Corporate Presentation

November 2024

Taysha GENE THERAPIES

Legal disclosure

FORWARD LOOKING STATEMENTS

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding the potential of TSHA-102, our research, development and regulatory plans, and our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements are subject to a number of risks, uncertainties and assumptions. Risks regarding our business are described in detail in our Securities and Exchange Commission filings, including in our Annual Report on Form 10-K for the year ended December 31, 2023, and our other filings with the SEC, which are available on the SEC’s website at www.sec.gov. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements contained in this presentation reflect our current views with respect to future events, and we assume no obligation to update any forward-looking statements except as required by applicable law.

This presentation includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties as well as our own estimates of potential market opportunities. All of the market data used in this prospectus involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions

Key investment highlights

TSHA-102: Lead Clinical Program in Rett Syndrome	○ Ongoing REVEAL Phase 1/2 adolescent/adult trial (Canada, U.S.) and ongoing REVEAL Phase 1/2 pediatric trial (U.S., U.K., Canada) ○ Novel miRARE technology designed to mediate *MECP2* expression on a cell-by-cell basis (enables protein production in *MECP2*-deficient cells, silences transgene expression in healthy cells) to address risks associated with under- and over-expression of *MECP2* ○ High unmet medical need and significant market opportunity of 15,000-20,000 (U.S., EU+U.K.)[1] with typical Rett syndrome caused by a *MECP2* mutation ○ Potential to obtain Priority Review Voucher (PRV)
Transformative Potential	○ Cohort one (low dose) data from both REVEAL trials showed early, sustained and new improvements/functional gains across multiple domains and an encouraging safety profile in adult and pediatric patients as of data cutoff* ○ Cohort two (high dose) data from two adolescent/adult patients and one pediatric patient across both REVEAL trials showed TSHA-102 was generally well tolerated with no SAEs or DLTs as of data cutoff*
Proven and Well-Characterized Delivery	○ Clinically and commercially proven AAV9 capsid with clinical activity and tolerability across multiple CNS indications ○ Intrathecal delivery achieves widespread, consistent biodistribution and minimizes viral load, potentially reducing risk of systemic inflammatory response, with potential for outpatient delivery ○ Self-complementary technology increases transduction efficiency and facilitates more rapid transgene expression
Well-Capitalized	○ Cash and cash equivalents expected to extend cash runway into Q4 of 2026
Proven Leadership	○ Led by former AveXis management, who developed and launched ZOLGENSMA, the second FDA approved one-time gene therapy ○ Strong relationships with key gene therapy stakeholders, including regulatory authorities, suppliers and other third parties
Key Upcoming Milestones	○ 1H 2025 – Report clinical data from cohort one and cohort two from both the REVEAL adolescent/adult and pediatric trials

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Source: [1]IRSF; NORD; Amir RE, Van den Veyver IB, Wan M, et al. Rett Syndrome Is Caused by Mutations in X-Linked Mecp2, Encoding Methyl-Cpg-Binding Protein 2. Nat Genet 232:185-188. 1999.

*Adolescent/adult trial low dose: safety data as of week 52 and 36 for patient one and two, respectively; Pediatric trial low dose: safety data as of week 22 and 11 for patient one and two, respectively; Adolescent/adult trial high dose: safety data as of week 20 and 9 for patient one and two, respectively; Pediatric high dose: safety data as of week 6 for patient one.

Progress in clinical-stage TSHA-102 program supports clinical evaluation across a broad range of ages and stages of Rett syndrome

Adolescent & Adult REVEAL Phase 1/2 Trial *in U.S. and Canada*

- ✓ Completed dosing of cohort 1 (low dose, n=2); encouraging longer-term safety and efficacy data*
- ✓ Expanded trial to include patients ≥12 years of age
- ✓ TSHA-102 was generally well-tolerated as of 20 and nine weeks, respectively, in first two patients in cohort two (high dose)
- ✓ RMAT, ODD, RPDD and FTD from U.S. FDA

Pediatric REVEAL Phase 1/2 Trial *in U.S., U.K. and Canada*

- ✓ Completed dosing of cohort 1 (low dose, n=2); encouraging preliminary safety and efficacy data*
- ✓ TSHA-102 was generally well-tolerated as of six weeks in first patient in cohort two (high dose)
- ✓ Health Canada cleared the CTA, enabling expansion of ongoing pediatric trial into Canada
- ✓ RMAT, ODD, RPDD and FTD from U.S. FDA, ODD from E.U. EMA and ILAP designation from U.K. MHRA

First half of 2025: expect clinical data from low and high dose cohorts in both trials

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*Adolescent/adult trial: based on week 52 safety and efficacy data for patient one, and week 36 safety data and week 25 efficacy data for patient two. Pediatric trial: based on week 22 safety data and week 12 efficacy data for patient one, and week 11 safety data and week 8 efficacy data for patient two.
ODD=Orphan Drug designation; RPDD=Rare Pediatric Disease designation; FTD=Fast Track designation; FDA=Food and Drug Administration; CTA=clinical trial application; E.U.=European Union; EMA=European Medicines Agency; ILAP=Innovative Licensing and Access Pathway designation; U.K.=United Kingdom; MHRA=Medicines and Healthcare products Regulatory Agency

Important regulatory progress for TSHA-102 program through Regenerative Medicine Advanced Therapy (RMAT) mechanism

Advanced FDA Discussions on Regulatory Pathway Following Initial RMAT Type B Meeting

- ✓ Advanced discussions on trial design, endpoints and potential use of an established natural history dataset for Part B of REVEAL Phase 1/2 trials
- ✓ Company intends to focus on objective measures that clinically capture functional gains in Part B
- ✓ Aligned on meeting cadence with the FDA to expedite the development and review of TSHA-102
- ✓ Aligned on the adequacy of the nonclinical data package submitted to date to support BLA submission

Aligned with FDA on Commercial Manufacturing Process Following Type D CMC Meeting

- ✓ Approved use of pivotal TSHA-102 product in REVEAL trials based on demonstration of comparability between the clinical product and product derived from the final commercial manufacturing process
- ✓ Released pivotal product for use in Part B of the REVEAL Phase 1/2 trials
- ✓ FDA endorsed proposed analytical methods and corresponding qualification and validation plans, including mechanism of action potency release assays

Rett syndrome: a rare, progressive X-linked neurodevelopmental disease with no approved disease-modifying treatments that address the genetic root cause

- Caused by mutations in the X-linked gene encoding MeCP2 protein, which inhibits neuronal developments[1]
- Primarily occurs in females
- Leads to impaired brain development and function, resulting in multisystem complications[1]
- Symptoms and severity vary due in part to random X-inactivation[2]

High unmet medical need

- Current standard of care focused on symptom management[1]
- Patients typically require 24/7 care and lifelong assistance with daily activities[3]
- High caregiver burden and significant impact on quality of life and activities of daily living[3]

Significant market opportunity

- Estimated prevalence of typical Rett syndrome caused by a *MECP2* mutation is between **15,000 and 20,000** patients in major global markets (U.S., EU+U.K.)[4]
- Rett syndrome occurs worldwide in **1 of every 10,000** female births[4]

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Sources: [1]Amir RE, Van den Veyver IB, Wan M, Tran CQ, Francke U, Zoghbi HY. Rett syndrome is caused by mutations in X-linked MECP2, encoding methyl-CpG-binding protein 2. Nat Genet. 1999;23(2):185-188. [2]Braunschweig D, Simcox T, Samaco RC, LaSalle JM. X-Chromosome inactivation ratios affect wild-type MeCP2 expression within mosaic Rett syndrome and Mecp2-/+ mouse brain. Hum Mol Genet. 2004;13(12):1275-1286. [3]Voice of the Patient Report Rett Syndrome Externally-Led Patient-Focused Drug Development Meeting. https://rettpfdd.org/site/assets/files/1/2022-rett-syndrome-voice-of-the-patient-report.pdf [4]IRSF; NORD; Amir RE, Van den Veyver IB, Wan M, et al. Rett Syndrome Is Caused by Mutations in X-Linked Mecp2, Encoding Methyl-Cpg-Binding Protein 2. Nat Genet 232:185-188. 1999.

Hallmark characteristics of Rett syndrome appear across multiple clinical domains impacting activities of daily living

The neurologic architecture and function abnormalities observed across the CNS in Rett syndrome can have a significant impact on motor function, communication/socialization, autonomic function and seizures

Gross Motor Function	Fine Motor Function	Communication / Socialization	Autonomic Function / Seizures
○ Mobility issues ○ Loss of movement and coordination abilities ○ Gait disturbances ○ Hypotonia ○ Dystonia	○ Loss of hand function ○ Loss of purposeful hand use ○ Repetitive hand movements	○ Loss of speech/ communication ○ Social withdrawal ○ Behavioral issues ○ Intellectual disability	○ Epilepsy ○ Sleep disturbances ○ Breathing issues ○ Gastrointestinal issues ○ Cardiac dysfunction ○ Vasomotor disturbances

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Sources: [1]Gold WA, Krishnarajy R, Ellaway C, Christodoulou J. Rett Syndrome: A Genetic Update and Clinical Review Focusing on Comorbidities. ACS Chem Neurosci. 2018 Feb 21;9(2):167-176. doi: 10.1021/acschemneuro.7b00346. Epub 2017 Dec 15. PMID: 29185709. [2]Armstrong, DD. J Child Neurol. 2005;20(9):747-753

TSHA-102 clinical development program designed to capture a broad range of ages and stages of patients with Rett syndrome

Rett syndrome is divided into four key stages

STAGE I

Developmental Arrest

6-18 months (typical)
≤6 months (early)

Symptom onset

STAGE II

Rapid Deterioration

1-4 years

Symptom progression

STAGE III

Pseudo Stationary

4-10 years

Symptom stabilization

STAGE IV

Late Motor Deterioration

>10 years

Muscle wasting with age

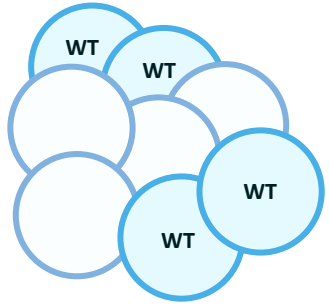
REVEAL Phase 1/2 Pediatric Trial

REVEAL Phase 1/2 Adolescent/Adult Trial

Source: Gold WA, Krishnarajy R, Ellaway C, Christodoulou J. Rett Syndrome: A Genetic Update and Clinical Review Focusing on Comorbidities. ACS Chem Neurosci. 2018 Feb 21;9(2):167-176. doi: 10.1021/acschemneuro.7b00346. Epub 2017 Dec 15. PMID: 29185709.

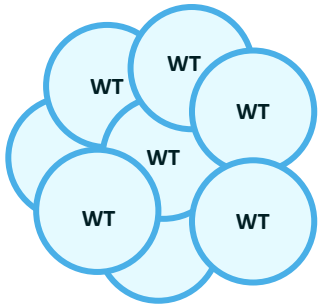
Gene Therapy Challenge: too much or too little *MECP2* expression is harmful in Rett syndrome

Rett syndrome



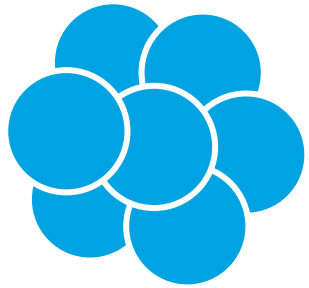
Some *MECP2* deficiency
occurs due to random X-inactivation, leading to a mixture of wild-type and deficient cells

Healthy individual



Normal *MECP2* levels
in all cells

***MECP2* duplication syndrome**



Overexpressed *MECP2*
leads to harmful effects and duplication syndrome

TSHA-102's novel miRNA-Responsive Auto-Regulatory Element (miRARE) technology is designed to correct *MECP2* deficiency and avoid toxic overexpression

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Source: Van Esch H, Bauters M, Ignatius J, et al. Duplication of the MECP2 region is a frequent cause of severe mental retardation and progressive neurological symptoms in males. Am J Hum Genet. 2005;77(3):442-453.

TSHA-102: an investigational one-time gene therapy that is designed to regulate *MECP2*

Strategically designed to enable optimal and controlled transgene expression across the CNS leveraging a clinically and commercially proven AAV9 capsid

Self-complementary vector (scAAV) enables more rapid, potent and efficient transgene expression vs. traditional single-stranded viral genome[1,2]

***miniMECP2* transgene** contains essential functional domains, and smaller size enables packaging of construct in self-complementary viral genome[3]

miRARE technology regulates transgene expression on a cell-by-cell basis to address risks associated with under- and over-expression by sensing both transgene and endogenous *MECP2* levels[4]

Intrathecal (IT) delivery leads to widespread and consistent biodistribution across the brain and spinal cord using a routine, minimally invasive procedure with potential for outpatient administration[5]

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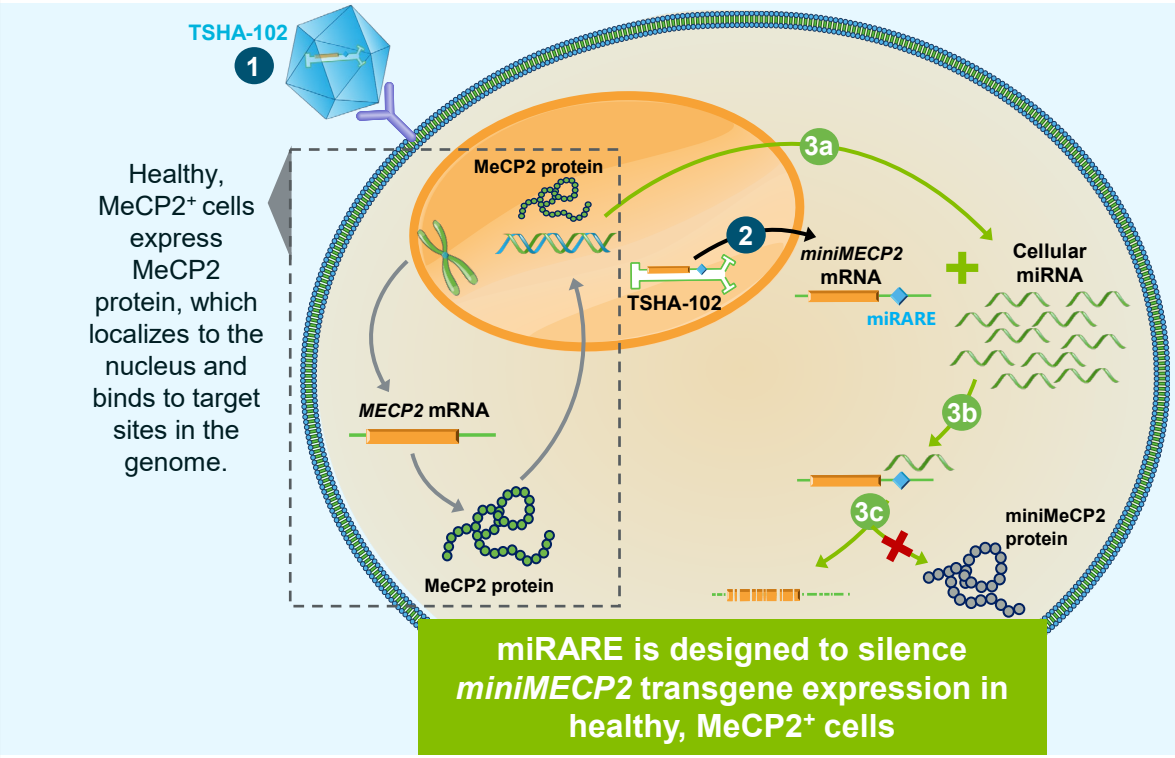
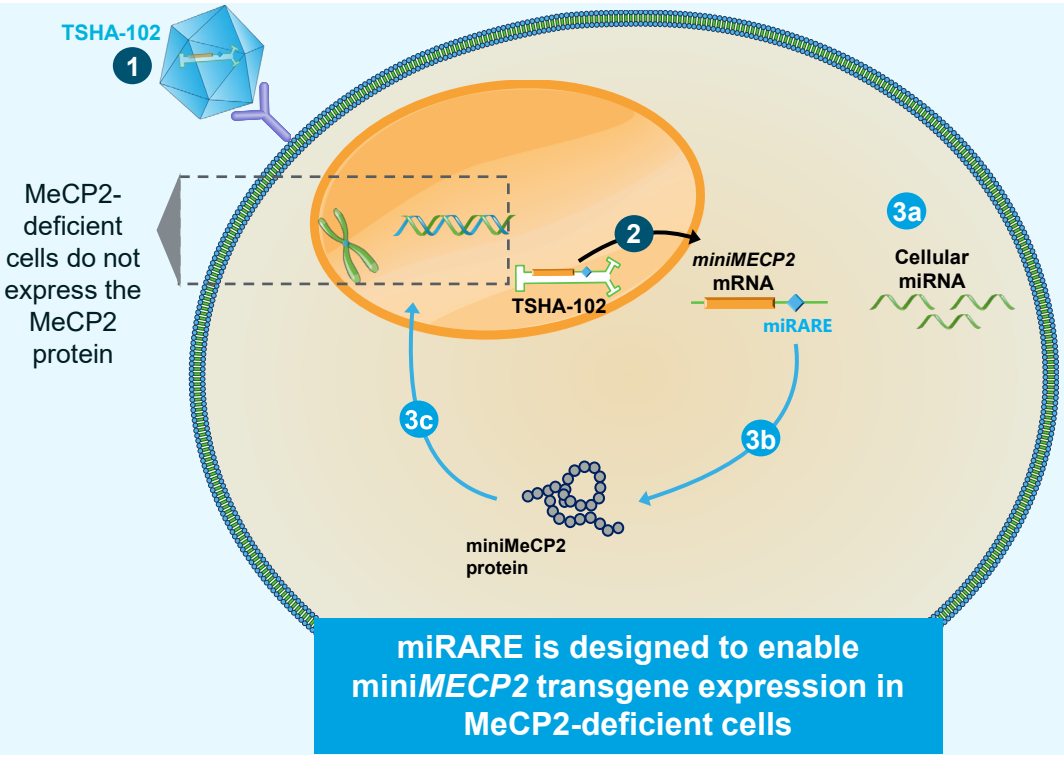
[1]Preclinical Differences of Intravascular AAV9 Delivery to Neurons and Glia: A Comparative Study of Adult Mice and Nonhuman Primates, Molecular Therapy, Volume 19, Issue 6, 2011, S. Gray, V. Matagne, L. Bachaboina, S. Yadav, S. Ojeda, R. Samulski, [2]Self-complementary AAV vectors; advances and applications. Mol Ther. 2008 Oct;16(10):1648-56. doi: 10.1038/mt.2008.171. Epub 2008 DM. McCarty [3]Tillotson R et al. 2017 *Nature;* 550:398-401; Sinnett SE et al. A New Approach for Designing a Feedback-Enabled AAV Genome Improves Therapeutic Outcomes of MiniMeCP2 Gene Transfer in Mice Modeling RTT. *23rd Annual meeting for the American Society of Gene & Cell Therapy*; April 28,2020. [4]Haque E et al. The microRNA-responsive autoregulatory element from TSHA-102 for Rett Syndrome modulates therapeutic transgene expression in response to cellular MeCP2 in mouse and human cell lines. 30th Annual Congress of the European Society for Gene and Cell Therapy, 24–27 Oct 2023, Brussels, Belgium. Poster #P435. [5]Haque E, Schultz M, Ashkenas J, Devidze N, Haque-Ahmed R, Porter F. Broad CNS Biodistribution of AAV9-based Gene Therapies Delivered by Intrathecal Lumbar Puncture in Non-Human Primates. Poster presented at: European Society of Gene & Cell Therapy Annual Congress; October 22-25, 2024; Rome, Italy.

miRARE: potential best-in-class approach to regulating *MeCP2* expression using RNA interference and binding sites for endogenous microRNA responsive to MeCP2[1]





In cells with normal MeCP2 function in the nucleus:

- 3a Cellular miRNAs are produced abundantly
- 3b These miRNAs interact with miRARE in the mini*MECP2* mRNA
- 3c This interaction signals the cell to degrade the mRNA and/or to suppress synthesis of the miniMeCP2 protein

In cells lacking normal MeCP2 function:

- 3a Fewer cellular miRNAs are produced
- 3b Therefore, the transgene mRNA is translated to produce mini-MeCP2 protein
- 3c The miniMeCP2 protein is imported into the nucleus, restoring MeCP2 function

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Source: [1]Sinnet, SE, et al. Engineered microRNA-based regulatory element permits safe high-dose miniMECP2 gene therapy in Rett mice. *Brain*. 2021 awab182.

Compelling preclinical safety, pharmacology, toxicology & biodistribution data supported clinical advancement of TSHA-102 in a broad age range of patients

- TSHA-102 improved survival rate, overall neurobehavioral function and growth in neonatal KO mouse models of Rett syndrome, and demonstrated a favorable safety profile in KO and WT mice
- TSHA-102 improved survival, body weight, motor function and respiratory health across all ages evaluated in KO mouse models of Rett syndrome, and demonstrated a favorable safety profile in KO and WT mice
- In six-month GLP toxicology studies, single intrathecal administration of TSHA-102 up to $2x10^{15}$ vg/animal was well-tolerated in WT rats and NHPs
- Broad biodistribution to brain and spinal cord demonstrated in mice, rats and NHPs
- Vehicle and WT treated animals demonstrated similar levels of *MECP2,* supporting the mechanism of miRARE regulation through minimizing transgene expression in the presence of endogenous *MECP2*
- miRARE downregulated *MECP2* transgene and protein expression in response to cellular levels of MeCP2 in human and mouse cell lines

Source: Company data

Robust preclinical data for TSHA-102 across age ranges

Species	Animal Model	Age	Study Size	Purpose	HED (vg / participant)	Route of Administration	Findings
Mouse	Wild-type and *Mecp2*$^{-/Y}$	Neonates (P2)	n=45	Survival	$2.9x10^{14}$	ICV	○ Improvement in survival rate, overall neurobehavioral function and growth in neonatal KO Rett mice ○ No impact on WT treated mice
Mouse	Wild-type and *Mecp2*$^{-/Y}$	P7, P14, P28	n=252	Pharmacology	$2.9x10^{14}$ $7.1x10^{14}$ 1.4×10^{15} $2.9x10^{15}$	IT	○ Significant improvement in survival, body weight, motor function and respiratory health across treatment ages ○ No signs of overexpression in WT treated mice
Mouse	Wild-type and *Mecp2*$^{-/Y}$	P28 - P35	n=137	Biodistribution and gene expression	$2.9x10^{15}$	IT	○ TSHA-102 vector DNA and transgene distribution demonstrated in the brain and spinal cord ○ mini*MECP2* RNA detected in brain and spinal cord
Rat	Wild-type	3.4 - 6.1 weeks	n=160	Toxicology	2.5×10^{14} 5.0×10^{14} 2.0×10^{15}	IT	○ Favorable safety profile of TSHA-102 ○ Nerve conduction metrics within functional physiological ranges for all groups at all timepoints
NHP	Wild-type	Juvenile (~2 yrs)	n=24	Toxicology	2.5×10^{14} 5.0×10^{14} 2.0×10^{15}	IT	○ TSHA-102 well-tolerated with no toxicity observed ○ Biodistribution demonstrated in brain and spinal cord, with low *miniMECP2* mRNA expression in the CNS, indicating miRARE mediated transgene expression in the presence of endogenous *MECP2*
Human and mouse cell lines	2v6.11, SH-SY5Y, and Neuro-2a	NA	NA	Gene and protein expression	NA	Cell transfection and transduction	○ Evidence that miRARE can control mini*MECP2* transgene and protein expression in cell culture models ○ miniMeCP2 protein expression induced by absence of cellular MeCP2

Source: Company data

Adolescent and Adult REVEAL Phase 1/2 trial in U.S. and Canada

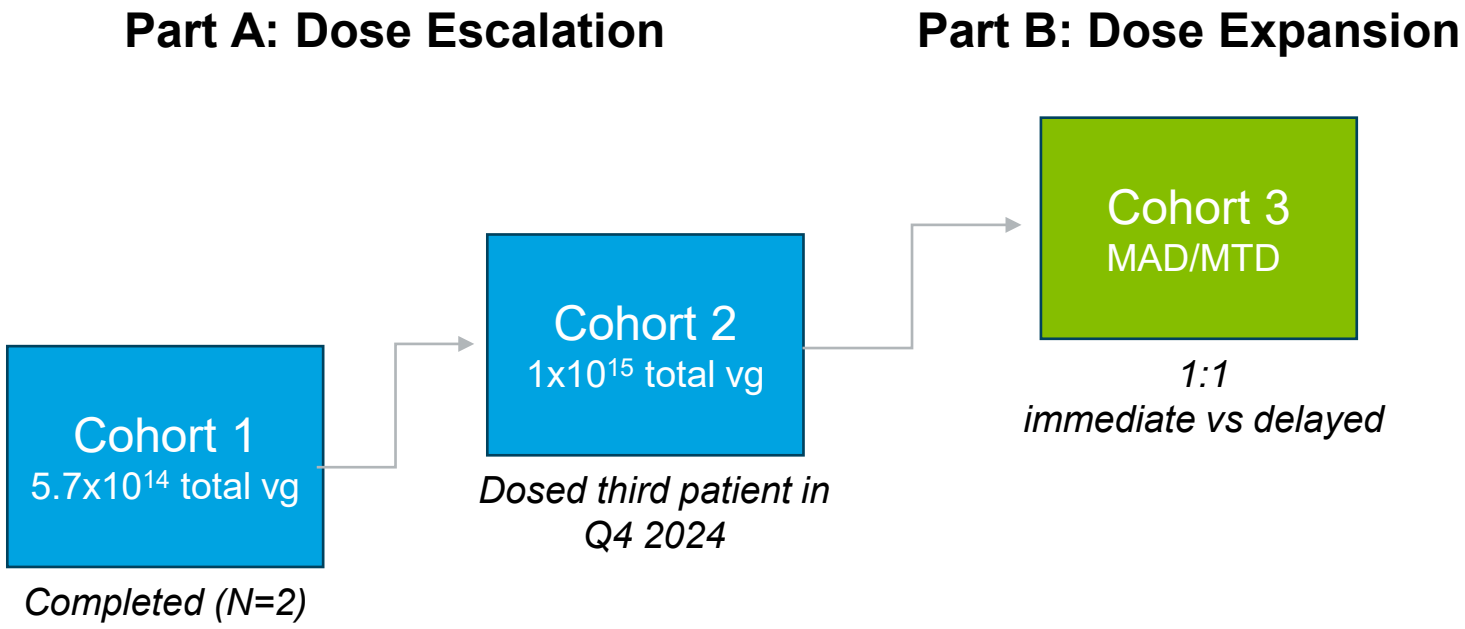
Open-label, dose-escalation and dose-expansion, randomized, multi-center trial for TSHA-102

Study Overview

Objectives
- Safety and preliminary efficacy of TSHA-102
- **Part A**: evaluates two dose levels; if possible, establishes MAD or MTD
- **Part B**: evaluates the MAD or MTD

Key inclusion criteria
- Females aged 12+ with pathogenic confirmation of *MECP2* mutation
- CGI-S score of ≥4 at screening

Key clinical assessments
- Revised Motor Behavior Assessment Scale (R-MBA)
- Clinical Global Impression Scale-Severity and Improvement (CGI-S and CGI-I)
- Parental Global Impressions Scale-Improvement (PGI-I)
- Rett Syndrome Hand Function Scale (RSHFS)



Clinical trial: NCT05606614; MAD: maximum administered dose; MTD: maximum tolerated dose

Adolescent/adult low dose cohort: Encouraging safety profile & early, sustained and new improvements across consistent clinical domains

Generally well-tolerated

No SAEs related to TSHA-102 or DLTs as of week 52 assessment (patient one) and week 36 assessment (patient two)

Improvements across multiple efficacy measures

Improvements as early as four weeks post-treatment, with sustained and new improvements across multiple efficacy measures at week 52 (patient one) and at week 25 (patient two) following completion of steroid taper

Functional gains across multiple clinical domains

Principal Investigator reported improvements and functional gains as early as four weeks post-treatment across multiple domains including motor skills, communication/socialization, autonomic function and seizures, that persisted and strengthened over time through week 52 (patient one) and week 25 (patient two) following completion of steroid taper

Durability of TSHA-102 supported by sustained and new functional gains over time across different clinical severity and genetic mutations

Two adult patients with stage four Rett syndrome in low dose cohort had different genetic mutation severity and phenotypic expression

Baseline Characteristics

Adult Patient One	Adult Patient Two
Diagnosed with stage four "late motor deterioration muscle wasting" Rett syndrome	
20 year-old female	21 year-old female
Large *MECP2* deletion	Missense *MECP2* mutation
Severe phenotype	**Milder** phenotype
"Severely ill" – CGI-S baseline score of 6	"Moderately ill" – CGI-S baseline score of 4
Motor Skills: Complete loss of ambulation and ability to sit unassisted; wheelchair-bound by age 8 Loss of hand function by age 6 **Communication/Socialization:** Mostly non-verbal by age 6 **Autonomic Function:** Frequent apnea and hyperventilation by age 3 **Seizures:** Seizures at age 5 (2-4 per year at baseline)	**Motor Skills:** Partial loss of ambulation by age 2 Walks with impaired gait and balance by age 18 Hand stereotypies with weak grasping by age 3 **Communication/Socialization:** Mostly non-verbal by age 2 **Autonomic Function:** Frequent hyperventilation by age 3 **Seizures:** Seizures by age 10 (2-4 per week at baseline)

Source: Company data | baseline characteristics based on pre-treatment observations, baseline assessments, pre-screening visits and patient's medical history.

Clinical improvements and functional gains seen in multiple domains in both adult patients in low dose cohort based on Principal Investigator observations

Adult Patient One – *20-year-old female (large MECP2 deletion; severe phenotype)*

Patient history

- **Age 3:** Apnea and hyperventilation
- **Age 5:** Seizures
- **Age 6:** Mostly non-verbal
- **Age 6:** Loss of hand function
- **Age 8:** Complete loss of ambulation and ability to sit unassisted

Age 20

52 weeks post-TSHA-102

- **MOTOR SKILLS:** Improved hand function; gained ability to sit unassisted and move legs for the first time in over a decade
- **COMMUNICATION/SOCIALIZATION:** Improved social interest, vocalization, and use of eye-driven communication device
- **AUTONOMIC FUNCTION:** Improved breathing patterns and circulation, and normalized sleep quality/duration with gained ability to sleep through night for the first time in 20 years
- **SEIZURES:** Stable seizure events with lower levels of anti-seizure medication relative to baseline

Adult Patient Two – *21-year-old female (missense MECP2 mutation; milder phenotype)*

Patient history

- **Age 2:** Partial loss of ambulation, mostly non-verbal
- **Age 3:** Hand stereotypies with weak grasp
- **Age 3:** Frequent hyperventilation
- **Age 10:** Seizures
- **Age 18:** Bradykinesia, walks with impaired gait and balance

Age 21

25 weeks post-TSHA-102

- **MOTOR SKILLS:** Improved hand stereotypies for the first time since regression at age three and improved posture
- **COMMUNICATION/SOCIALIZATION:** Improved social interest
- **AUTONOMIC FUNCTION:** Improved breathing patterns and circulation
- **SEIZURES:** Significantly reduced seizure events with 25% lower levels of anti-seizure medication relative to baseline; seizure free for 8.5 months*

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Clinical observations made by the Principal Investigator are based on post-treatment assessments, pre-treatment observations, baseline assessments, pre-screening visits and patient's medical history. Subject to change as the trial progresses.
*Seizure data for adult patient two is based on Seizure Diary and caregiver reports as of week 36 post-TSHA-102

Clinical improvement demonstrated across multiple efficacy measures in patient one (13-months) and patient two (6-months) in low dose cohort

	CGI-S		CGI-I, with Rett anchors		PGI-I		R-MBA		RSHFS	
Scale Description	Clinician-reported 7-point assessment of illness severity 1=*normal* 7=*among the most extremely ill*		Clinician-reported 7-point assessment of overall improvement 1=*very much improved* 7=*very much worse*		Caregiver-reported 7-point assessment of overall improvement 1=*considerably better* 7=*very much worse*		Clinician-reported 24-question scale measuring disease behaviors of Rett syndrome *Higher scores indicate greater severity*		Clinician-reported assessment of hand function in Rett syndrome by an independent experienced physical therapist, being reported as best score for large objects 1=*no active grasping* 4=*independent grasp*	
	P1	**P2**	**P1**	**P2**	**P1**	**P2**	**P1**	**P2**	**P1**	**P2**
Screening, Baseline	6 Severely ill	4 Moderately ill	-	-	-	-	43	38	DH: 3 NH: NA*	DH: NE* NH: 1
Week 4	5 Markedly ill	4 Moderately ill	2 Much improved	3 Minimally improved	3 A little better	3 A little better	48	31		DH: NE* NH: 1
Week 8	5 Markedly ill	4 Moderately ill	2 Much improved	3 Minimally improved	3 A little better	3 A little better	51	24	DH: 2 NH: 1	DH: 4 NH: 1
Week 12	5 Markedly ill	4 Moderately ill	2 Much improved	3 Minimally improved	2 Much better*	3 A little better	37	21	DH: 3 NH: 3*	DH: NE* NH: 1
Week 25	5 Markedly ill	4 Moderately ill	2 Much improved	3 Minimally improved	2 Much better	3 A little better	42	15	DH: 3 NH: 2	DH: 4 NH: 1
Week 52	5 Markedly ill		3 Minimally improved		1 Considerably better		26			
Overall Change	+	=	+	+	+	+	+	+	+	=

DH = dominant hand; NH = non-dominant hand; = *not assessed; NE = not evaluable* = *improvement from baseline* = *no change from baseline* = *decline from baseline*

**PGI-I week 12 assessment for patient one was captured at week 16; RSHFS week 12 assessment for patient one was captured on week 11; RSHFS assessment for patient one was not conducted at baseline; RSHFS assessment for patient two's DH was not conducted as defined in the guidelines at baseline, week 4 and week 12, therefore the data is not evaluable at these time points. Rett syndrome Behavior Questionnaire (RSBQ) has been removed as it is no longer being considered as a primary/secondary endpoint in Part B of our TSHA-102 clinical studies based on discussions with the U.S. FDA and focus on objective endpoints.*

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Data presented reflects current data in the Electronic Data Capture System, subject to change

Pediatric REVEAL Phase 1/2 trial in the U.S., U.K. and Canada

Open-label, dose-escalation and dose-expansion, randomized, multi-center trial for TSHA-102

Study Overview

Objectives

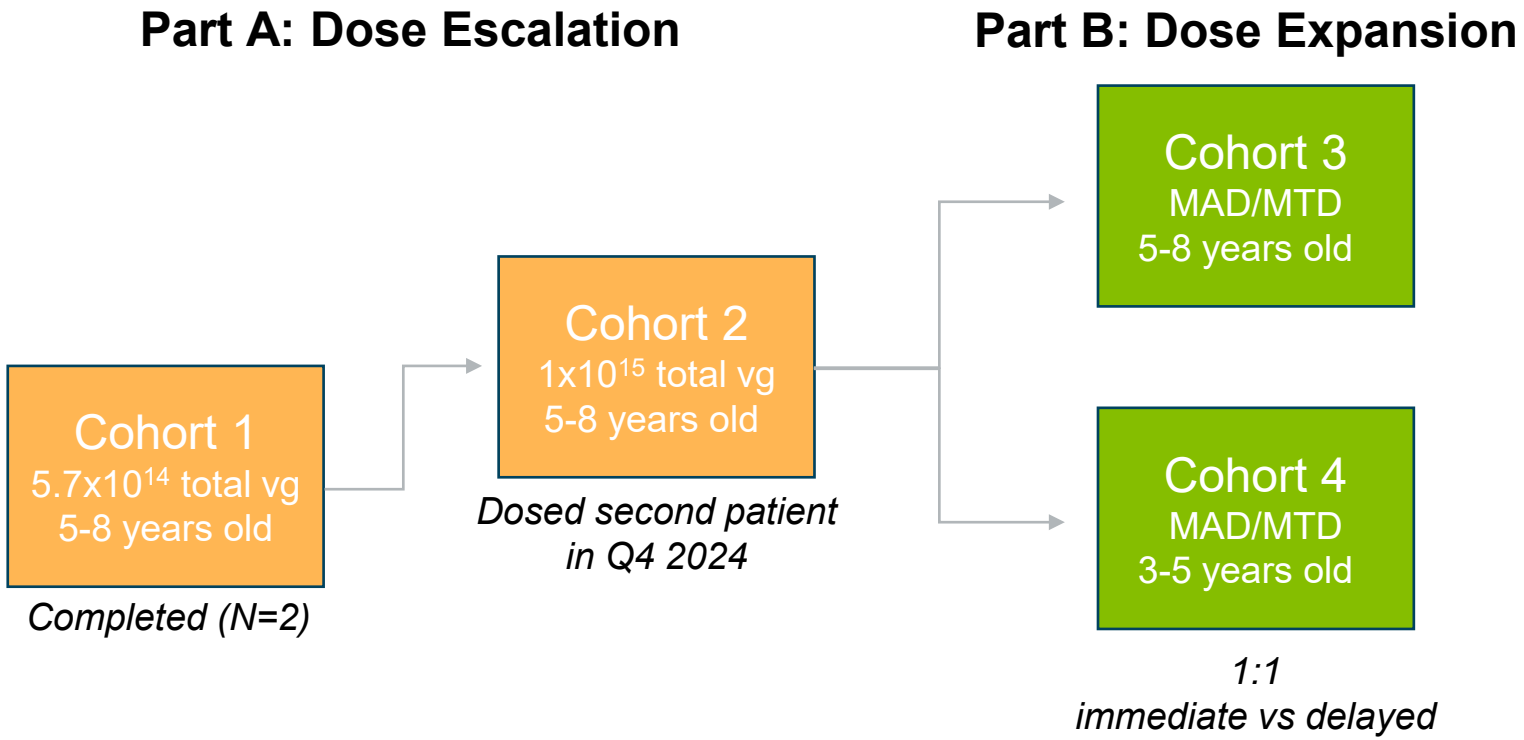
- Safety and preliminary efficacy of TSHA-102
- **Part A**: evaluates two dose levels; if possible, establishes the MAD or MTD
- **Part B**: evaluates the MAD or MTD in two age cohorts

Key inclusion criteria

- Females 5-8 years old with pathogenic confirmation of *MECP2* mutation (Part A)
- CGI-S score of ≥4 at screening

Key clinical assessments

- R-MBA
- CGI-S and CGI-I
- PGI-I
- Adapted Mullen Scales for Early Learning (MSEL-A)



Clinical trial: NCT06152237

Pediatric low dose cohort: Encouraging safety profile & early improvements across consistent clinical domains

Generally well-tolerated	No SAEs related to TSHA-102 or DLTs as of week 22 assessment (patient one) and week 11 assessment (patient two)*
Improvements across multiple efficacy measures	Improvements as early as four weeks post-treatment, with sustained and new improvements across multiple efficacy measures at week 12 (patient one) and at week 8 (patient two)
Functional gains across multiple clinical domains	Principal Investigator reported improvements and functional gains as early as four weeks post-treatment across multiple domains including motor skills, communication/socialization, autonomic function and seizures through week 12 (patient one) and week 8 (patient two)

Initial data support early functional gains in pediatric patients with different clinical severity and genetic mutations

Taysha GENE THERAPIES

*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 have both resolved.

Two pediatric patients with stage three Rett syndrome in low dose cohort had different genetic mutation severity and phenotypic expression

Baseline Characteristics

Pediatric Patient One	Pediatric Patient Two
Diagnosed with stage three "pseudo stationary" Rett syndrome	
6 year-old female	7 year-old female
MECP2 deletion	Missense *MECP2* mutation
Moderate phenotype	**Milder** phenotype
"Markedly ill" – CGI-S baseline score of 5	"Moderately ill" – CGI-S baseline score of 4
Motor Skills: Non-ambulatory Sits unassisted for 30 seconds/stands with support by age 3 Impaired hand function by age 1.5 **Communication/Socialization:** Mostly non-verbal by age 1 **Autonomic Function:** Breath holding **Seizures:** Seizures by age 3 (1 seizure every 3 months at baseline)	**Motor Skills:** Partial loss of ambulation by age 1.5 Impaired hand function by age 1 **Communication/Socialization:** Non-verbal by age 1 **Autonomic Function:** Frequent hyperventilation by age 4 **Seizures:** Seizures by age 3 (2-4 seizures daily at baseline)

Source: Company data | baseline characteristics based on pre-treatment observations, baseline assessments, pre-screening visits and patient's medical history.

Clinical improvements and functional gains seen in multiple domains in both pediatric patients in low dose cohort based on Principal Investigator observations

Pediatric Patient One – *6-year-old female (MECP2 deletion; moderate phenotype)*

Patient history

- **Age 1.5** – Impaired hand function
- **Age 1** – Mostly non-verbal
- **Age 3** – Non-ambulatory: Sits unassisted for 30 seconds/stands with support
- **Age 3** – Seizures
- **Age 6** – 

12 weeks post-TSHA-102

- **MOTOR SKILLS:** Improved hand function/grasping with ability to hold object up to 3 minutes; improved truncal stability and balance with gained ability to move leg to take step on own without assistance and sit unassisted for longer duration
- **COMMUNICATION/SOCIALIZATION:** Improved communication and use of eye-gaze driven communication device; gained new visual reception and receptive language skills
- **AUTONOMIC FUNCTION:** Improved breathing patterns
- **SEIZURES:** Stable seizure events relative to baseline

Pediatric Patient Two – *7-year-old female (missense MECP2 mutation; milder phenotype)*

Patient history

- **Age 1** – Impaired hand function
- **Age 1** – Mostly non-verbal
- **Age 1.5** – Partial loss of ambulation
- **Age 3** – Seizures
- **Age 4** – Hyperventilation
- **Age 7** – 

8 weeks post-TSHA-102

- **MOTOR SKILLS:** Improved hand function with ability to reach more quickly; improved gait, speed and stability when walking with new skills gained including the ability to stand up from a chair and walk up a stair
- **COMMUNICATION/SOCIALIZATION:** Improved social interest and eye contact
- **AUTONOMIC FUNCTION:** Improved breathing patterns
- **SEIZURES:** Increased number of seizure-free days compared to baseline*

Clinical observations made by the Principal Investigator are based on post-treatment assessments, pre-treatment observations, baseline assessments, pre-screening visits and patient's medical history. Subject to change as the trial progresses.
*A new anti-seizure medication was added to patient two's regimen week 4, which has been maintained through week 11

Clinical improvements demonstrated across multiple efficacy measures in patient one (3-months) and patient two (2-months) in low dose cohort

	CGI-S		CGI-I, with Rett anchors		PGI-I		R-MBA		MSEL-A	
Scale Description	Clinician-reported 7-point assessment of illness severity 1=*normal* 7=*among the most extremely ill*		Clinician-reported 7-point assessment of overall improvement 1=*very much improved* 7=*very much worse*		Caregiver-reported 7-point assessment of overall improvement 1=*very much improved* 7=*very much worse*		Clinician-reported 24-question scale measuring disease behaviors of Rett syndrome *Higher scores indicate greater severity*		Clinician-reported 4 subscale scores to assess cognitive function for visual reception (VR), receptive language (RL), expressive language (EL) and fine motor (FM) reported as age equivalent score *Higher score indicates improvement*	
	P1	**P2**	**P1**	**P2**	**P1**	**P2**	**P1**	**P2**	**P1**	**P2**
Screening, Baseline	5 Markedly ill	4 Moderately ill	–	–	–	–	40	41	VR=25 mos RL=22 mos EL=7 mos FM=3 mos	VR=39 mos RL=13 mos EL=7 mos FM=6 mos
Week 4	5 Markedly ill	4 Moderately ill	3 Minimally improved	3 Minimally improved	3 A little better	3 A little better	35			
Week 8	5 Markedly ill	4 Moderately ill	3 Minimally improved	2 Much improved	3 A little better*	2 Much better	30	30		
Week 12	5 Markedly ill		3 Minimally improved		3 A little better		36		VR=26 mos RL=24 mos EL=7 mos FM=5 mos	
Overall Change	=	=	+	+	+	+	+	+	+	

= *not assessed* = *improvement from baseline* = *no change from baseline* = *decline from baseline*

**Patient one's RSBQ and R-MBA week 8 assessment was collected week 11. RSBQ has been removed as it is no longer being considered as a primary/secondary endpoint in Part B of our TSHA-102 clinical studies based on discussions with the U.S. FDA and focus on objective endpoints.*

Improvements across consistent clinical domains in all patients treated with low-dose TSHA-102 based on clinician and caregiver assessments and video evidence

Adult Patient One (week 52)
Severe phenotype

- Gained **motor skills** with ability to sit unassisted and move legs for first time in over a decade
- Improved **communication** with gained ability to use eye-gaze driven communication device
- Improved **autonomic function** including normalized sleep behaviors for first time in 20 years
- **Stabilized seizures** at lower level of anti-seizure medication

Adult Patient Two (week 25)
Milder phenotype

- Improved **motor skills,** with reduced hand stereotypies for first time since regression at age 3 and improved posture
- Improved **social interest** with increased response to words and eye contact
- Improved **autonomic function** including breathing patterns
- **Seizure-free for 8.5 months** at 25% lower levels of anti-seizure medication relative to baseline (2-4 per week)

Pediatric Patient One (week 12)
Moderate phenotype

- Improved **motor skills** including hand function and grasping with ability to hold object up to 3 minutes vs. 12 seconds pre-treatment
- Improved **communication** and use of eye-driven communication device with new words communicated using device
- Improved swallowing and oral intake relative to gastrostomy tube feeding
- **Stabilized seizures**

Pediatric Patient Two (week 8)
Milder phenotype

- Gained new **motor skills** of standing up from a chair walking up a stair
- Improved **social interest** and eye contact
- Improved **autonomic function** including breathing patterns
- Increase in **seizure-free** days since dosing (a new anti-seizure medication was added to patient two's regimen at week 4)

Anticipated TSHA-102 program milestones

First Half of 2025	Report update on longer-term safety and efficacy data from cohort one (low dose) in both the REVEAL Phase 1/2 adolescent and adult trial and the REVEAL Phase 1/2 pediatric trial
	Report safety and efficacy data from cohort two (high dose) in both the REVEAL Phase 1/2 adolescent and adult trial and the REVEAL Phase 1/2 pediatric trial

Financial Position

- Cash and cash equivalents of $157.7 million as of September 30, 2024
- Cash runway expected to fund operating expenses and capital requirements into the fourth quarter of 2026 through key TSHA-102 inflection points

TSHA-102: *a differentiated treatment approach for all patients with Rett syndrome*

Designed to safely address the root cause of Rett syndrome with a minimally invasive route of administration

Encouraging preliminary Phase 1/2 data in adults and pediatric patients with advanced disease

Well-capitalized through key inflection points