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

High dose TSHA-102 was generally well tolerated with no SAEs or DLTs in two adolescent/adult patients and one pediatric patient as of data cutoff; IDMC approved continued enrollment in cohort two (high dose) across both REVEAL trials; eight patients dosed to date (low dose=4, high dose=4)

Advanced discussions with the FDA on trial design, endpoints and potential use of established natural history dataset for Part B of REVEAL trials, and aligned on a meeting cadence to expedite the development plan for TSHA-102 following initial RMAT Type B meeting

FDA approved use of pivotal TSHA-102 product in REVEAL trials based on successful demonstration of analytical comparability; Company released pivotal product manufactured with the final commercial manufacturing process following Type D CMC meeting

Clinical data from cohort two (high dose) and cohort one (low dose) of both REVEAL trials expected in H1 2025

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

DALLAS, Nov. 13, 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 third quarter ended September 30, 2024, and provided a corporate update.

“We are pleased with the progress made with the FDA on further elucidating the potential regulatory pathway for TSHA-102 as we advanced discussions on the trial design, endpoints and potential use of an established natural history dataset for Part B of our REVEAL trials. Additionally, we aligned on a meeting cadence to expedite the development plan for TSHA-102,” said Sean P. Nolan, Chairman and Chief Executive Officer of Taysha. “We are in a strong position with CMC, having obtained FDA approval to use the pivotal product in our REVEAL trials based on the successful demonstration of analytical comparability. Subsequently, we released the pivotal product manufactured with the final commercial manufacturing process that we intend to use in Part B.”

Mr. Nolan continued, “Clinical data presented from the adult patients with the most advanced stage of the disease treated with the low dose of TSHA-102 indicate a pattern of early clinical improvements and functional gains across multiple domains within four weeks post-treatment that persisted and strengthened over time. As the pediatric data mature, we anticipate that the early clinical improvements and functional gains observed should also persist and strengthen over time in the pediatric patients treated with TSHA-102. We look forward to reporting longer-term data from the low dose cohort and data from the high dose cohort of both REVEAL trials in the first half of 2025. We plan to continue working closely with the FDA through the RMAT mechanism to solidify the regulatory pathway for TSHA-102 based on the totality of data and remain focused on execution as we prepare for what we expect to be an impactful year ahead.”

Recent Corporate and TSHA-102 Program Highlights

- **Completed Regenerative Medicine Advanced Therapy (RMAT) Type B Meeting.** Advanced discussions on regulatory pathway for TSHA-102 following initial RMAT Type B multidisciplinary meeting with the United States (U.S.) Food and Drug Administration (FDA)
    - Advanced discussions with the FDA on trial design, endpoints and potential use of an established natural history dataset for Part B of the REVEAL Phase 1/2 trials
    - Based on FDA feedback from ongoing discussions, the Company intends to focus on objective measures that clinically capture functional gains; the Rett Syndrome Behavior Questionnaire (RSBQ) will not be included as a primary or secondary endpoint in Part B of the REVEAL trials
    - Aligned with the FDA on the Company’s proposed meeting cadence to expedite the development and review of TSHA-102 and on the adequacy of the nonclinical data package submitted to date to support Biologics License Application submission
- **Reached FDA Alignment on Commercial Manufacturing Process.** Completed Type D Chemistry Manufacturing and Controls (CMC) meeting with the FDA regarding TSHA-102
    - The FDA approved use of the pivotal product in the REVEAL trials based on the successful demonstration of analytical comparability between the clinical product and the product derived from the final commercial manufacturing process
    - The Company released the pivotal product manufactured with the final commercial manufacturing process for use in Part B of the REVEAL Phase 1/2 trials
    - The FDA endorsed the intended commercial manufacturing process, proposed analytical methods, and corresponding qualification and validation plans, including mechanism of action potency release assays
- **High Dose of TSHA-102 was Generally Well Tolerated.** TSHA-102 was generally well tolerated with no serious adverse

events (SAEs) or dose-limiting toxicities (DLTs) in the first two adolescent/adult patients as of 20 and nine weeks, respectively, and in the first pediatric patient as of six weeks

- **Continued Enrollment in High Dose Cohorts.** Received Independent Data Monitoring Committee (IDMC) approval to continue with enrollment in cohort two (high dose, $1x10^{15}$ total vector genomes (vg)) across both REVEAL Phase 1/2 trials, following review of available clinical data from the first two adolescent/adult patients and the first pediatric patient treated with the high dose of TSHA-102
    - Dosed the third adolescent/adult patient in cohort two and enrolled the second pediatric patient in cohort two, with dosing scheduled for the current quarter

- **Presented Positive Previously Disclosed Clinical Data on Low Dose TSHA-102.** Clinical data from cohort one (low dose, $5.7x10^{14}$ total vg) in both the ongoing REVEAL Phase 1/2 adolescent/adult trial and the REVEAL Phase 1/2 pediatric trial were presented during an oral presentation at the 9th World Rett Syndrome Congress in October 2024
    - **Adolescent/Adult Trial (n=2):**
        - Generally well tolerated with no SAEs related to TSHA-102 or DLTs as of 52 and 36 weeks for patient one and two, respectively
        - Early and consistent clinical improvements and functional gains demonstrated across multiple clinical domains (fine and gross motor skills, communication/socialization, autonomic function and seizure events) as early as four weeks post-treatment, with sustained and new improvements through 52- and 25-weeks post-treatment for patient one and two, respectively, based on clinician and caregiver assessments and video evidence
    - **Pediatric Trial (n=2):**
        - Generally well tolerated with no SAEs related to TSHA-102 or DLTs as of 22 and 11 weeks for patient one and two, respectively
        - Early and consistent clinical improvements and functional gains demonstrated across multiple clinical domains (fine and gross motor skills, communication/socialization, autonomic function and seizure events) as early as four weeks post-treatment, with sustained and new improvements through 12- and eight-weeks post-treatment for patient one and two, respectively, based on clinician and caregiver assessments and video evidence

- **Presented Biodistribution Data Further Supporting the Clinical Potential of Intrathecal Delivery.** Data from an analysis of 28 non-human primates (NHP) across five studies evaluating AAV9 gene therapy delivery were presented during a poster presentation at the 31st Annual Congress of the European Society of Gene & Cell Therapy in October 2024
    - Both intrathecal and intra-cisterna magna administration showed comparable, consistent and widespread biodistribution of AAV9 vector throughout the brain and spinal cord regions in NHPs
    - Findings reaffirm the clinical potential of intrathecal administration as an effective, safe and minimally invasive delivery approach for broad targeting of the CNS that has potential for outpatient delivery in both children and adults

Anticipated Milestones

REVEAL Adolescent and Adult Trial

- Safety and efficacy data in cohort two (high dose; n=3) and an update on safety and efficacy data in cohort one (low dose; n=2) expected in the first half of 2025

REVEAL Pediatric Trial

- Safety and efficacy data in cohort two (high dose; n=3) and an update on safety and efficacy data in cohort one (high dose; n=2) expected in the first half of 2025

Third Quarter 2024 Financial Highlights

Research and Development Expenses: Research and development expenses were $14.9 million for the three months ended September 30, 2024, compared to $11.8 million for the three months ending September 30, 2023. The $3.1 million increase was driven by an $0.8 million increase in GMP batch activities during the three months ended September 30, 2024, which is representative of the intended commercial manufacturing process for TSHA-102 in Rett syndrome. Additionally, compensation for R&D employees increased as a result of higher headcount, and this was partially offset by lower consultant and contractor expenses.

General and Administrative Expenses: General and administrative expenses were $7.9 million for the three months ended September 30, 2024, compared to $8.6 million for the three months ended September 30, 2023. The decrease of $0.7 million was primarily due to the decrease in issuance costs allocated to the liability-classified 2023 pre-funded warrants associated with the August 2023 financing.

Net loss: Net loss for the three months ended September 30, 2024, was $25.5 million, or $0.1 per share, compared to a net loss of $117.1 million, or $0.93 per share, for the three months ended September 30, 2023. The reduction in net loss in 2024 was primarily due to a non-cash loss of $100.5 million recorded in 2023 from a change in fair value of warrant liability from the 2023 pre-funded warrants associated with the August 2023 financing.

Cash and cash equivalents: As of September 30, 2024, Taysha had $157.7 million in cash and cash equivalents. Taysha expects that its current cash resources will support planned operating expenses and capital requirements into the fourth quarter of 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 13748703. The live webcast and replay may be accessed by visiting Taysha's website.

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, including with respect to functional milestones, 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, the clinical potential of intrathecal administration and our current cash resources supporting our planned operating expenses and capital requirements into the fourth quarter of 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 September 30,		For the Nine Months Ended September 30,	
	2024	2023	2024	2023
Revenue	$ 1,788	$ 4,746	$ 6,311	$ 11,847
Operating expenses:				
Research and development	14,946	11,791	50,676	44,096
General and administrative	7,902	8,589	22,324	23,328
Impairment of long-lived assets	4,838	616	4,838	616
Total operating expenses	27,686	20,996	77,838	68,040
Loss from operations	(25,898)	(16,250)	(71,527)	(56,193)

Other income (expense):				
Change in fair value of warrant liability	75	(100,456)	(67)	(100,456)
Change in fair value of term loan	(1,703)	-	(4,035)	-
Interest income	2,107	1,109	5,240	1,651
Interest expense	(24)	(1,471)	(80)	(4,285)
Other expense	(81)	(19)	(44)	(24)
Total other income (expense), net	374	(100,837)	1,014	(103,114)
Net loss	**$ (25,524)**	**$ (117,087)**	**$ (70,513)**	**$ (159,307)**
Net loss per common share, basic and diluted	$ (0.10)	$ (0.93)	$ (0.29)	$ (1.88)
Weighted average common shares outstanding, basic and diluted	267,824,045	125,700,799	244,052,057	84,630,796

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

	September 30, 2024	December 31, 2023
ASSETS		
Current assets:		
Cash and cash equivalents	$ 157,688	$ 143,940
Restricted cash	449	449
Prepaid expenses and other current assets	3,418	3,479
Assets held for sale	-	2,000
Total current assets	161,555	149,868
Restricted cash	2,151	2,151
Property, plant and equipment, net	7,613	10,826
Operating lease right-of-use assets	8,678	9,582
Other non-current assets	220	304
Total assets	**$ 180,217**	**$ 172,731**
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 4,932	$ 6,366
Accrued expenses and other current liabilities	12,608	12,284
Deferred revenue	11,795	18,106
Total current liabilities	29,335	36,756
Term loan, net	42,971	40,508
Operating lease liability, net of current portion	17,751	18,953
Other non-current liabilities	1,363	1,577
Total liabilities	91,420	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 September 30, 2024 and December 31, 2023	-	-
Common stock, $0.00001 par value per share; 400,000,000 shares authorized and 204,943,306 and 186,960,193 issued and outstanding as of September 30, 2024 and December 31, 2023, respectively	2	2
Additional paid-in capital	674,643	587,942
Accumulated other comprehensive income	(2,328)	-
Accumulated deficit	(583,520)	(513,007)
Total stockholders' equity	88,797	74,937
Total liabilities and stockholders' equity	**$ 180,217**	**$ 172,731**

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