study CRO activities, and consulting for regulatory and clinical studies.

General and Administrative (G&A) Expenses: General and administrative expenses were $11.8 million for the three months ended December 31,

2021, compared to $6.1 million for the three months ended December 31, 2020. General and administrative expenses were $41.3 million for the full year ended December 31, 2021, compared to $11.1 million for the full year ended December 31, 2020. The full year increase of approximately $30.2 million was primarily attributable to $16.3 million of incremental compensation expense, which included $7.7 million of non-cash stock-based compensation, due to increases in employee headcount. We also incurred an increase of $13.9 million 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 December 31, 2021 was $50.4 million or $1.32 per share, as compared to a net loss of $18.3 million, or $0.50 per share, for the three months ended December 31, 2020. Net loss for the full year ended December 31, 2021 was $174.5 million or $4.64 per share, as compared to a net loss of $60.0 million, or $3.40 per share, for the full year ended December 31, 2020.

Cash and cash equivalents: As of December 31, 2021, Taysha had $149.1 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 13727816. 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, the forecast of our cash runway and the implementation and potential impacts of our strategic pipeline prioritization initiatives. 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, 2021, 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.
Condensed Consolidated Statements of Operations
(in thousands, except share and per share data)
(Unaudited)

	For the Three Months Ended December 31,		For the Year Ended December 31,	
	2021	2020	2021	2020
Operating expenses:				
Research and development	$ 37,918	$ 12,260	$ 131,943	$ 31,893
General and administrative	11,806	6,107	41,324	11,109
Total operating expenses	49,724	18,367	173,267	43,002
Loss from operations	(49,724)	(18,367)	(173,267)	(43,002)
Other income (expense):				
Change in fair value of preferred stock tranche liability	-	-	-	(17,030)
Interest income	29	49	172	49
Interest expense	(691)	-	(1,428)	(28)
Total other expense, net	(662)	49	(1,256)	(17,009)
Net loss	**$ (50,386)**	**$ (18,318)**	**$ (174,523)**	**$ (60,011)**
Net loss per common share, basic and diluted	$ (1.32)	$ (0.50)	$ (4.64)	$ (3.40)
Weighted average common shares outstanding, basic and diluted	38,110,597	36,992,377	37,650,566	17,665,683

Taysha Gene Therapies, Inc.

Condensed Consolidated Balance Sheet Data
(in thousands, except share and per share data)
(Unaudited)

	December 31, 2021	December 31, 2020
ASSETS		
Current assets:		
Cash and cash equivalents	$ 149,103	$ 251,253
Prepaid expenses and other current assets	10,499	6,626
Total current assets	159,602	257,879
Restricted cash	2,637	-
Deferred lease asset	667	715
Property, plant and equipment, net	50,610	287
Other non-current assets	440	-
Total assets	**$ 213,956**	**$ 258,881**
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities		
Accounts payable	$ 21,763	$ 1,994
Accrued expenses and other current liabilities	29,983	5,135
Total current liabilities	51,746	7,129
Build-to-suit lease liability	25,900	-
Term Loan, net	37,192	-
Other non-current liabilities	3,735	450
Total liabilities	118,573	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 December 31, 2021 and December 31, 2020	-	-
Common stock, $0.00001 par value per share; 200,000,000 shares authorized and 38,473,945 and 37,761,435 issued and outstanding as of December 31, 2021 and December 31, 2020	-	-
Additional paid-in capital	331,032	312,428
Accumulated deficit	(235,649)	(61,126)
Total stockholders' equity	95,383	251,302
Total liabilities and stockholders' equity	**$ 213,956**	**$ 258,881**

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