Taysha Gene Therapies Reports First Quarter 2024 Financial Results and Provides Corporate Update

Completed dosing in cohort one (low dose, 5.7x10^{14} total vg) of REVEAL Phase 1/2 adolescent and adult trial with longer-term data supporting the safety profile and durable response of TSHA-102; enrolled first patient in cohort two (high dose, 1x10^{15} total vg) with dosing scheduled for Q2 2024

Dosed second pediatric patient in cohort one (low dose, 5.7x10^{14} total vg) of REVEAL Phase 1/2 pediatric trial in Q1 2024

FDA granted Regenerative Medicine Advanced Therapy designation following review of available safety and efficacy data from the first three patients dosed with the low dose of TSHA-102 across both REVEAL trials (adolescent/adult and pediatric)

Initial data from cohort one (low dose, 5.7x10^{14} total vg) in REVEAL pediatric trial and update from cohort one in REVEAL adolescent and adult trial expected mid-2024; initial data from cohort two (high dose, 1x10^{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, May 14, 2024 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA) (Taysha or the Company), a clinical-stage biotechnology company focused on advancing adeno-associated virus (AAV)-based gene therapies for severe monogenic diseases of the central nervous system (CNS), today reported financial results for the first quarter ended March 31, 2024, and provided a corporate update.

"We are pleased with the recent progress we have made to advance our TSHA-102 program in clinical evaluation for Rett syndrome, including enrolling the first patient in the high dose cohort of our REVEAL adolescent and adult trial earlier than planned and dosing the second patient in our REVEAL pediatric trial. We recently received RMAT designation for TSHA-102 following the FDA's review of safety and efficacy data from the first three patients dosed with the low dose of TSHA-102 across both of our REVEAL trials, which we believe reinforces the therapeutic potential of TSHA-102," said Sean P. Nolan, Chairman and Chief Executive Officer of Taysha. "We look forward to the year ahead as we remain focused on moving to the high dose cohort and generating critical longer-term clinical data across a broad population of patients with Rett syndrome that will guide the next phase of our studies. We expect to report initial clinical data from our REVEAL pediatric trial and provide an update on the completed low dose cohort from our REVEAL adolescent and adult trial in mid-2024."

Recent Corporate and Program Highlights

Received Regenerative Medicine Advanced Therapy (RMAT) designation for TSHA-102 from the United States Food and Drug Administration (FDA): A regenerative medicine therapy is eligible for RMAT designation if it is intended to treat, modify, reverse or cure a serious condition and preliminary clinical evidence indicates the therapy has the potential to address unmet medical needs for such condition. RMAT designation follows the FDA's review of available safety and efficacy data from the first three patients with Rett syndrome dosed with the low dose of TSHA-102 across the REVEAL Phase 1/2 adolescent and adult trial and the REVEAL Phase 1/2 pediatric trial. RMAT designation will enable increased dialogue with the FDA to support the potential expedited development and review of TSHA-102.

REVEAL Phase 1/2 Adolescent and Adult Trial (Canada and U.S.): a first-in-human, open-label, randomized, dose-escalation and dose-expansion study evaluating the safety and preliminary efficacy of TSHA-102 in adolescent and adult females aged 12 years and older with Rett syndrome due to *MECP2* loss-of-function mutation. TSHA-102 is administered as a single lumbar intrathecal injection. 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.

- Completed dosing in cohort one (low dose, n=2) of 5.7x10^{14} total vg
- Announced longer-term data from cohort one including two adult patients with late motor deterioration stage four Rett syndrome and different genetic mutation severity and phenotypic expression:
    - **Adult patient one**: TSHA-102 was generally well tolerated with no treatment-emergent serious adverse events (SAEs) as of the 35-week assessment, with sustained and new improvement across key efficacy measures at decreased steroid levels six-months post-treatment. The Principal Investigator observed sustained and new improvements across multiple clinical domains including autonomic function, socialization/communication, motor skills and stable seizure events, through 35-weeks post-treatment following completion of steroid taper.
    - **Adult patient two**: TSHA-102 was generally well tolerated with no treatment-emergent SAEs as of the 19-week assessment, with sustained and new improvement across key efficacy measures at 12-weeks post-treatment. The Principal Investigator observed sustained and new improvements across multiple clinical domains including autonomic function, socialization/communication, motor skills and significantly reduced seizures, through 19 weeks post-treatment at decreased steroid levels.
- Enrolled the first patient in cohort two (high dose, n=3) of 1x10^{15} total vg and scheduled dosing for the second quarter of 2024 following Independent Data Monitoring Committee (IDMC) approval of the Company's request to dose escalate immediately, which enabled early advancement to cohort two

REVEAL Phase 1/2 Pediatric Trial (U.S. and U.K.): an open-label, randomized, dose-escalation and dose-expansion study evaluating the safety and

preliminary efficacy of TSHA-102 in pediatric females with Rett syndrome due to *MECP2* loss-of-function mutation. TSHA-102 is administered as a single lumbar intrathecal injection. Part A of the study will focus on determining MAD and MTD in patients aged 5 to 8 years old. Part B is the dose expansion phase and will evaluate TSHA-102 at the MAD or MTD in two age cohorts (5 to 8 years and 3 to 5 years).

- Dosed the second pediatric patient in cohort one (low dose, n=3) of $5.7x10^{14}$ total vg in the first quarter of 2024 following IDMC review of six-week post-treatment assessment data from the first pediatric patient dosed

Anticipated 2024 Milestones

- **REVEAL Adolescent and Adult Trial**
  - Dosing of the first patient in cohort two (high dose) of $1x10^{15}$ total vg scheduled for the second quarter of 2024
  - Update on available safety and efficacy data from completed cohort one (low dose) of $5.7x10^{14}$ total vg expected in mid-2024
  - Initial available safety and efficacy data from cohort two expected in the second half of 2024
- **REVEAL Pediatric Trial**
  - Initial available safety and efficacy data from cohort one (low dose) of $5.7x10^{14}$ total vg expected in mid-2024
  - Initial available safety and efficacy data from cohort two (high dose) of $1x10^{15}$ total vg expected in the second half of 2024

First Quarter 2024 Financial Highlights

Research and Development Expenses: Research and development expenses were $20.7 million for the three months ended March 31, 2024, compared to $12.5 million for the three months ending March 31, 2023. The $8.2 million increase was primarily driven by an increase in Good Manufacturing Practice (GMP) batch activities during the three months ended March 31, 2024, which is representative of the intended commercial manufacturing process for TSHA-102. Additionally, clinical trial expenses increased primarily due to ongoing activities in the REVEAL adolescent/adult and pediatric trials.

General and Administrative Expenses: General and administrative expenses were $7.1 million for the three months ended March 31, 2024, compared to $8.8 million for the three months ended March 31, 2023. The decrease of $1.7 million was due to reduced general and administrative compensation as a result of lower headcount and a reduction in consulting and professional fees.

Net loss: Net loss for the three months ended March 31, 2024, was $24.1 million, or $0.10 per share, as compared to a net loss of $17.6 million, or $0.28 per share, for the three months ended March 31, 2023.

Cash and cash equivalents: As of March 31, 2024, Taysha had $124.0 million in cash and cash equivalents. Taysha 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 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 13745689. The live webcast and replay may be accessed by visiting Taysha's website at https://ir.tayshagtx.com/news-events/events-presentations.

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 Regenerative Medicine Advanced Therapy, Fast Track and Orphan Drug and Rare Pediatric Disease designations from the FDA, Orphan Drug designation from the European Commission and Innovative Licensing and Access Pathway designation from the 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 patients 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 Three Months Ended March 31,	
	2024	**2023**
Revenue	$ 3,411	$ 4,706
Operating expenses:		
Research and development	20,657	12,514
General and administrative	7,084	8,751
Total operating expenses	27,741	21,265
Loss from operations	(24,330)	(16,559)
Other income (expense):		
Change in fair value of warrant liability	(337)	—
Change in fair value of term loan	(1,053)	—
Interest income	1,693	319
Interest expense	(29)	(1,374)
Other expense	(5)	(8)
Total other income (expense), net	269	(1,063)
Net loss	**$ (24,061)**	**$ (17,622)**
Net loss per common share, basic and diluted	$ (0.10)	$ (0.28)
Weighted average common shares outstanding, basic and diluted	231,249,344	63,260,905

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

	March 31, 2024	**December 31, 2023**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 123,980	$ 143,940
Restricted cash	449	449
Prepaid expenses and other current assets	4,168	3,479
Assets held for sale	2,000	2,000
Total current assets	130,597	149,868
Restricted cash	2,151	2,151
Property, plant and equipment, net	10,686	10,826
Operating lease right-of-use assets	9,261	9,582
Other non-current assets	304	304
Total assets	**$ 152,999**	**$ 172,731**
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 10,380	$ 6,366
Accrued expenses and other current liabilities	13,562	12,284
Deferred revenue	14,695	18,106
Total current liabilities	38,637	36,756
Term loan, net	40,512	40,508
Operating lease liability, net of current portion	18,499	18,953
Other non-current liabilities	1,502	1,577

Total liabilities	99,150	97,794
Stockholders' equity		
Preferred stock, $0.00001 par value per share; 10,000,000 shares authorized and no shares issued and outstanding as of March 31, 2024 and December 31, 2023	—	—
Common stock, $0.00001 par value per share; 400,000,000 shares authorized and 187,018,275 and 186,960,193 issued and outstanding as of March 31, 2024 and December 31, 2023, respectively	2	2
Additional paid-in capital	591,166	587,942
Accumulated other comprehensive loss	(251)	—
Accumulated deficit	(537,068)	(513,007)
Total stockholders' equity	53,849	74,937
Total liabilities and stockholders' equity	**$ 152,999**	**$ 172,731**

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