



Taysha Gene Therapies Reports Initial Clinical Data from First Adult Rett Syndrome Patient Dosed in REVEAL Phase 1/2 Trial and Provides Corporate Update with Second Quarter 2023 Financial Results

Data from first adult patient dosed in REVEAL Phase 1/2 trial showed TSHA-102 was well-tolerated with no treatment-emergent serious adverse events (SAEs) as of six-week assessment and improvement in key efficacy measures, including Clinical Global Impression – Improvement (CGI-I), Clinical Global Impression – Severity (CGI-S) and Rett Syndrome Behavior Questionnaire (RSBQ), four weeks post-treatment

Principal Investigator (PI) observed clinical improvement in multiple domains, including autonomic function (sleep and breathing), vocalization, as well as gross motor skills (gained ability to sit unassisted for three minutes) and fine motor skills (gained ability to hold objects), supported by initial clinical data and video evidence

United States (U.S.) Food and Drug Administration (FDA) cleared the Investigational New Drug (IND) application for TSHA-102 in pediatric patients with Rett syndrome

Clinical Trial Application (CTA) submitted to the United Kingdom (U.K.) Medicines and Healthcare products Regulatory Agency (MHRA) for TSHA-102 in pediatric patients with Rett syndrome

Private placement financing ("PIPE") is expected to result in gross proceeds of approximately \$150 million from new and existing investors and, net proceeds from PIPE, along with existing cash and cash equivalents, extends cash runway into the third quarter of 2025

Conference call and live webcast today at 8:30 AM Eastern Time

DALLAS, Aug. 14, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-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), today reported financial results for the second quarter ended June 30, 2023, and provided a corporate update.

"We are pleased with the progress we have made this quarter in the clinical evaluation of our two lead investigational programs. For TSHA-102 in Rett syndrome, we believe the initial safety profile and significant clinical improvements seen in the first adult patient with severe disease four weeks post-treatment reinforces the transformative potential of our gene therapy to address the root cause of Rett syndrome. Importantly, these early data indicate that the miRNA-Responsive Auto-Regulatory Element (miRARE) technology is mediating *MECP2* expression in the CNS on a cell-by-cell basis, supporting the regulatory control of miRARE. We are highly encouraged by the initial data for TSHA-102 and are focused on continuing to explore its therapeutic potential, with the dosing of the second patient expected in the third quarter. We also received FDA clearance to initiate clinical development of TSHA-102 in pediatric patients in the U.S. and have submitted a CTA to the MHRA for TSHA-102 in pediatric patients with Rett syndrome, which will expand our clinical evaluation to children with earlier stages of disease progression," said Sean P. Nolan, Chairman and Chief Executive Officer of Taysha. "For TSHA-120 in GAN, our new comprehensive data analysis utilizing the Disease Progression Model (DPM) was submitted to the FDA, and we plan to review the potential regulatory pathway for TSHA-120 with the Agency expected in the third quarter."

Mr. Nolan continued, "Our successful completion of a \$150 million PIPE from top-tier investors significantly bolsters our balance sheet and we believe highlights the enthusiasm for our TSHA-102 program and the early clinical readout of the first patient treated in the REVEAL trial. By extending our cash runway into the third quarter of 2025, we can focus on execution as we endeavor to deliver on key value-creating milestones."

Dr. Elsa Rossignol, M.D., FRCP, FAAP, Associate Professor Neuroscience and Pediatrics at CHU Sainte-Justine, affiliated to the Université de Montréal, and Principal Investigator of the REVEAL trial added, "The efficacy response observed following treatment with TSHA-102 in the first adult with an advanced stage of Rett syndrome is promising. Prior to treatment, the patient was in a constant state of hypertonia, had limited body movement, required constant back support, and had lost fine and gross motor function early in childhood. Following treatment, we have observed improvements in breathing patterns, vocalization and motor skills. The patient was able to sit unassisted for the first time in over a decade, and she demonstrated the ability to unclasp her hands and hold an object steadily for the first time since infancy. I believe that the patient achieving these milestones so early in treatment, coupled with the improvements in breathing patterns and quality of sleep that we have observed, are highly encouraging and support the potential of TSHA-102. I am honored to work with the Rett syndrome community and help patients and families suffering from this devastating disease."

Rett syndrome is a rare neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene. The disorder is characterized by intellectual disabilities, loss of communication, seizures, slowing and/or regression of development, motor and respiratory impairment, and shortened life expectancy. 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 UK.

Recent Corporate Highlights

\$150 million private placement financing strengthens balance sheet and, together with existing cash and cash equivalents, extends cash runway into the third quarter of 2025

- Private placement led by new investor, RA Capital Management, with participation from a large institutional investor, PBM Capital, RTW Investments, LP, Venrock Healthcare Capital Partners, TCGX, Acuta Capital Partners, Kynam Capital Management, LP, Octagon Capital, Invus, GordonMD® Global Investments LP, and B Group Capital
- Cash runway expected to fund operational plans into the third quarter of 2025
- Net proceeds to primarily fund clinical development of TSHA-102 in Rett syndrome and provide support for program

activities for TSHA-120 in GAN, working capital, and other general corporate purposes

Recent Clinical Highlights

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 platform designed to mediate levels of *MECP2* in the CNS on a cell-by-cell basis without risk of overexpression. 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.

TSHA-102 is being evaluated in the [REVEAL Phase 1/2 trial](#), a first-in-human, open-label, randomized, dose-escalation and dose-expansion study evaluating the safety and preliminary efficacy of TSHA-102 in adult females with Rett syndrome due to *MECP2* loss-of-function mutation. Primary efficacy endpoints are patient assessments by clinicians using the Clinical Global Impressions Scale – Improvement (CGI-I), Rett Syndrome Hand Function Scale, and Revised Motor Behavior Assessment (R-MBA). Secondary endpoints include patient assessments by clinicians and caregivers using the Clinical Global Impressions Scale – Severity (CGI-S), the Rett Syndrome Behavior Questionnaire (RSBQ) and other clinical assessment scales.

Results from the first adult patient dosed in cohort one (low dose) with TSHA-102 in the REVEAL Phase 1/2 trial:

- Well-tolerated safety profile with no treatment-emergent SAEs as of six-week assessment post-treatment
- The following were demonstrated in key efficacy measures four weeks post-treatment:
 - Clinical Global Impressions – Improvement (CGI-I) scale adapted to Rett syndrome, a clinician-reported assessment of overall improvement using a seven-point scale (one=“very much improved” and seven=“very much worse”), demonstrated a score of two indicating “much improved”
 - Clinical Global Impressions – Severity (CGI-S) scale, a clinician-reported assessment of overall severity of a patient’s illness using a seven-point scale, demonstrated a one-point improvement from the baseline score of six (“severely ill”) to a score of five (“markedly ill”)
 - Rett Syndrome Behavior Questionnaire (RSBQ), a 45-item questionnaire to assess Rett syndrome characteristics, demonstrated a total score improvement of 23 points from the baseline score of 52 to a score of 29
- Seizure diary demonstrated no quantifiable seizure events through week five post-treatment
- No marked changes observed four weeks post-treatment in the Revised Motor Behavior Assessment (R-MBA), a 24-question clinician-reported scale measuring disease behaviors of Rett syndrome
- Initial efficacy data and clinical observations supported by video evidence from PI six-weeks post-treatment indicate clinical improvements in multiple domains, including:
 - Autonomic function with improvements in breathing patterns and sleep quality/duration, including the normalization of night-time behavior
 - Vocalization with increased social interest
 - Gross motor skills with the gained ability to sit unassisted for three minutes
 - Fine motor skills and hand function with the gained ability to hold an object, unclasp her hands and use her fingers to touch a screen
- Further updates on available clinical data expected quarterly
- Dosing of second patient cleared by the Independent Data Monitoring Committee (IDMC) and expected in Q3 2023, with continued dosing of adult patients in second half of 2023
- U.S. FDA cleared the IND application for TSHA-102 in pediatric patients with Rett syndrome
- CTA submitted to U.K. MHRA for TSHA-102 in pediatric patients with Rett syndrome

TSHA-120 for giant axonal neuropathy (GAN): a self-complementary intrathecally delivered AAV9 gene therapy in clinical evaluation for GAN, an ultra-rare inherited genetic neurodegenerative disorder with no approved treatments. TSHA-120 has received Orphan Drug and Rare Pediatric Disease designations from the FDA and has been granted Orphan Drug designation from the European Commission.

- At R&D Day in June 2023, Taysha provided an overview of new comprehensive data analysis and development of disease progression model (DPM), which the Company believes has the potential to address FDA feedback regarding the heterogeneity of GAN and effort-dependent nature of MFM32 as the primary endpoint in an unblinded study
- New comprehensive data analysis utilizing the DPM submitted as meeting request to the FDA; feedback for a potential regulatory pathway for TSHA-120 expected in Q3 2023

- FDA feedback on CMC module 3 amendment concluded that the analytical data is sufficient to support the comparability of pivotal lot and release for use in clinical studies

Second Quarter 2023 Financial Highlights

Research and Development Expenses: Research and development expenses were \$19.8 million for the three months ended June 30, 2023, compared to \$23.5 million for the three months ending June 30, 2022. The \$3.7 million decrease was due to lower compensation expense as a result of reduced headcount and fewer manufacturing batches and raw material purchases.

General and Administrative Expenses: General and administrative expenses were \$6.0 million for the three months ended June 30, 2023, compared to \$9.9 million for the three months ended June 30, 2022. The decrease of \$3.9 million was due to reduced general and administrative compensation as a result of lower headcount, consulting and professional fees.

Net loss: Net loss for the three months ended June 30, 2023 was \$24.6 million or \$0.38 per share, as compared to a net loss of \$34.1 million, or \$0.85 per share, for the three months ended June 30, 2022.

Cash and cash equivalents: As of June 30, 2023, Taysha had \$45.1 million in cash and cash equivalents. Taysha expects to receive gross proceeds of \$150 million from the Private Placement, which is expected to close August 16, 2023, before deducting placement agent commissions and offering expenses. The net proceeds from the private placement, combined with the current cash and cash equivalents, are expected to fund its operational plans and capital requirements into the third quarter of 2025.

Conference Call and Webcast Information

Taysha management will hold a conference call and webcast today at 8:30 a.m. ET 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 13740092. The live webcast can be accessed here: https://viaid.webcasts.com/starthere.jsp?ei=1624983&tp_key=25b742b70a. An archived version of the webcast will be available for 30 days and can be accessed by visiting Taysha's website at <https://ir.tayshagtx.com/news-events/events-presentations>.

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. Together, we leverage our fully integrated platform with a goal 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 the reproducibility and durability of any favorable results initially seen in our first patient dosed in the REVEAL trial and 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, statements associated with the timing, size and completion of the Private Placement, the forecast of our cash runway and the Company's expectations regarding funding, operating and working capital expenditures. 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, 2022, and our Quarterly Report on Form 10-Q for the quarter ended March 31, 2023, both of which are 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
Balance Sheet Data
(in thousands, except share and per share data)
(Unaudited)

	June 30, 2023	December 31, 2022
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 45,083	\$ 87,880
Prepaid expenses and other current liabilities	9,032	8,537
Total current assets	54,115	96,417

Restricted cash	2,637	2,637
Property, plant and equipment, net	14,139	14,963
Operating lease right-of-use assets	10,348	10,943
Other non-current assets	304	1,316
Total assets	\$ 81,543	\$ 126,276

LIABILITIES AND STOCKHOLDERS' (DEFICIT) EQUITY

Current liabilities:		
Accounts payable	\$ 10,766	\$ 10,946
Accrued expenses and other current liabilities	19,631	18,287
Deferred revenue	26,909	33,557
Total current liabilities	50,641	62,790
Deferred revenue, net of current portion	6,212	
Term loan, net	38,354	37,967
Operating lease liability, net of current portion	19,528	20,440
Other non-current liabilities	3,922	4,130
Total liabilities	118,657	125,327

Stockholders' (deficit) equity

Preferred stock, \$0.00001 par value per share; 10,000,000 shares authorized and no shares issued and outstanding as of June 30, 2023 and December 31, 2022

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Common stock, \$0.00001 par value per share; 200,000,000 shares authorized and 64,432,637 and 63,207,507 issued and outstanding as of June 30, 2023, and December 31, 2022, respectively

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Additional paid-in capital	406,546	402,389
Accumulated deficit	(443,661)	(401,441)
Total stockholders' (deficit) equity	(37,114)	949
Total liabilities and stockholders' (deficit) equity	\$ 81,543	\$ 126,276

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

	For the three months ended June 30, 2023	For the three months ended June 30, 2022	For the six months ended June 30, 2023	For the six months ended June 30, 2022
Revenue:				
Service Revenue	\$ 2,395	\$ -	\$ 7,101	\$ -
Operating expenses:				
Research and development	19,791	23,506	32,305	61,688
General and administrative	5,988	9,867	14,739	21,336
Total operating expenses	25,779	33,373	47,044	83,024
Loss from operations	(23,384)	(33,373)	(39,943)	(83,024)
Other income (expense):				
Interest Income	223	27	542	41
Interest expense	(1,440)	(743)	(2,814)	(1,415)
Other expense	3	(3)	(5)	(11)
Total other income (expense)	(1,214)	(719)	(2,277)	(1,385)
Net loss	\$ (24,598)	\$ (34,092)	\$ (42,220)	\$ (84,409)
Net loss per common share, basic and diluted	\$ (0.38)	\$ (0.85)	\$ (0.66)	\$ (2.16)
Weighted average common shares outstanding, basic and diluted	64,244,531	40,142,403	63,755,435	39,163,996

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Source: Taysha Gene Therapies, Inc.