UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 25, 2024

Taysha Gene Therapies, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-39536**	**84-3199512**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

3000 Pegasus Park Drive, Suite 1430
Dallas, Texas **75247**
(Address of Principal Executive Offices) **(Zip Code)**

(214) 612-0000
(Registrant's telephone number, including area code)

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.00001 par value	TSHA	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition.

The information contained in the section titled "Preliminary Financial Information" in Exhibit 99.2 to this Current Report on Form 8-K is hereby incorporated into this Item 2.02 by reference.

The information set forth in this Item 2.02 of this Current Report on Form 8-K is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "***Exchange Act***"), or otherwise subject to the liabilities of that section, nor shall it be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

On June 25, 2024, Taysha Gene Therapies, Inc. (the "***Company***") issued a press release announcing that it had commenced an underwritten public offering of shares of its common stock and pre-funded warrants (the "***Offering***") pursuant to an effective shelf registration statement on Form S-3 (File No. 333-260069) (the "***Registration Statement***") and a related prospectus and prospectus supplement, in each case filed with the Securities and Exchange Commission (the "***SEC***"). A copy of the press release is attached hereto as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

In connection with the Offering, the Company filed a preliminary prospectus supplement to the Registration Statement on June 26, 2024, the date of its first use. The preliminary prospectus supplement described certain elements of the Company's business strategy, preclinical and clinical pipeline, the Company's cash position as of May 31, 2024 and certain updated and additional risk factors, including those attached as Exhibit 99.2 and incorporated by reference herein.

The disclosures on this Current Report on Form 8-K shall not constitute an offer to sell or the solicitation of an offer to buy these securities, nor shall there be any sale of these securities in any state or jurisdiction in which such an offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.

Forward-Looking Statements

This Current Report on Form 8-K 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 Company's anticipated public offering, including the uncertainties related to market conditions and the completion of the public offering on the anticipated terms, if at all. 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 the Company's business are described in detail in its SEC filings, including in the Company's Annual Report on Form 10-K for the full-year ended December 31, 2023, and the Company's Quarterly Report on Form 10-Q, which is available on the SEC's website at www.sec.gov. Additional information will be made available in other filings that the Company makes from time to time with the SEC. These forward-looking statements speak only as of the date hereof, and the Company disclaims any obligation to update these statements except as may be required by law.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Exhibit Description
99.1	Press Release, dated June 25, 2024.
99.2	Additional Business Information.
104	Cover Page Interactive Data File (the cover page XBRL tags are embedded within the inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Taysha Gene Therapies, Inc.

By: /s/ Kamran Alam
Kamran Alam
Chief Financial Officer

Date: June 26, 2024

Taysha Gene Therapies Announces Proposed Public Offering of Common Stock and Pre-Funded Warrants

Dallas – June 25, 2024—Taysha Gene Therapies, Inc. (Nasdaq: TSHA), 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 announced that it has commenced an underwritten public offering of up to $75 million of shares of its common stock and, in lieu of common stock to certain investors that so choose, pre-funded warrants to purchase shares of its common stock. All of the securities will be offered by Taysha. Taysha also intends to grant the underwriters a 30-day option to purchase up to an additional 15% of the shares of its common stock offered in the public offering under the same terms and conditions (including shares underlying the pre-funded warrants). The offering is subject to market conditions, and there can be no assurance as to whether or when the offering may be completed, or the actual size or terms of the offering.

Jefferies and Goldman Sachs & Co. LLC are acting as joint book-running managers for the offering, and Cantor is also serving as a book-running manager for the proposed offering.

A shelf registration statement relating to the securities offered in the public offering described above was filed with the Securities and Exchange Commission (the "SEC") on October 5, 2021, and declared effective by the SEC on October 14, 2021. The offering will be made only by means of a written prospectus and prospectus supplement that form a part of the registration statement. A preliminary prospectus supplement and accompanying prospectus relating to the offering will be filed with the SEC and will be available on the SEC's website at www.sec.gov. Copies of the preliminary prospectus supplement and the accompanying prospectus, when available, may also be obtained by contacting Jefferies LLC, Attention: Equity Syndicate Prospectus Department, 520 Madison Avenue, New York, NY 10022, or by telephone at (877) 821-7388, or by e-mail at Prospectus_Department@Jefferies.com; or Goldman Sachs & Co. LLC, Attention: Prospectus Department, 200 West Street, New York, NY 10282, by telephone at (866) 471-2526, or by email at Prospectus-ny@ny.email.gs.com.

This press release shall not constitute an offer to sell or the solicitation of an offer to buy the securities being offered, nor shall there be any sale of the securities being offered in any state or other jurisdiction in which such offer, solicitation or sale would be unlawful prior to the registration or qualification under the securities laws of any such state or other jurisdiction.

About Taysha Gene Therapies

Taysha Gene Therapies (Nasdaq: TSHA) is a clinical-stage biotechnology company focused on advancing 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.

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 and Taysha's other product candidates, to positively impact

quality of life and alter the course of disease in the patients Taysha seeks to treat, its research, development and regulatory plans for its product candidates, and its anticipated public offering, including the uncertainties related to market conditions and the completion of the public offering on the anticipated terms, if at all. 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 Taysha's business are described in detail in its SEC filings, including in Taysha's 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 Taysha makes from time to time with the SEC. These forward-looking statements speak only as of the date hereof, and Taysha disclaims any obligation to update these statements except as may be required by law.

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Company Overview

We are a clinical-stage biotechnology company focused on advancing AAV-based gene therapies for the treatment of severe monogenic diseases of the central nervous system, or CNS. Our lead clinical program TSHA-102 is in development for the treatment of 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, we aim to address severe unmet medical needs and dramatically improve the lives of patients and their caregivers. Our management team has proven experience in gene therapy development and commercialization. We leverage this experience, our manufacturing process and a clinically and commercially proven AAV9 capsid in an effort to rapidly translate treatments from bench to bedside.

We are evaluating TSHA-102 in the REVEAL Phase 1/2 adolescent and adult trial, which is 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. The trial is taking place in Canada and the United States. We dosed the first two adult patients with Rett syndrome in 2023. TSHA-102 was generally well-tolerated with no serious adverse events, or SAEs, related to TSHA-102 or dose-limiting toxicities, or DLTs, as of the 52-week assessment post-treatment for patient one and 36-week assessment post-treatment for patient two. The independent data monitoring committee, or IDMC, meeting to review the clinical data from the first two adult patients and the first pediatric patient took place in February 2024. The IDMC approved our request to proceed to earlier dose escalation in the adolescent and adult trial, enabling early advancement to cohort 2. The first patient in cohort 2 (high dose, $1x10^{15}$ total vg) was dosed in the second quarter of 2024. We expect to report initial available safety and efficacy data from cohort 2 (high dose, $1x10^{15}$ total vg) in the second half of 2024.

We are also evaluating TSHA-102 in the REVEAL Phase 1/2 pediatric trial, which is 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. The trial is taking place in the United States. We submitted submitted an IND application for pediatric patients with Rett syndrome to the U.S. Food and Drug Administration, or the FDA, for TSHA-102 early in the third quarter of 2023.

We have received orphan drug designation and rare pediatric disease designation from the FDA and orphan drug designation from the European Commission for TSHA-102 for the treatment of Rett syndrome. We also received Fast Track Designation from the FDA for TSHA-102 for the treatment of Rett syndrome. We also received Clinical Trial Authorisation, or CTA, clearance from the United Kingdom’s Medicines and Healthcare Products Regulatory Agency, or U.K. MHRA, in early 2024 for pediatric patients with Rett syndrome. In February 2024, we received Innovative Licensing and Access Pathway, or ILAP, designation for TSHA-102 from the 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. In April 2024, the FDA granted Regenerative Medicine Advanced Therapy, or RMAT, designation for TSHA-102 in Rett syndrome. 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 (5.7x1014 total vg) across the REVEAL Phase 1/2 adolescent and adult trial and the REVEAL Phase 1/2 pediatric trial. RMAT designation was designed to expedite the development and review of regenerative medicine therapies. 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. Sponsor companies receiving RMAT designation can benefit from increased interactions with the FDA involving senior managers, with the goal of expediting drug development.

Our Pipeline

We are focused on discovering, developing and commercializing gene therapies for the treatment of monogenic diseases of the CNS in both rare and large patient populations. Our primary focus is advancing our lead clinical program in Rett syndrome, while our pipeline of CNS programs offers the potential for additional development opportunities in the future. The stage of development of our Rett syndrome program, including the progress in our ongoing clinical trials, is represented in the below table:

REVEAL Phase 1/2 Clinical Trials Update

We currently are conducting two Phase 1/2 clinical trials for TSHA-102: an adolescent/adult study in the United States and Canada and a pediatric study in the United States. In addition, approval has been granted to expand the pediatric study into the United Kingdom. The trials are described below:

Study	Primary Study Objectives	Study Population	TSHA-102 Single IT Dosing Regimen	Active Geographies
REVEAL Phase 1/2 Adolescent and Adult Trial	To assess the safety, tolerability, and preliminary efficacy of TSHA-102 as a single lumbar IT administration	Adolescent and adult females with Rett syndrome, ≥12 years old	Part A: Cohort 1: 5.7 x 10^{14} vg IT Cohort 2: 1.0 x 10^{15} vg IT Part B: Dose Expansion with MTD or MAD	Canada, US
REVEAL Phase 1/2 Pediatric Trial	To assess the safety, tolerability, and preliminary efficacy of TSHA-102 as a single lumbar IT administration	Pediatric females with Rett syndrome Part A: 5-8 years old Part B: 3-8 years old	Part A: Cohort 1: 5.7 x 10^{14} vg IT Cohort 2: 1.0 x 10^{15} vg IT Part B: Dose Expansion with MTD or MAD in two age cohorts	US, UK

IT – Intrathecal; MTD – Maximum Tolerated Dose; MAD – Maximum Administered Dose.

We dosed the first adult patient with Rett syndrome in May 2023. The second adult patient was dosed in September 2023. We dosed the first pediatric patient with Rett syndrome in the Phase 1/2 REVEAL pediatric trial in December 2023, and the second pediatric patient was dosed in the first quarter of 2024. In early 2024, we announced that the U.K. MHRA authorized the CTA for TSHA-102 in pediatric patients with Rett syndrome, enabling expansion of our ongoing pediatric trial into the United Kingdom. In February 2024, we announced the expansion of the ongoing REVEAL Phase 1/2 adolescent and adult trial in Canada into the United States following submission of the adolescent and adult trial protocol to the FDA.

Cohort 1, which evaluates the low dose of TSHA-102 of $5.7x10^{14}$ total vg, is considered complete for both REVEAL trials. Two adult patients have been dosed in cohort 1 in the REVEAL adolescent and adult trial, and TSHA-102 was generally well-tolerated with no SAEs related to TSHA-102 or DLTs as of the 52-week assessment post-treatment for patient one and 36-week assessment post-treatment for patient two. Following review of available clinical data from the first two adult patients and first pediatric patient showing that TSHA-102 was generally well-tolerated, and in light of the potential for improved benefit at the higher dose ($1x10^{15}$ total vg), in February 2024, the Independent Data Monitoring Committee, or IDMC, approved our request to proceed to earlier dose escalation in the adolescent and adult trial, enabling earlier advancement to cohort 2 evaluating the $1x10^{15}$ total vg dose. The first patient in cohort 2 of the adolescent and adult trial was dosed in the second quarter of 2024.

Additionally, two pediatric patients have been dosed in cohort 1 in the REVEAL pediatric trial, and TSHA-102 was generally well-tolerated with no SAEs related to TSHA-102 or DLTs as of the 22-week assessment post-treatment for patient one and 11-week assessment post-treatment for patient two. There were two SAEs reported in the second pediatric patient that were not deemed treatment related. Both were related to underlying disease and one was also attributed to immunosuppression, and both have resolved. In May 2024, the IDMC approved our request to proceed to earlier dose escalation in the REVEAL pediatric trial, enabling earlier advancement to

cohort 2 evaluating the $1x10^{15}$ total vg dose, with dosing to occur following IDMC review of the 42-day safety data from the patient treated with the high dose of TSHA-102 in the adolescent and adult trial. We expect to dose the first pediatric patient in cohort 2 in the third quarter of 2024. We expect to report initial available safety and efficacy data from cohort 2 of both the adolescent and adult trial and the pediatric trial in the second half of 2024.

The maximum tolerated dose, or MTD, or maximum administered dose, or MAD, established in Part A will be administered during dose expansion in Part B. Data from Part A will be assessed by regulatory agencies and the IDMC to determine key elements of Part B of the study, including efficacy endpoints, study duration and the MTD or MAD.

TSHA-102 REVEAL Phase 1/2 Adolescent / Adult Trial Safety and Efficacy Summary

Efficacy endpoints include patient assessments performed by clinicians, including the Clinical Global Impressions Scale – Improvement, or CGI-I, the Clinical Global Impressions Scale – Severity, or CGI-S, Rett Syndrome Hand Function Scale, or RSHFS, and Revised Motor Behavior Assessment, or R-MBA. Additional efficacy endpoints also include patient assessments by caregivers, including Parental Global Impressions Improvement, or PGI-I, the Rett Syndrome Behavior Questionnaire, or RSBQ, and seizure diaries.

Overview of Cohort 1 Patients and Results

The first adult patient, a 20-year-old female at the time of dosing, has the most advanced stage of Rett syndrome, Stage IV, with a genetic change consisting of a large deletion within the *MECP2* gene that is known to cause Rett syndrome. This patient's phenotypic manifestation is severe. She lost the ability to walk, stand, and sit without support by age eight (non-ambulatory, wheelchair bound, limited movements of her lower extremities), lost fine motor and hand function by age six (unable to grasp and hold objects of any size, with essentially no function in non-dominant hand) and speak around age six (non-verbal, minimal vocalizations). She experienced frequent apnea and hyperventilation episodes by age three and has a history of seizures since the age of five. Per the Principal Investigator, or PI, the first adult patient's baseline reported seizure frequency was approximately two to four seizures per year.

In the first adult patient, TSHA-102 was generally well-tolerated with no SAEs related to TSHA-102 or DLTs as of the 52-week assessment post-treatment. Per the protocol, prophylactic immunosuppressant therapy began seven days prior to TSHA-102 administration. The first adult patient's steroid taper was completed by week 36, and her sirolimus taper was completed by week 43. At week 52 post-treatment, the first adult patient demonstrated sustained and new improvements across multiple clinical domains compared to baseline after the completion of her immunosuppression taper. Specifically, the PI reported that the patient sustained improvements in motor function, with the gained ability to kick her legs against gravity and sit unassisted for the first time in over a decade, and sustained improvements in fine motor and hand function with gained function in her non-dominant hand. Additionally, she could open her hands, dissociate her fingers, scratch her nose and touch a screen through week 52 post-treatment. The PI reported sustained improvements in communication and socialization at week 52 post-treatment as the patient was more alert and socially interactive, with increased communication using vocalizations. Caregivers reported an enhanced ability to use an eye-gaze driven communication device at week 25, which she had not expressed interest in before treatment. The first adult patient also demonstrated sustained improvements in autonomic function at week 52 post-treatment, including improved breathing patterns with infrequent hyperventilation and fewer breath holding spells compared to before treatment, normalized sleep/night-time behaviors with the ability to sleep through the night for the first time in 20 years, and improved circulation with the patient's hands and feet restored to normal temperature and color (whereas before treatment, her hands and feet were usually cold and blue). The PI also reported that the first patient's seizures were overall well-controlled through week 52 following treatment at lower levels of anti-seizure medication, relative to baseline, and the patient no longer experienced unprovoked seizures. The PI's clinical observations are supported by clinical, caregiver and video evidence.

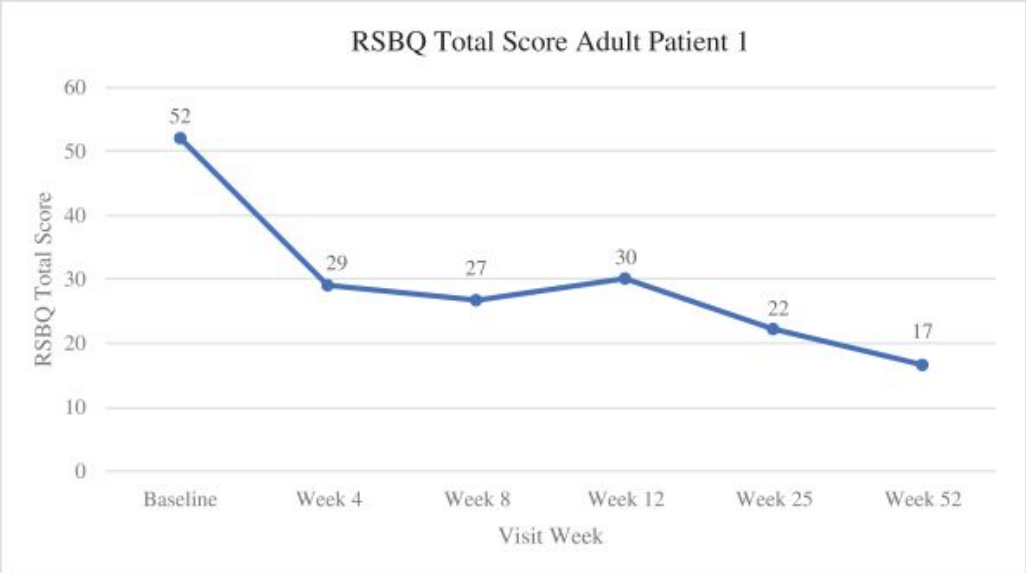
The second adult patient, a 21-year-old female at the time of dosing, has the most advanced stage of Rett syndrome, Stage IV, with a missense mutation in the *MECP2* gene, which has been reported to cause Rett syndrome. This patient's phenotypic manifestation is milder than the first adult patient. Prior to treatment, she had partial loss of ambulation (able to walk/stand without support, but she had impaired gait and balance that developed at age 18) and impaired fine motor and hand function (significant stereotypies that emerged by age three, and she mostly held her hands firmly together, with weak ability to reach and grasp objects). She has been mostly nonverbal since the age of two and experienced frequent hyperventilation episodes by age three. She had a history of seizures since the age of 10. Per the PI, the second adult patient's baseline reported seizure frequency was approximately two to four seizures per week.

In the second adult patient, TSHA-102 was generally well-tolerated with no SAEs related to TSHA-102 or DLTs as of the 36-week assessment post-treatment. The PI reported that the second adult patient demonstrated sustained and new improvements across multiple clinical domains compared to baseline following completion of her steroid taper at week 25 post-treatment. Her sirolimus taper was completed by week 31. She sustained improvements in motor skills, with a reduction in hand stereotypies (repetitive, purposeless hand movements and a diagnostic hallmark of Rett syndrome) for the first time since regression at age three. Before treatment, the patient mostly held her hands firmly together, and post-treatment, she displays less forceful hand wringing and more open and relaxed hands. The second patient also sustained improvements in communication and socialization through week 25, including increased response to spoken words and eye contact compared to baseline. The PI also reported sustained improvements in autonomic function, with improvements in breathing dysrhythmia, including hyperventilation and reduced apneic spells, and circulation at week 25 post-treatment, evident by the restoration of the patient's hands and feet to normal temperature and color compared to the cold and blue appearance before treatment. Additionally, the second adult patient demonstrated new improvements in gross motor skills at week 25 post treatment, with improved posture and stability. Notably, she also demonstrated pronounced improvements in seizure frequency at week 25, with a significant reduction in seizures at 25% lower levels of anti-seizure medication, relative to the baseline seizure frequency of two to four seizures per week. Following treatment with TSHA-102, the second patient had a single seizure event, with 8.5 months reported seizure free as of week 36 post-treatment.

Adult Patient 1 Efficacy Data (Cohort 1)

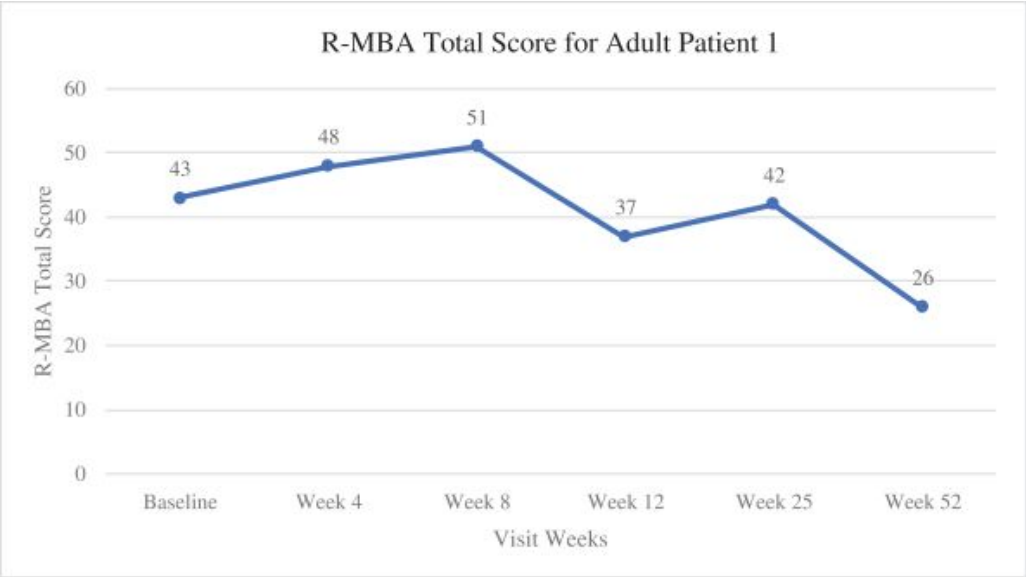
The first adult patient showed clinically significant improvement in CGI-S from a score of six (severely ill) at baseline to a score of five (markedly ill) in this measure four weeks post-TSHA-102 administration, which was sustained through week 52 post-treatment. Similarly, the patient demonstrated sustained improvement in CGI-I post-TSHA-102 administration with a score of three (minimally improved) at week 52 and new improvement in PGI-I with a score of one (considerably better) as of the week 52 assessment post-TSHA-102 administration.

The first adult patient demonstrated continued improvement in RSBQ Total Score at week 52 post-TSHA-102 administration as depicted in the graph below.



A 35-point improvement was reported in RSBQ Total Score at week 52 compared to baseline, which was driven by improvements in hand behaviors, general mood, breathing, repetitive face movements, body rocking and expressionless face, nighttime behaviors and fear and anxiety.

The first adult patient demonstrated continued improvement in R-MBA Total Score at week 52 post-TSHA-102 administration as depicted in the graph below.



A 17-point improvement was reported in R-MBA Total Score at week 52 compared to baseline, which was driven by improvements in motor dysfunction, functional skills, social skills and respiratory behaviors.

Per the seizure diary and caregiver reports, the first adult patient demonstrated stable seizure events relative to baseline through week 52 post-treatment, based on caregiver-reported medical history, and seizures are confined to periods where phenytoin level declines to <50 mmol/L (previously <100 mmol/L). The first adult patient had been on phenytoin as antiepileptic therapy prior to treatment, which she has continued following TSHA-102. Prior to treatment and per the patient's medical history, she required phenytoin levels of >100 µmol/L to control her seizures. The first adult patient had seizures prior to TSHA-102 administration on day –8 and day –7, and post-administration she had seizures on days 45-49 and day 82 associated with lower than target phenytoin levels. Specifically, the seizures on days 45-49 corresponded with a phenytoin level of 45.9 µmol/L, and the seizure on day 82 corresponded with a phenytoin level of 35.9 umol/L.

Loss of hand function is a hallmark characteristic of Rett syndrome and a key area of concern for caregivers. It impacts a patient's ability to communicate and impedes daily activities, which ultimately limits independence. The RSHFS is a scale designed to evaluate hand function in patients with Rett syndrome. Hand function is evaluated by an experienced independent physical therapist with expertise in evaluating hand function in patients with Rett syndrome. Sessions are videotaped in which the patient's caregiver offers the patient both large (e.g. a toy, cup, or spoon) and small (e.g. a grape or small piece of sandwich) objects so that she may demonstrate her ability to grasp, pick up, and hold the objects. The independent physical therapist then codes the demonstrated hand function in each video at the demonstrated level of hand function, ranging from no active grasping of any objects to independent grasping and function.

The first adult patient showed an improvement in the RSHFS at 25 weeks post-TSHA-102 administration as depicted in the tables below. As of week 25 following treatment, the first adult patient was using her non-dominant hand for some basic grasping whereas before treatment, she was not able to grasp at all. As of the week 25 assessment, her dominant hand function improved from baseline with the demonstrated ability to grasp two different objects (spoon and toy) rather than just one object (spoon). These clinical observations reported by the independent physical therapist are supported by video evidence. The RSHFS for week 52 was not completed as of the cutoff date.

Dominant Hand		
Visit	**Best Level for Large Object**	**Number of Objects Grasped**
Baseline	3	1
Week 8	2	2
Week 10	3	2
Week 11	3	2
Week 25	3	2

Non-Dominant Hand		
Visit	**Best Level for Large Object**	**Number of Objects Grasped**
Baseline	NA*	0
Week 8	1	0
Week 10	2	2
Week 11	3	2
Week 25	2	1

***RSHFS for patient 1's non-dominant hand was not assessed at baseline**

Best Level Scoring Criteria:

Level	Description
1	No Active Grasping
2	Assisted to Grasp (hold 2 seconds)
3	Hold (at least 2 seconds)
4	Independent Grasp (pick up and hold)

Adult Patient 2 Efficacy Data (Cohort 1)

While the two adult patients dosed in cohort 1 in our REVEAL trial both have the most advanced stage of Rett syndrome, Stage IV, they possess different genetic backgrounds and mutation types, which manifest in different phenotypes and clinical severity.

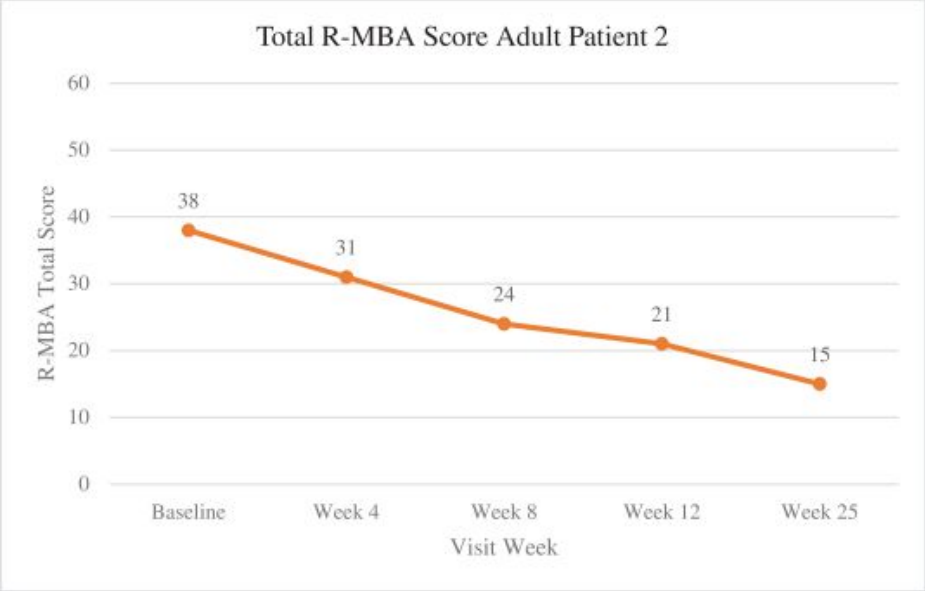
While there was no change at week 25 post-TSHA-102 administration in the second adult patient's CGI-S

baseline score of four (moderately ill), her CGI-I and PGI-I scores showed sustained improvement at week 25 (score of three, minimally improved and a little better, respectively) post-TSHA-102 administration.

An increase in RSBQ Total Score was reported at week 25 post-TSHA-102 administration as depicted in the graph below.

A two-point increase was reported in the RSBQ Total Score at week 25 compared to baseline. Improvements in RSBQ were reported by caregivers in breathing and general mood. However, there was an increase in hand behaviors and fear and anxiety compared to baseline, impacting the total score.

The second adult patient demonstrated continued improvement in the R-MBA Total Score at week 25 post-TSHA-102 administration as depicted in the graph below.



A 23-point improvement was reported in the R-MBA Total Score at week 25 compared to baseline. Improvements were reported in all domains, including social skills, respiratory behaviors, seizures, functional skills, motor dysfunction, aberrant behavior, and truncal rocking and stereotypic hand movements.

Per the seizure diary and caregiver reports, the second adult patient demonstrated significantly reduced seizure events relative to baseline through 36 weeks post-treatment at 25% lower levels of anti-seizure medication, based on caregiver-reported medical history. Pre-treatment, the second adult patient had approximately two to four seizures per week, and there has been a significant reduction in seizures post-treatment with TSHA-102 as of the 36-week visit. Post-treatment, the second adult patient had a single seizure event on day 13. The seizure was an unknown type, with motor manifestations and lasted less than one minute duration. The patient has been seizure-free for eight and a half months as of the week 36 post-treatment time point.

Hand function in the dominant hand for the second adult patient is challenging to interpret due to inconsistency in the video recording. At the week 25 post-treatment assessment, the second adult patient's dominant hand received a hand function score of four, an independent grasp (pick up and hold) and was able to grasp two objects. There was no change reported in the patient's non-dominant hand score at week 25 compared to baseline. However, the rater reported that the patient displayed nice opening of her non-dominant hand and the ability to grasp three objects weakly (hold for about one second). These clinical observations reported by the independent physical therapist are supported by video evidence.

Dominant Hand		
Visit	**Best Level for Large Object**	**Number of Objects Grasped**
Baseline*	NE	0
Week 4*	NE	0
Week 8	4	3
Week 12*	NE	1
Week 25	4	2

Non-Dominant Hand		
Visit	**Best Level for Large Object**	**Number of Objects Grasped**
Baseline*	1	0
Week 4*	1	0
Week 8	1	0
Week 12*	1	0
Week 25	1	0

Best Level Scoring Criteria:

Level	Description
1	No Active Grasping
2	Assisted to Grasp (hold 2 seconds)
3	Hold (at least 2 seconds)
4	Independent Grasp (pick up and hold)

** Video evaluation at baseline, week 4 and week 12 - due to inadequate initial caregiver training and inconsistency by caregiver when recording video assessment, the assessment was not conducted as defined in the guidelines. Therefore the data may not be accurately represented.*

TSHA-102 REVEAL Phase 1/2 Pediatric Trial Safety and Efficacy Summary

Efficacy endpoints include patient assessments performed by clinicians, including CGI-I, CGI-S, R-MBA and Adapted Mullen Scales for Early Learning, or MSEL-A. Additional efficacy endpoints also include patient assessments by caregivers, including PGI-I, RSBQ and seizure diaries.

Overview of Cohort 1 Patients and Results

The first pediatric patient, a six-year-old female at the time of dosing, has Stage III Rett syndrome, with a deletion within her *MECP2* gene that manifests as a moderate phenotype. The patient's severity is evident by her clinical presentation at baseline. Prior to treatment, the patient was non-ambulatory (unable to walk without assistance), with impaired gross motor function (could sit unassisted for only up to 30 seconds and stand with support by age three) and impaired fine motor and hand function (lost the ability to use eating utensils at one and half years old and lost pincer grasp by age two). The patient could hold an object for a maximum of 12 seconds at baseline based on medical records and video evidence. She has been mostly non-verbal since the age of one (could use her eye-gaze driven communication device and speak three words inconsistently at baseline). The first pediatric patient experienced breath holding spells and had a history of seizures since three years old. Per the PI, the patient's baseline reported seizure frequency was approximately one seizure every three months.

In the first pediatric patient, TSHA-102 was generally well-tolerated with no SAEs related to TSHA-102 or DLTs as of the 22-week assessment post-treatment. The PI reported significant challenges with adverse events, or AEs, due to the immunosuppressive regimen. As of 12 weeks post-treatment, the PI reported improvements across multiple clinical domains and early evidence of developmental gains, compared to baseline, including motor skills, with improved hand function and grasping. The first pediatric patient demonstrated the ability to hold an object in her hand for up to three minutes while moving her arm (compared to baseline where she could hold an object for up to 12 seconds, but would drop objects when she moved her arm), and improved truncal stability and balance with the gained ability to move her leg on her own to better take a step with assistance for the first time and the ability to sit unassisted for one minute (compared to 30 seconds at baseline). In addition, the first pediatric patient showed improvement in oral motor and autonomic function, with improved swallowing and oral intake relative to the use of a gastrostomy tube for feeding at week 12 post-treatment. Importantly, we believe this indicates that TSHA-102 impacts both motor and autonomic function in a coordinated manner to further improve functional capabilities for patients with Rett syndrome impacting activities of daily living. The PI also observed improvements in the patient's communication and socialization, with enhanced use of an eye-gaze driven communication device, including the use of new words, and the gained ability to string multiple words together and identify object functions for the first time. The patient also gained new skills in visual reception and receptive language, including the ability to identify an object from memory, follow two unrelated commands and identify the function of objects and action words, which she was unable to do pre-treatment. Further, the first pediatric patient showed improvements in autonomic function with improved breathing patterns at week 12. The PI observed that the first pediatric patient had stable seizure events as of 22 weeks post-treatment, relative to baseline.

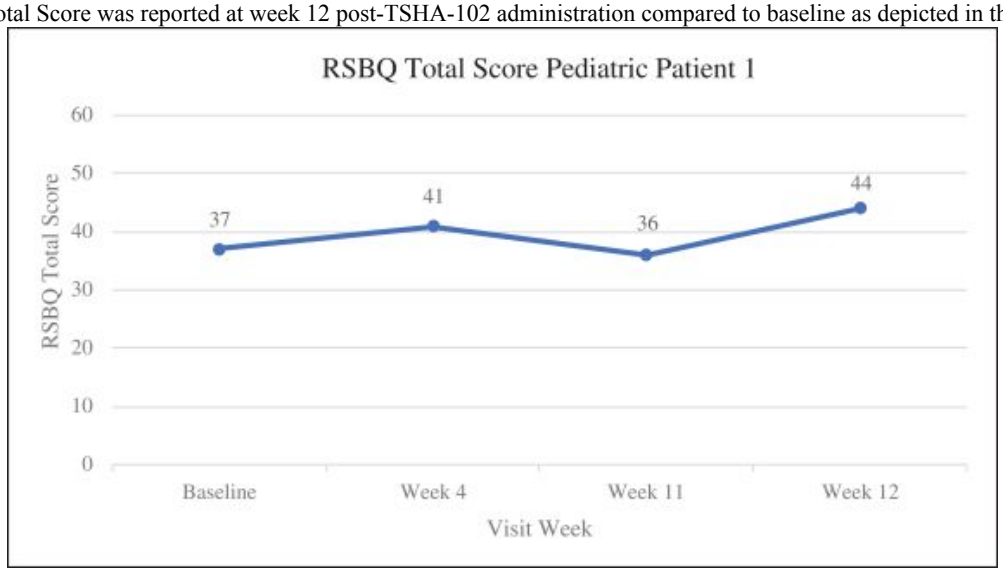
The second pediatric patient, a seven-year-old female at the time of dosing, has Stage III Rett syndrome, with a missense mutation in the *MECP2* gene that manifests as a milder phenotype as compared to the first pediatric patient, which is reflected in her clinical presentation at baseline as well as her baseline scores across multiple efficacy measures. Prior to treatment, the second patient was ambulatory (could stand and walk independently, but developed a mildly apraxic gait at one and half years old, impacting her gait and balance), with impaired fine motor and hand function by age one (could reach, swipe and transfer objects between hands at baseline, but her ability to reach and grasp objects was weak). The patient has been non-verbal since she was one year old (could use her eye-gaze driven communication device at baseline), and she experienced frequent hyperventilation by the age of four and had a history of seizures since the age of three. Per the PI, the patient's baseline reported seizure frequency was approximately two to four seizures daily.

In the second pediatric patient, TSHA-102 was generally well-tolerated with no SAEs related to TSHA-102 or DLTs as of the 11-week assessment post-treatment. There were two SAEs reported in the second pediatric patient that were not deemed treatment-related. Both were related to underlying disease, and one was also attributed to immunosuppression. Both events have resolved. The PI reported significant challenges with AEs due to the patient's immunosuppressive regimen. As of eight weeks post-treatment, the PI observed improvements across multiple clinical domains compared to baseline and early evidence of developmental gains in the second pediatric patient. Specifically, following treatment, the patient showed improvements in motor skills, with improved hand function and the ability to reach more quickly, as well as improved gait, speed and stability when walking, with new skills gained that were lost pre-treatment, including the ability to stand up from a chair and walk up a stair. The PI also observed improvements in the patient's communication and socialization, including improved social interest and eye contact. The second pediatric patient also showed improvements in autonomic function, including improved breathing patterns with less hyperventilation and breath holding episodes. The second pediatric patient also had an increase in days reported seizure-free since dosing as of week 11 post-treatment, which was one of the most severe aspects of disease impacting the patient and her caregivers' quality of life prior to treatment (although, a new anti-seizure medication was added to the regimen at week four, which has been maintained through week 11).

Pediatric Patient 1 Efficacy Data (Cohort 1)

There was no change at week 12 post-TSHA-102 administration in the first pediatric patient's CGI-S baseline score of five (markedly ill). The patient demonstrated an improvement in CGI-I and PGI-I at week four post-treatment with a score of three (minimally improved and a little better, respectively), which was sustained through week 12.

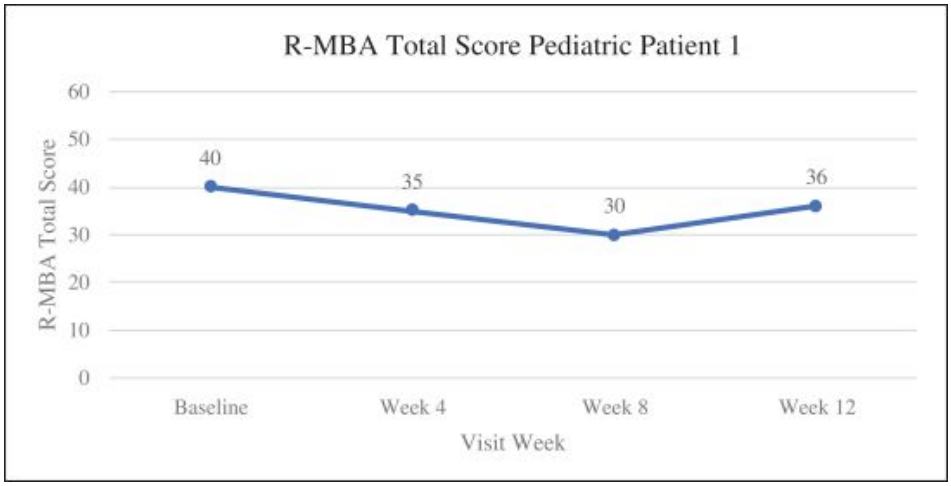
An increase in RSBQ Total Score was reported at week 12 post-TSHA-102 administration compared to baseline as depicted in the graph below.



**Pediatric patient one's RSBQ week eight assessment was collected week 11.*

A seven-point increase was reported in RSBQ Total Score at week 12 compared to baseline. The first pediatric patient demonstrated an improvement in hand behaviors and fear and anxiety compared to baseline. However, the patient's observed increase in mood changes, body rocking and expressionless face, nighttime behavior, and repetitive face movements also impacted the RSBQ Total Score. These increased behaviors are attributed to impacts of the immunosuppresion regimen on the patient, per the PI.

The first pediatric patient demonstrated an improvement in R-MBA Total Score at week 12 post-TSHA-102 administration compared to baseline as depicted in the graph below.



**Pediatric patient one's R-MBA week eight assessment was collected week 11.*

A four-point improvement was reported in R-MBA Total Score at week 12 compared to baseline, which was driven by an improvement in respiratory behavior, aberrant behavior and motor dysfunction.

Per the seizure diary and caregiver reports, the first pediatric patient demonstrated stable seizure events relative to baseline through 22 weeks post-treatment, based on caregiver-reported medical history. Pre-treatment, the patient had approximately one seizure every three months. Following treatment, the patient had three seizure episodes. The patient has been seizure-free as of week nine following treatment through week 22.

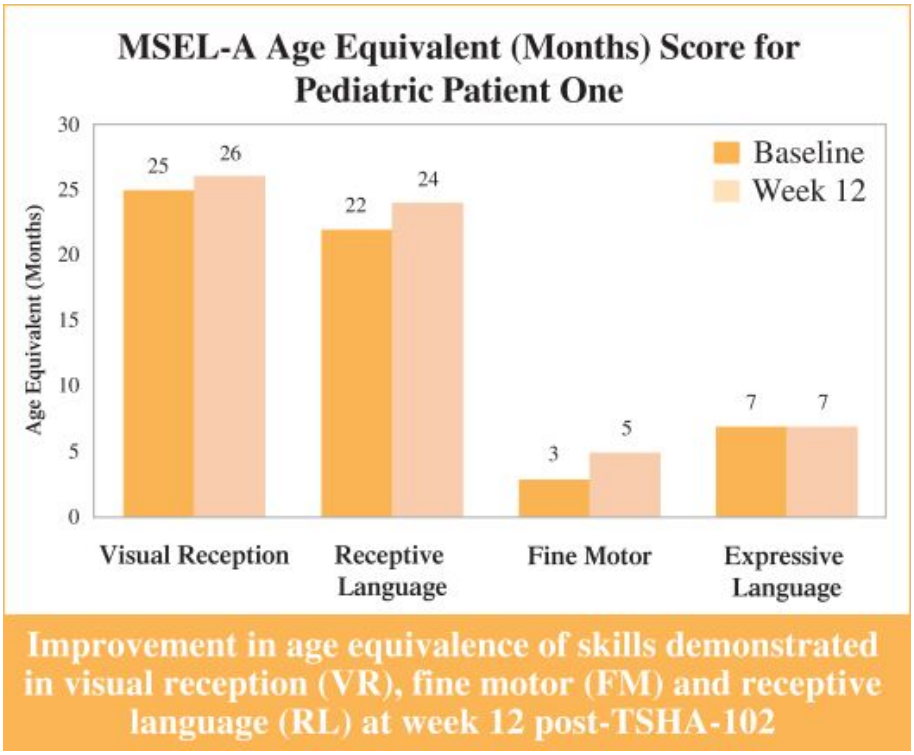
The Adapted Mullen Scales of Early Learning, or MSEL-A, is a standardized cognitive developmental assessment adapted for use in patients with Rett syndrome. The MSEL-A functionally evaluates skills compared to developmental milestones across four subscales, including visual reception - which is one's ability to visually interpret the surrounding environment, receptive language – one's ability to comprehend spoken language, fine motor - one's ability to use their hands to manipulate an object and communicate, and expressive language - one's ability to produce language and communication. The MSEL-A is administered by a trained psychologist or psychometrician, and the scores are reviewed by a certified, central rater.

The assessment evaluates where patients with Rett syndrome fall on a developmental curve compared to standard developmental milestones. For each domain assessed, the patient's developmental age equivalence is calculated based on standardized developmental norms.

At week 12 following treatment with TSHA-102, which is the first post-treatment assessment of the Mullen scale, the first pediatric patient showed an improvement in the age equivalence of skills she was able to demonstrate across multiple domains compared to baseline, including visual reception, receptive language and fine motor, with new developmental gains demonstrated, as depicted in the graph.

Before treatment, the patient was able to identify objects from a picture, resulting in an age equivalent baseline score of 25 months for visual reception. At week 12 post-treatment, she gained the ability to identify an object from memory based on three choices, resulting in an improvement in the age equivalent score of 26 months at week 12. Additionally, before treatment, the patient was able to follow one unrelated command and comprehend questions from a picture, resulting in an age equivalent baseline score of 22 months for receptive language.

Post-treatment, she gained the ability to follow two unrelated commands and identify the function of objects and action words, such as eating, sleeping, or washing, resulting in an improvement in her age equivalent score of 24 months at week 12. Further, the patient lost her ability to grasp at age two and displayed limited hand function at baseline, resulting in an age equivalent baseline score of three months for fine motor. At week 12 post-treatment, she gained the ability to use a refined thumb grasp, resulting in an improvement in the age equivalent score of five months as noted in the below chart. There was no change in the expressive language score at week 12.



Improvement in age equivalence of skills demonstrated in visual reception (VR), fine motor (FM) and receptive language (RL) at week 12 post-TSHA-102

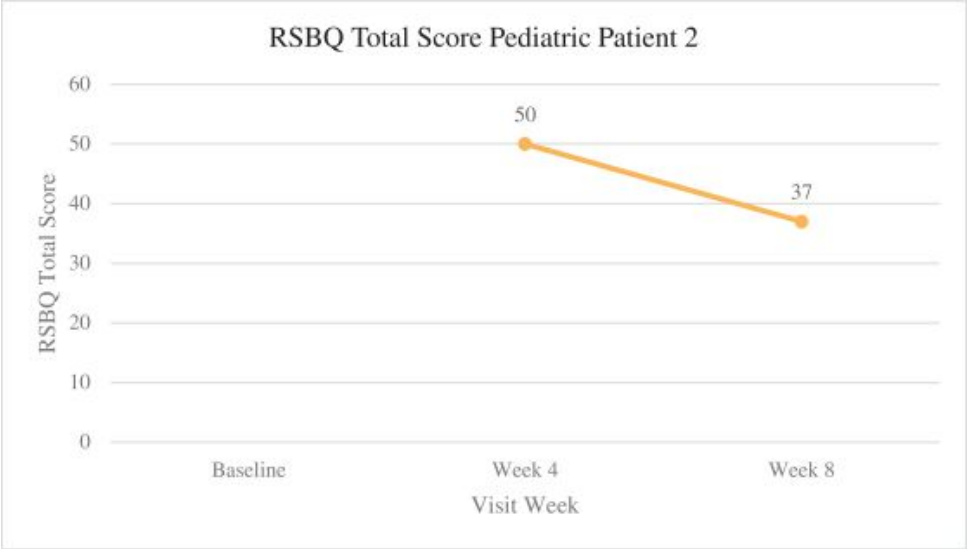
The patient was not able to demonstrate these skills before treatment per the MSEL-A baseline assessment, medical history, and caregiver reports. These developmental gains suggest clinically meaningful improvements for the patient as she has generalized these newly gained skills beyond demonstrating them during the MSEL-A assessment. Specifically, per the PI and administrating psychometrician, the patient used her eye-gaze driven communication device to identify object functions while using the device at home, and she held an object for up to three minutes at week 12 compared to up to 12 seconds pre-treatment, which supports her grasping improvements captured on the MSEL-A.

Pediatric Patient 2 Efficacy Data (Cohort 1)

The two pediatric patients dosed to date in our REVEAL trial possess different genetic backgrounds and mutation types, which manifest in different phenotypes and clinical severity.

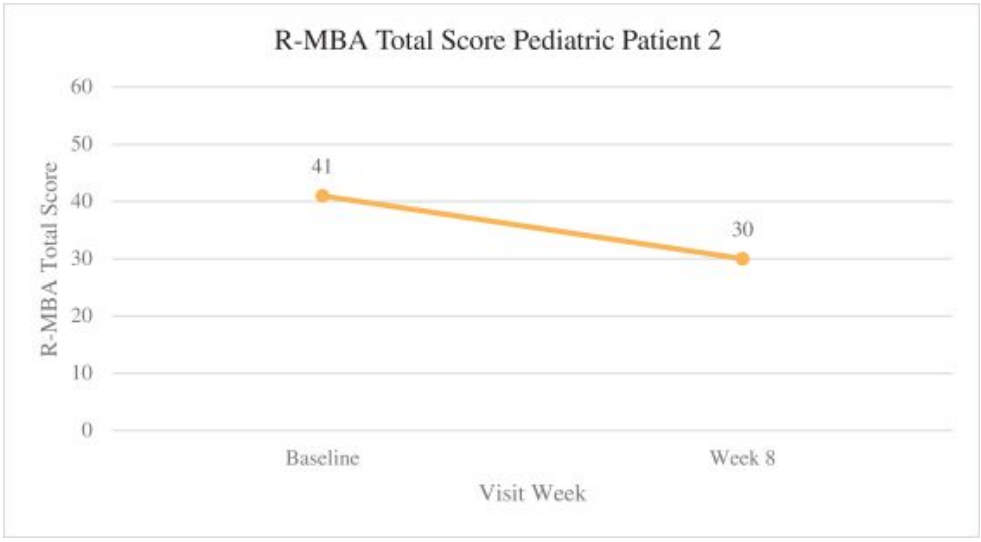
There was no change at week eight post-TSHA-102-administration in the second pediatric patient's CGI-S score of four (moderately ill) at baseline. The patient demonstrated an improvement in CGI-I and PGI-I of three (minimally improved and a little better, respectively) at week four. At week eight, the patient demonstrated continued improvement in CGI-I and PGI-I, with a CGI-I score of two (much improved) and a PGI-I score of two (much better).

The second pediatric patient demonstrated an improvement in RSBQ Total Score eight weeks post-TSHA-102 administration compared to the week four assessment as depicted in the graph below. RSBQ was not assessed at baseline.



At week eight, the second pediatric patient demonstrated a 13-point improvement in RSBQ Total Score, compared to week four, which was driven by improvements in breathing, repetitive face movements, nighttime behaviors, and fear and anxiety.

The second pediatric patient demonstrated an improvement in R-MBA Total Score at week eight post-TSHA-102 administration compared to baseline as depicted in the graph below.



At week eight, the second pediatric patient demonstrated an 11-point improvement in R-MBA Total Score. The most notable improvements were reported in respiratory behaviors, seizures and truncal rocking.

Per the seizure diary and caregiver reports, the second pediatric patient had an increase in days reported seizure-free since dosing through 11 weeks post-treatment, based on caregiver-reported medical history. Pre-treatment, the patient had approximately two to four seizures per day, with a medical history of seizure disorder including prior hospitalizations for seizure control since the age of three. Two weeks post-TSHA-102, the patient demonstrated a reduction in seizure frequency, with several days reported seizure-free. The patient experienced an episode of seizures during the week four post-treatment assessment, resulting in hospitalization, which was deemed unrelated to TSHA-102 and due to underlying disease, a concurrent urinary tract infection and Propofol sedation for protocol requirement MRI. Although her seizures improved prior to discharge, a new anti-seizure medication was added to the patient's regimen at week four, which she has maintained through week 11 post-treatment. The second pediatric patient had an increase in days reported seizure-free post-treatment since dosing through week 11.

Preliminary Financial Information

We estimate that we had cash and cash equivalents of approximately $105 million, as of May 31, 2024. However, this estimate is preliminary and subject to the completion of our unaudited financial statements as of and for the three and six months ended June 30, 2024. The actual cash and cash equivalents that we report as of June 30, 2024 will be subject to the completion of our financial closing procedures and any final adjustments that may be made prior to the time our financial results for the quarter ended June 30, 2024, are finalized and filed with the SEC. Our independent registered public accounting firm has not audited, reviewed, compiled, or performed any procedures with respect to our cash and cash equivalents and, accordingly, does not express an opinion or any other form of assurance on it. This estimate should not be viewed as a substitute for financial statements prepared in accordance with accounting principles generally accepted in the United States and is not necessarily indicative of the results to be achieved in any future period. Accordingly, you should not draw any conclusions based on the foregoing estimate and should not place undue reliance on this preliminary estimate. We assume no duty to update this preliminary estimate except as required by law.

Risks Related to the Development of our Product Candidates

Interim "top-line" and preliminary results from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim top-line or preliminary results from our clinical trials. Interim results from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or top-line results also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. For example, in June 2024, we announced initial clinical data from the first two pediatric patients and interim clinical data from the first two adult patients treated in the Phase 1/2 REVEAL trials of TSHA-102. However, those observations may not endure or be repeated in subsequently dosed patients or any age or disease severity, including patients receiving higher doses of TSHA-102 in either the adolescent/adult or pediatric trial. Initial clinical observations also may not translate into success on primary endpoints of the REVEAL trial. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly.

Risks Related to Legal and Regulatory Compliance Matters

We are subject to legal proceedings and claims from time to time that may seek material damages or otherwise may have a material adverse effect on our business. The costs we incur in defending ourselves or associated with settling any of these proceedings, as well as a material final judgment or decree against us, could materially adversely affect our financial condition.

We are subject to legal proceedings and claims from time to time that may seek material damages or otherwise may have a material adverse effect on our business. For example, in January 2024 and April 2024, we were named a nominal defendant in a shareholder derivative lawsuits against certain of our current and former directors in the Court of Chancery of the State of Delaware. These lawsuits seek unspecified monetary damages, disgorgement of profits, and reasonable costs and expenses, including attorneys' fees, and other relief. See "Item 3-Legal Proceedings" and "Part II, Item 8, Note 13-Commitments and Contingencies" in our Annual Report on Form 10-K and "Part I, Item 2, Note 13-Commitments and Contingencies in our Quarterly Report on Form 10-Q" for more information. Due to the inherent uncertainties in legal proceedings, we cannot accurately predict the ultimate outcome of any such proceedings. This or any future litigation, regardless of the merits of any such proceeding, could harm our reputation and result in substantial costs and diversion of management's attention and resources, which could adversely impact our business. Although we have directors' and officers' liability insurance, it provides for a substantial retention of liability and is subject to limitations and may not cover a significant portion, or any, of the expenses or liabilities we may incur or be subject to in connection with these lawsuits or other litigation to which we are party. The costs we incur in defending ourselves or associated with settling such proceedings, as well as a material final judgment or decree against us, that are not covered by our directors' and officers' liability insurance could materially adversely affect our financial condition. In addition, additional lawsuits may be filed, the conclusion of which in a manner adverse to us and for which we incur substantial costs or damages not covered by our directors' and officers' liability insurance could have a material adverse effect on our financial condition and business.