



Taysha Gene Therapies Reports Full Year 2023 Financial Results and Provides Corporate and Clinical Updates

Data from first adult patient in REVEAL Phase 1/2 trial showed TSHA-102 (low dose, 5.7×10^{14} total vg) was well-tolerated with no treatment-emergent SAEs as of 35-week assessment, with sustained improvement across key efficacy measures at decreased steroid levels and new improvement in RSBQ at month six

Data from second adult patient showed TSHA-102 (low dose, 5.7×10^{14} total vg) was well-tolerated with no treatment-emergent SAEs as of 19-week assessment, with sustained improvement across key efficacy measures, significantly reduced seizure events and new improvement in R-MBA at week 12

Principal Investigator observed sustained and new improvements across multiple clinical domains following completion of steroid taper for patient one through 35-weeks post-treatment and for patient two through 19-weeks post-treatment at decreased steroid levels

Received Independent Data Monitoring Committee approval of Company's request to proceed to early advancement to cohort two (high dose, 1×10^{15} total vg) in REVEAL adolescent and adult trial, and approval to dose second pediatric patient in cohort one (low dose, 5.7×10^{14} total vg) in REVEAL pediatric trial

*Initial data from cohort one (low dose, 5.7×10^{14} total vg) in REVEAL pediatric trial expected mid-2024;
initial data from cohort two (high dose, 1×10^{15} total vg) in both trials (adolescent/adult and pediatric) expected in 2H 2024*

Conference call and live webcast today at 4:30 PM Eastern Time

DALLAS, March 19, 2024 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA) (Taysha or the Company), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of severe monogenic diseases of the central nervous system (CNS), today reported financial results for the full-year ended December 31, 2023, and provided corporate and clinical updates.

"We are highly encouraged by the safety profile and durable response reported in the longer-term data from the low dose cohort in our REVEAL adolescent and adult trial. Importantly, following completion of the steroid taper for the first patient and at decreased steroid levels for the second patient, both patients showed sustained improvements across multiple clinical domains, as well as new improvements compared to earlier post-treatment assessments, which supports the transformative potential of TSHA-102," said Sean P. Nolan, Chairman and Chief Executive Officer of Taysha. "These continued improvements in both adult patients with advanced stage four Rett syndrome and the initial clinical data from the first pediatric patient were reviewed by the Independent Data Monitoring Committee (IDMC) and enabled us to proceed to earlier dose escalation in the adolescent and adult trial, which will expedite and further inform our clinical development and regulatory strategy for the dose expansion portion of the studies. With this progress, we believe we are well-positioned to focus on generating clinical data in a broad range of ages and stages of patients with Rett syndrome across multiple geographies this year."

Dr. Elsa Rossignol, M.D., FRCP, FAAP, Associate Professor in Neuroscience and Pediatrics at the Université de Montréal, and Principal Investigator of the REVEAL trial at the CHU Sainte-Justine added, "Both adult patients treated with TSHA-102 showed sustained and new improvements across key areas of disease impacting activities of daily living, including multiple aspects of autonomic function, social communication, motor skills, and experienced stabilized or significantly reduced seizures. The first patient sustained improvements at week 35 post-treatment after the completion of her steroid taper, with restored movement in her legs, the gained ability to sit unassisted for the first time in over a decade and gained function in her non-dominant hand. She has also sustained improvements in breathing dysrhythmia and sleep quality and duration, including the gained ability to sleep through the night for the first time in 20 years. Notably, she has vastly increased interest in social communication and activities at week 35 compared to earlier post-treatment assessments. She is more alert and socially interactive, with increased vocalizations and enhanced ability to use an eye-driven communication device. The second patient showed sustained improvements at decreased steroid levels at week 19 post-treatment, including reduced hand stereotypies for the first time since regression at age three, and sustained improvements in breathing dysrhythmia, including hyperventilation and reduced apneic spells. As of week 19 post-treatment, she's experienced a significant reduction in seizures at a lower dose of anti-seizure medication. Collectively, these continued improvements in both adult patients with different genetic mutation severity and phenotypic expression are encouraging and support the potential of TSHA-102 to bring meaningful change to the lives of patients and their caregivers."

Data Summary from Cohort One (Low Dose, 5.7×10^{14} total vg) of the REVEAL Phase 1/2 Adolescent and Adult Trial

TSHA-102 in Rett syndrome: a self-complementary intrathecally delivered AAV9 gene transfer therapy in clinical evaluation for Rett syndrome, a rare genetic neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene. TSHA-102 utilizes a novel miRARE technology designed to mediate levels of *MECP2* in the CNS on a cell-by-cell basis without risk of overexpression. The safety and preliminary efficacy of TSHA-102 are being evaluated in female patients aged 12-years and older with Rett syndrome due to *MECP2* loss-of-function mutation in the [REVEAL Phase 1/2 adolescent and adult trial](#), a first-in-human, open-label, randomized, dose-escalation and dose-expansion study taking place in Canada and the United States (U.S.). Dose escalation will evaluate two dose levels of TSHA-102 sequentially. The maximum tolerated dose (MTD) or maximum administered dose (MAD) established in Part A will then be administered during dose expansion in Part B of the study.

Results from the first patient (large *MECP2* deletion; associated with severe phenotype) and second patient (missense *MECP2* mutation; associated with milder phenotype) with late motor deterioration stage four Rett syndrome dosed with TSHA-102 in the low dose cohort (5.7×10^{14} total vg):

- Generally well-tolerated with no treatment-emergent serious adverse events (SAEs) as of 35-week assessment post-treatment for patient one and 19-week assessment post-treatment for patient two
- Sustained and new improvements observed across multiple clinical domains, as of 35-weeks post-treatment for patient one following completion of steroid taper at week 33, and 19-weeks post-treatment for patient two at decreased steroid levels (taper began at week 17), based on clinical observations by the Principal Investigator (PI), including:
 - **Autonomic function:** improved breathing patterns, sleep quality/duration and circulation (patient one), and improved breathing patterns and circulation (patient two)
 - **Socialization/Communication:** improved social interest, vocalization and ability to use eye-driven communication device (patient one), and improved social interest (patient two)
 - **Motor skills:** improved hand function and gained ability to sit unassisted and move legs (patient one), and improved hand stereotypies (patient two)
 - **Seizures:** stable seizure events (patient one), and significantly reduced seizure events (patient two)
- Seizure Diary showed stable seizure events at lower levels of anti-seizure medication relative to baseline through 35-weeks post-treatment in patient one, and significantly reduced seizure events with lower levels of anti-seizure medication relative to baseline through 19-weeks post-treatment in patient two, based on caregiver-reported medical history
- Clinical improvements seen across key efficacy measures in both patients include:
 - **Patient one at six-month assessment:** *Sustained improvement* in Clinical Global Impression–Improvement (CGI-I), Clinical Global Impression–Severity (CGI-S), Parental Global Impressions–Improvement (PGI-I), Revised Motor Behavior Assessment (R-MBA), Rett Syndrome Hand Function Scale (RSHFS) and Seizure Diaries, at decreased steroid levels, with *new improvement* in Rett Syndrome Behavior Questionnaire (RSBQ)
 - **Patient two at 12-week assessment:** *Sustained improvement* in CGI-I, PGI-I and RSBQ, with *new improvement* in R-MBA and Seizure Diaries
- **Figure accompanying this announcement is available [here](#).**

Recent Corporate and Program Highlights

- Strengthened clinical and regulatory leadership with the promotion of Meredith Schultz, M.D., M.S., to Chief Medical Officer and Rumana Haque-Ahmed to Chief Regulatory Officer, reporting to Sukumar Nagendran, M.D., President and Head of R&D. Dr. Schultz is a board-certified, licensed pediatric neurologist experienced in treating patients with Rett syndrome and leading gene therapy clinical trials. She brings more than 17 years of clinical experience and will lead the Company's clinical development, clinical operations, medical affairs and safety activities. Rumana Haque-Ahmed brings nearly 30 years of experience in regulatory strategy and product development in the biopharmaceutical space. She will continue to lead the Company's regulatory affairs department and initiatives.
- **REVEAL Phase 1/2 Adolescent and Adult Trial (Canada and U.S.):**
 - Completed dosing in cohort one (low dose, n=2) of 5.7×10^{14} total vg.
 - Received IDMC approval of the Company's request to dose escalate immediately, enabling early advancement to cohort two (high dose, n=3) of 1×10^{15} total vg.
 - Announced expansion of ongoing trial in Canada into the U.S. and initiated site activation.
- **REVEAL Phase 1/2 Pediatric Trial (U.S. and United Kingdom (U.K.)):**
 - Received IDMC approval to dose the second pediatric patient in cohort one (low dose, n=3) of 5.7×10^{14} total vg following review of initial clinical data from the six-week post-treatment assessment.
 - Received authorization from U.K. Medicines and Healthcare Products Regulatory Agency (MHRA) of Clinical Trial Application (CTA) for TSHA-102, enabling expansion of ongoing trial in U.S. into the U.K.
 - Received Innovative Licensing and Access Pathway (ILAP) designation for TSHA-102 from U.K. MHRA. The ILAP aims to facilitate patient access to novel treatments by accelerating time to market through opportunities for enhanced engagements with U.K. regulatory authorities and other stakeholders.

Anticipated 2024 Milestones

- **REVEAL Adolescent and Adult Trial**

- Dosing of the first patient in cohort two (high dose, n=3) of 1×10^{15} total vg expected in the second quarter of 2024.
- Initial safety and efficacy data from cohort two expected in the second half of 2024.

- **REVEAL Pediatric Trial**

- Dosing of the second patient in cohort one (low dose, n=3) of 5.7×10^{14} total vg expected in the first quarter of 2024.
- Initial safety and efficacy data from cohort one expected in mid-2024.
- Initial safety and efficacy data from cohort two (high dose, n=3) of 1×10^{15} total vg expected in the second half of 2024.

Full-Year 2023 Financial Highlights

Revenue: Revenue for the full year ended December 31, 2023, was \$15.5 million compared to \$2.5 million for the full year ended December 31, 2022, as revenue was derived entirely from the Company's Option Agreement with Audentes Therapeutics, Inc. (d/b/a Astellas Gene Therapies). The increase in revenue is primarily a result of Rett syndrome research and development activities performed in 2023.

Research and Development Expenses: Research and development expenses were \$56.8 million for the full year ended December 31, 2023, compared to \$91.2 million for the full year ended December 31, 2022. The decrease was due to reduced research and development headcount, lower research and development manufacturing expenses and a reduction in third-party research and development consulting fees, mainly related to pre-clinical studies and IND-enabling toxicology studies.

General and Administrative Expenses: General and administrative expenses were \$30.0 million for the full year ended December 31, 2023, compared to \$37.4 million for the full year ended December 31, 2022. The decrease was primarily attributable to a reduction in compensation expenses as a result of lower headcount and reduced corporate insurance and consulting expenses.

Net loss: Net loss for the full year ended December 31, 2023, was \$111.6 million, or \$0.96 per share, as compared to a net loss of \$166.0 million, or \$3.78 per share, for the full year ended December 31, 2022. The net loss includes a non-recurring and non-cash expense of \$34.5 million related to the change in fair value from the pre-funded warrants as a result of the August 2023 private placement financing.

Cash and cash equivalents: As of December 31, 2023, Taysha had \$143.9 million in cash and cash equivalents. The Company continues to expect that its current cash resources will support planned operating expenses and capital requirements into 2026.

Conference Call and Webcast Information

Taysha management will hold a conference call and webcast today at 4:30 p.m. ET to review its financial and operating results and to provide corporate and clinical updates. 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 13744574. 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 TSHA-102

TSHA-102 is a self-complementary intrathecally delivered AAV9 investigational gene transfer therapy in clinical evaluation for Rett syndrome. Designed as a one-time treatment, TSHA-102 aims to address the genetic root cause of the disease by delivering a functional form of *MECP2* to cells in the CNS. TSHA-102 utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) technology designed to mediate levels of *MECP2* in the CNS on a cell-by-cell basis without risk of overexpression. TSHA-102 has received Fast Track designation and Orphan Drug and Rare Pediatric Disease designations from the FDA and has been granted Orphan Drug designation from the European Commission. TSHA-102 has also received Innovative Licensing and Access Pathway designation from the U.K. Medicines and Healthcare Products Regulatory Agency.

About Rett Syndrome

Rett syndrome is a rare neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene encoding methyl CpG-binding protein 2 (MeCP2), which is essential for regulating neuronal and synaptic function in the brain. The disorder is characterized by loss of communication and hand function, slowing and/or regression of development, motor and respiratory impairment, seizures, intellectual disabilities and shortened life expectancy. Rett syndrome progression is divided into four key stages, beginning with early onset stagnation at 6 to 18 months of age followed by rapid regression, plateau and late motor deterioration. Rett syndrome primarily occurs in females and is one of the most common genetic causes of severe intellectual disability. Currently, there are no approved disease-modifying therapies that treat the genetic root cause of the disease. Rett syndrome caused by a pathogenic/likely pathogenic *MECP2* mutation is estimated to affect between 15,000 and 20,000 patients in the U.S., EU, and U.K.

About Taysha Gene Therapies

Taysha Gene Therapies (Nasdaq: TSHA) is a clinical-stage biotechnology company focused on advancing adeno-associated virus (AAV)-based gene therapies for severe monogenic diseases of the central nervous system. Its lead clinical program TSHA-102 is in development for Rett syndrome, a rare neurodevelopmental disorder with no approved disease-modifying therapies that address the genetic root cause of the disease. With a singular focus on developing transformative medicines, Taysha aims to address severe unmet medical needs and dramatically improve the lives of patients and their caregivers. The Company's management team has proven experience in gene therapy development and commercialization. Taysha leverages this experience, its manufacturing process and a clinically and commercially proven AAV9 capsid in an effort to rapidly translate treatments from bench to bedside. For more information, please visit 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 TSHA-102, including the reproducibility and durability of any favorable results initially seen in patient dosed to date in clinical trials, and our other 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, including the timing of initiating

additional trials and reporting data from our clinical trials, the potential for these product candidates to receive regulatory approval from the FDA or equivalent foreign regulatory agencies, and our current cash resources supporting our planned operating expenses and capital requirements into 2026. 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, 2023, 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. 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)

	For the Year Ended December 31,	
	2023	2022
Revenue	\$ 15,451	\$ 2,502
Operating expenses:		
Research and development	56,778	91,169
General and administrative	30,047	37,360
Impairment of long-lived assets	1,065	36,420
Total operating expenses	87,890	164,949
Loss from operations	(72,439)	(162,447)
Other income (expense):		
Change in fair value of warrant liability	(34,718)	—
Loss on debt extinguishment	(1,398)	—
Change in fair value of term loan	(1,538)	—
Interest income	3,572	249
Interest expense	(4,998)	(3,798)
Other expense	(47)	(18)
Total other expense, net	(39,127)	(3,567)
Net loss	\$ (111,566)	\$ (166,014)
Net loss per common share, basic and diluted	\$ (0.96)	\$ (3.78)
Weighted average common shares outstanding, basic and diluted	116,121,482	43,952,015

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

	December 31, 2023	December 31, 2022
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 143,940	\$ 87,880
Restricted cash	449	—
Prepaid expenses and other current assets	3,479	8,537
Assets held for sale	2,000	—
Total current assets	149,868	96,417
Restricted cash	2,151	2,637
Property, plant and equipment, net	10,826	14,963
Operating lease right-of-use assets	9,582	10,943
Other non-current assets	304	1,316
Total assets	\$ 172,731	\$ 126,276
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	\$ 6,366	\$ 10,946
Accrued expenses and other current liabilities	12,284	18,287
Deferred revenue	18,106	33,557
Total current liabilities	36,756	62,790
Term loan, net	40,508	37,967

REVEAL Phase 1/2 Adolescent and Adult Trial Data from Cohort One