Bringing New Treatments to Life

Corporate Presentation | November 2026

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, the durability and reproducibility of the clinical data from the REVEAL trials, our research, development, manufacturing and regulatory plans, our strategy, future operations, communications with and feedback from the FDA and Health Canada on the regulatory pathway for TSHA-102, future financial position and cash runway, future revenues, projected costs, prospects, plans, objectives of management, our ability to successfully commercialize our product candidates and our potential nomination of additional gene therapy programs and the timing thereof 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, 2025, our Quarterly Report on Form 10-Q for the quarter ended September 30, 2026, 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 presentation 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: potential one-time treatment designed to address root cause of Rett syndrome, with a clear path to registration

High Unmet Need and Significant Market Opportunity	○ No approved therapies address genetic root cause of Rett syndrome ○ 15,000-20,000 patients (U.S., EU+U.K.); 1 of 8,700 female births worldwide[1-3]
Differentiated Approach Designed to Support Commercial Uptake	○ Clinically and commercially proven AAV9 capsid with well-established safety profile, based on third-party gene therapy studies ○ Delivered intrathecally as a routine, minimally invasive procedure with outpatient potential, enabling broad, scalable access
Transformative Potential Supported by Part A Data[4]	○ 100% response rate in REVEAL Part A (N=12) for pivotal trial primary endpoint exceeds 33% minimum threshold for success ○ Patients consistently demonstrated durable, multidomain functional gains that deepened over time regardless of age/disease severity ○ No treatment-related SAEs or DLTs
Clear Path Toward Registration for Broad ≥2 Years Label	○ Completed dosing (N=17, 6 to <22 years) in FDA-aligned REVEAL pivotal trial; 6-month interim analysis may enable BLA submission ○ FDA alignment on product comparability enables REVEAL Part A data to be included in the BLA; robust 6 and ≥12-month Part A results further support potential BLA submission based on pivotal trial interim analysis ○ Completed dosing (N=4, 2 to <4 years) in FDA-aligned ASPIRE trial; ≥3 months safety data in BLA may support broad ≥2 years label

[1]Amir, R E et al. "Rett syndrome is caused by mutations in X-linked MECP2, encoding methyl-CpG-binding protein 2." *Nature genetics* vol. 23,2 (1999): 185-8. doi:partners.10.1038/13810. (estimated prevalence of *15,000-20,000 patients with typical Rett syndrome caused by a MECP2 mutation*). [2]Sarajlija, Adrijan, et al. "Epidemiology of Rett Syndrome in Serbia: Prevalence, Incidence and Survival." *Neuroepidemiology*, vol. 44, no. 1, 2015, pp. 1–5, https://doi.org/10.1159/000369494. [3]Laurvick, Crystal L., et al. "Rett Syndrome in Australia: A Review of the Epidemiology." *The Journal of Pediatrics*, vol. 148, no. 3, 2006, pp. 347–52. [4]Based on May 2026 data cutoff (N=12).
CNS=Central nervous system; SAP=Statistical analysis plan; BLA=Biologics license application; SAE=Serious adverse event; DLT=Dose-limiting toxicity

TSHA-102 Rett syndrome program strongly positioned for rapid execution toward BLA submission

Compelling Part A Clinical Data

supported FDA Breakthrough Therapy designation and indicates pivotal trial is well powered to establish efficacy

Completed BLA-enabling PPQ Campaign

Met predefined product acceptance criteria for comparability under FDA-aligned strategy and may enable pooling Phase 1/2 and pivotal data for BLA submission

Potential for Expedited Path to BLA Submission

FDA alignment that REVEAL pivotal trial 6-month interim analysis may serve as the basis for BLA submission

Potential for Broad Label Aged 2+ Years

FDA alignment on inclusion of ≥3 months of ASPIRE safety data in BLA submission to support a broad label

Next Steps

Q1 2027: Expected FDA feedback following CMC Type B meeting

1H 2027: Topline data from REVEAL pivotal trial 6-month interim analysis and FDA feedback on BLA submission pathway expected

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BLA=Biologics license application; PPQ=Process Performance Qualification

Commercial readiness activities designed to position TSHA-102 for successful launch and adoption

Deep Commercial and Manufacturing Expertise

Seasoned commercial leadership with expertise across gene therapy commercialization, market development and market access

Catalent to serve as primary commercial manufacturing partner at its FDA-licensed gene therapy facility in Maryland



Market Research Supports Potentially Strong Demand, Access and Broad Adoption

High clinician intent to treat across all ages, with the vast majority of caregivers likely to pursue gene therapy upon approval[1]

Strong payer support for TSHA-102's value proposition and reimbursement outlook due to its transformative potential and one-time outpatient IT delivery[2]



Intrathecal Administration Enables Broad Access

Strong preference for IT delivery over direct-to-brain due to familiarity, accessibility and scalability[1]

Routine outpatient procedure enables scalable access beyond COEs, with ~75% of patients managed outside large Rett COEs[3]



[1]2026 market research conducted by a third party with U.S. clinicians and caregivers of individuals with Rett syndrome. [2]2026 U.S. payer research conducted by a third party. [3]Based on U.S. claims data
IT=intrathecal; COEs=centers of excellence

Completed BLA-enabling PPQ campaign for TSHA-102 supporting potential future commercialization

Successfully produced commercial-scale drug product batches required to validate final commercial manufacturing process

Completed BLA-enabling PPQ manufacturing campaign for TSHA-102, which met predefined product specifications as well as comparability criteria for commercial product and clinical material, supporting potential inclusion of REVEAL Part A Phase 1/2 data in the planned BLA:

- Commercial product comparable to clinical material used in REVEAL and ASPIRE clinical trials supporting potential inclusion of REVEAL Part A data in planned BLA package
- High-quality product at commercial scale, including an encouraging **single-digit empty capsid percentage** contributing to patient safety
- Process consistency, efficiency and scalability support potential commercial demand

Expect to report FDA feedback following CMC Type B meeting in Q1 2027

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BLA=Biologics Licensing Application; PPQ=Process Performance Qualification

Rett syndrome: a devastating, rare and progressive X-linked neurodevelopmental disease

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



[1]Amir, R E et al. "Rett syndrome is caused by mutations in X-linked MECP2, encoding methyl-CpG-binding protein 2." *Nature genetics* vol. 23,2 (1999): 185-8. doi:10.1038/13810 [2]Braunschweig, Daniel et al. "X-Chromosome inactivation ratios affect wild-type MeCP2 expression within mosaic Rett syndrome and Mecp2-/+ mouse brain." *Human molecular genetics* vol. 13,12 (2004): 1275-86. doi:10.1093/hmg/ddh142.

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

Results in **loss of functional abilities and developmental milestones** and the emergence of hallmark symptoms by 6 years that progress over time[1]



Gross Motor Function

- Mobility issues
- Loss of movement and coordination abilities
- Gait disturbances
- Hypotonia
- Dystonia



Fine Motor Function

- Loss of hand function
- Loss of purposeful hand use
- Repetitive hand movements



Communication / Socialization

- Loss of speech / communication
- Social withdrawal
- Behavioral issues
- Intellectual disability



Autonomic Function / Seizures

- Epilepsy
- Sleep disturbances
- Breathing issues
- Gastrointestinal issues
- Cardiac dysfunction
- Vasomotor disturbances

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[1]Gold, Wendy A et al. "Rett Syndrome: A Genetic Update and Clinical Review Focusing on Comorbidities." *ACS chemical neuroscience* vol. 9,2 (2018): 167-176. doi:10.1021/acschemneuro.7b00346. [2]Armstrong, Dawna Duncan. "Neuropathology of Rett syndrome." *Journal of child neurology* vol. 20,9 (2005): 747-53. doi:10.1177/08830738050200090901.

There are no approved disease-modifying treatments that address the genetic root cause of Rett syndrome

High Unmet Medical Need

- Current standard of care focused on symptom management[1]
- Patients typically require 24/7 care and lifelong assistance[2]
- High caregiver burden with significant impact on quality of life and activities of daily living[2]

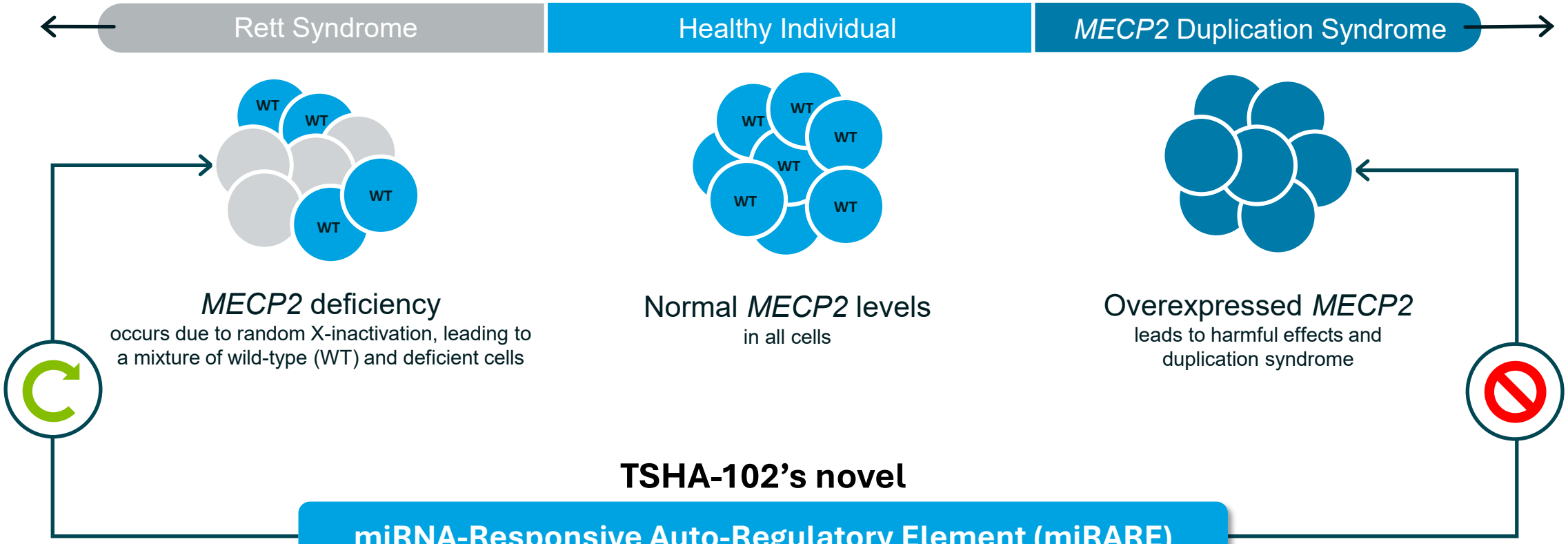
Significant Market Opportunity

- **~15,000 to 20,000 patients in major global markets** (U.S., EU+U.K.)[3]
  - >85% of prevalent U.S. population >10 years of age[4]
- **1 of every 8,700 female births worldwide**[5,6]
- Commercial launch and uptake of DAYBUE highlights market demand[6]

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[1]Fu, Cary et al. "Consensus guidelines on managing Rett syndrome across the lifespan." *BMJ paediatrics* open vol. 4,1 e000717. 13 Sep. 2020, doi:10.1136/bmjpo-2020-000717. [2]Coenraads, Monica et al. "Voice of the Patient Report: *Rett Syndrome Externally-Led Patient-Focused Drug Development Meeting*." 9 Aug. 2022, https://rettpfdd.org/site/assets/files/1/2022-rett-syndrome-voice-of-the-patient-report.pdf. [3]Amir, R E et al. "Rett syndrome is caused by mutations in X-linked MECP2, encoding methyl-CpG-binding protein 2." *Nature genetics* vol. 23,2 (1999): 185-8. doi:10.1038/13810. (estimated prevalence of *15,000-20,000 patients with typical Rett syndrome caused by a MECP2 mutation*). [4]Based on U.S. claims data. [5]Sarajlija, Adrijan, et al. "Epidemiology of Rett Syndrome in Serbia: Prevalence, Incidence and Survival." *Neuroepidemiology*, vol. 44, no. 1, 2015, pp. 1–5, https://doi.org/10.1159/000369494. [6]Laurvick, Crystal L., et al. "Rett Syndrome in Australia: A Review of the Epidemiology." *The Journal of Pediatrics*, vol. 148, no. 3, 2006, pp. 347–52. [6]Based on net product sales for the first quarter ended March 31, 2026 (source: Acadia Pharmaceuticals Reports First Quarter 2026 Financial Results and Operating Overview).

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



TSHA-102's novel

miRNA-Responsive Auto-Regulatory Element (miRARE)

technology is designed to correct *MECP2* deficiency and avoid toxic overexpression

[1]Van Esch, Hilde et al. "Duplication of the MECP2 region is a frequent cause of severe mental retardation and progressive neurological symptoms in males." *American journal of human genetics* vol. 77,3 (2005): 442-53. doi:10.1086/444549.

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

AAV9 Capsid

Clinically and commercially proven CNS capsid

Self-complementary Vector

Enables more rapid, potent and efficient transgene expression vs. traditional single-stranded viral genome[1]

***miniMECP2* Transgene**

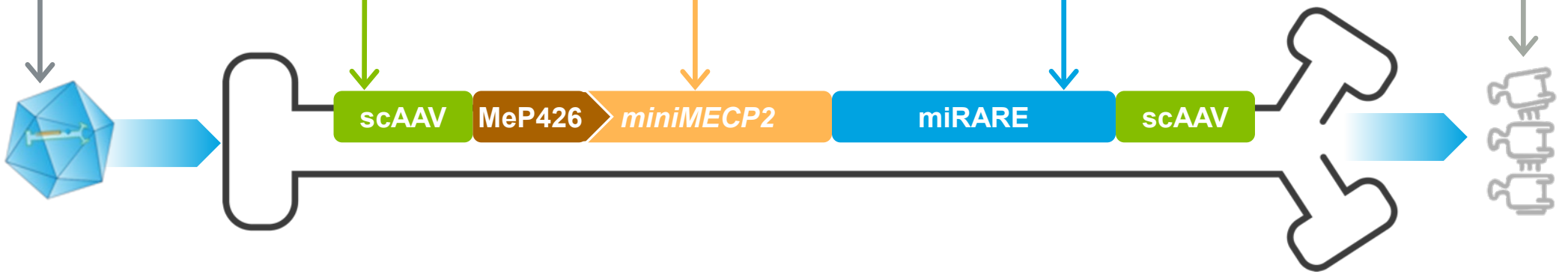
Contains essential functional domains, and smaller size enables packaging of construct in self-complementary viral genome[2]

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[3]

Intrathecal (IT) Delivery

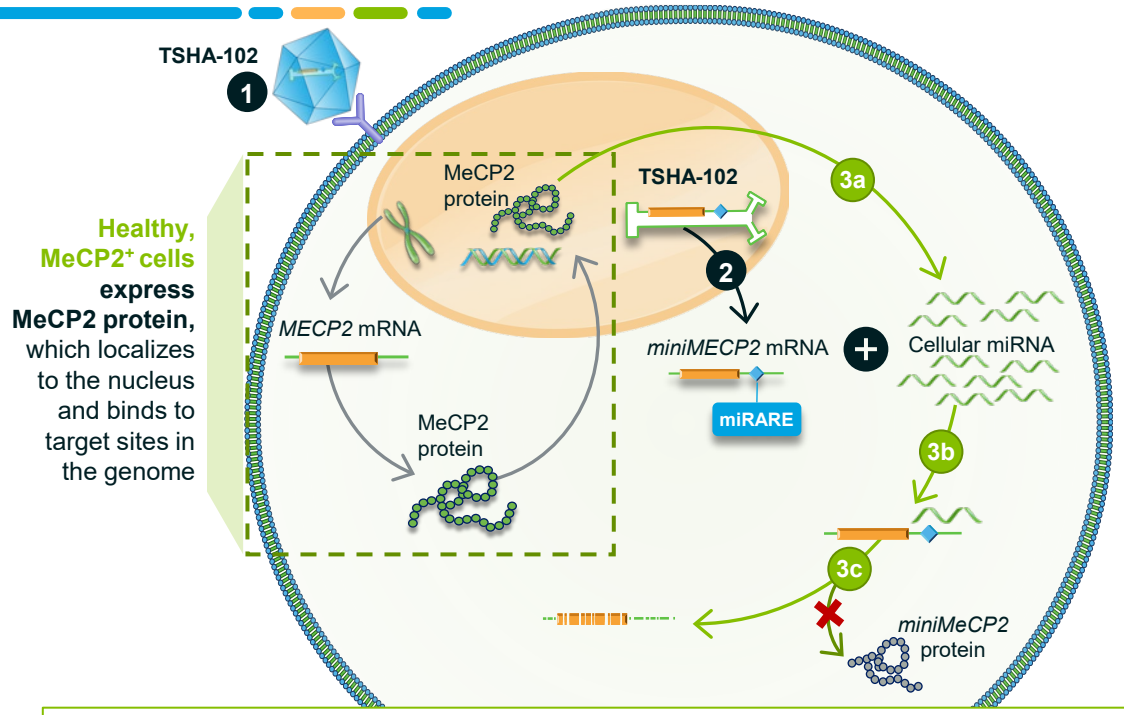
Leads to widespread and consistent biodistribution across the brain and spinal cord using a routine, minimally invasive procedure with potential for outpatient administration[4]

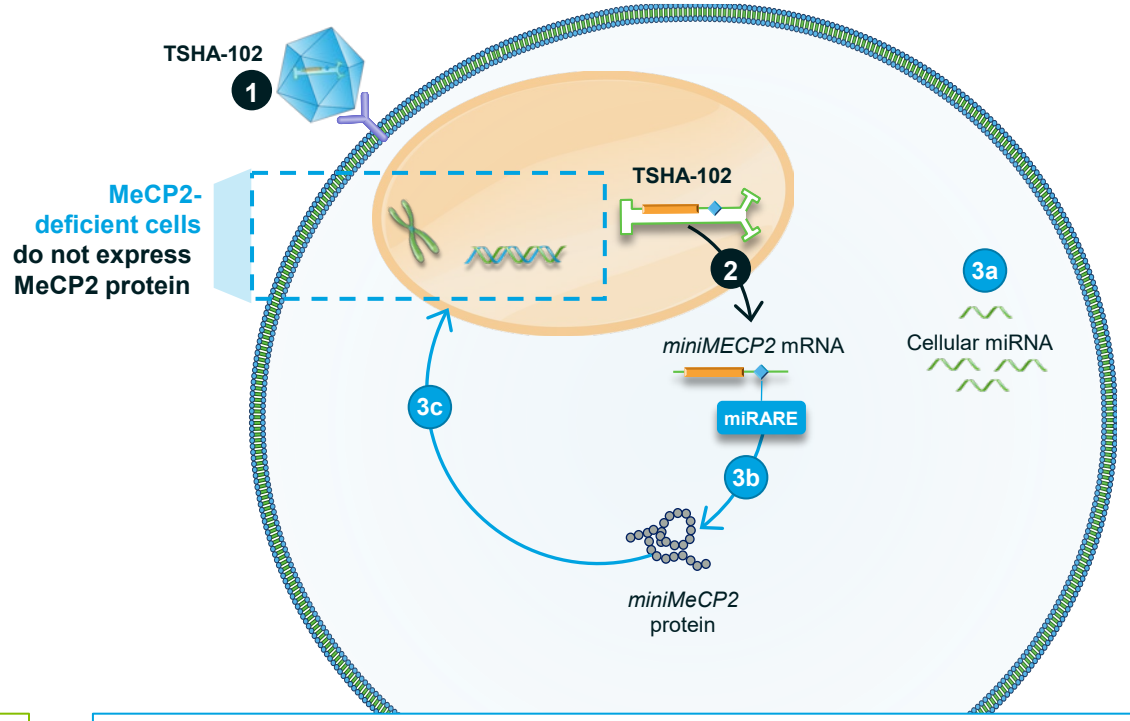


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[1]Gray, Steven J et al. "Preclinical differences of intravascular AAV9 delivery to neurons and glia: a comparative study of adult mice and nonhuman primates." Molecular therapy : *the journal of the American Society of Gene Therapy* vol. 19,6 (2011): 1058-69. doi:10.1038/mt.2011.72. [2]Tillotson, Rebekah et al. "Radically truncated MeCP2 rescues Rett syndrome-like neurological defects." *Nature* vol. 550,7676 (2017): 398-401. doi:10.1038/nature24058. [3]Haque, Emdadul 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, 25-26 Oct. 2023, Brussels, Belgium. [4]Haque et al. "rAAV9 vector biodistribution in nonhuman primate brain and spinal cord following lumbar intrathecal infusion" *Front. Med.* 13:1819594. doi: 10.3389/fmed.2026.1819594

miRARE: potential best-in-class approach to regulating *MECP2* expression using RNA interference and binding sites for endogenous microRNA responsive to MeCP2[1]





miRARE is designed to SILENCE *miniMECP2* transgene expression in healthy, MeCP2+ cells

In cells with normal MeCP2 function in the nucleus:

3a Cellular miRNAs are produced abundantly

3b 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**

miRARE is designed to ENABLE *miniMECP2* transgene expression in MeCP2-deficient cells

In cells lacking normal MeCP2 function:

3a Fewer cellular miRNAs are produced

3b Therefore, the transgene mRNA is translated to produce miniMeCP2 protein

3c The miniMeCP2 protein is imported into the nucleus, **restoring MeCP2 function**

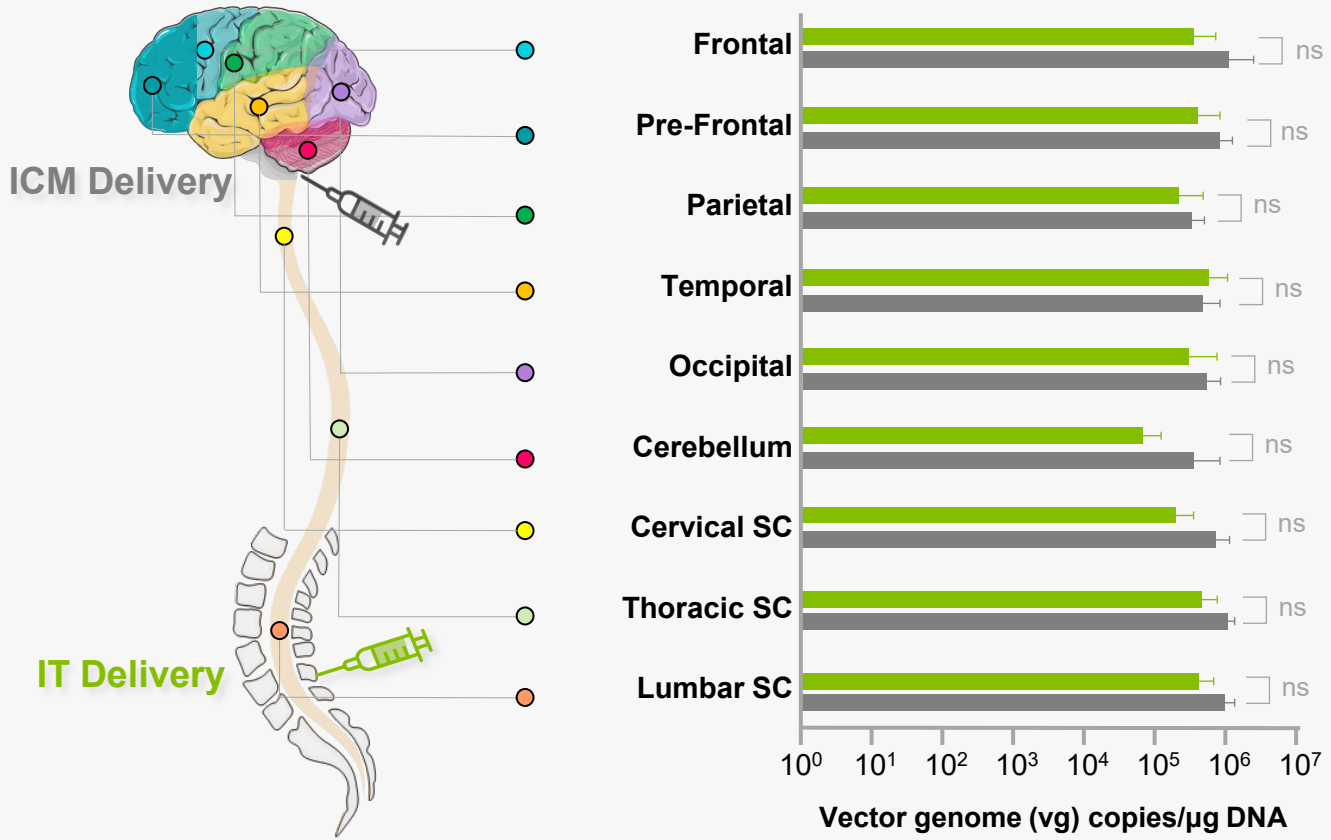
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[1]Sinnett, Sarah E et al. "Engineered microRNA-based regulatory element permits safe high-dose miniMECP2 gene therapy in Rett mice." *Brain*: a journal of neurology vol. 144,10 (2021): 3005-3019. doi:10.1093/brain/awab182.

Intrathecal (IT) Administration: a potentially effective, safe and minimally invasive delivery approach for broad targeting of the CNS[1]

- IT and ICM administration achieved **comparable, consistent and broad biodistribution** in the brain and spinal cord
- Supports TSHA-102 clinical development approach **leveraging the minimally invasive IT administration** with potential for **outpatient administration**
- IT administration **minimizes systemic exposure**, potentially reducing risk of immune responses and systemic toxicities

Biodistribution data comparing IT vs. ICM delivery using the same dose and volume in NHPs[1]



TSHA-102 (ICM): $2x10^{15}$ total vg HED, TSHA-105 (IT): $2x10^{15}$ total vg HED

[1]Haque et al. "rAAV9 vector biodistribution in nonhuman primate brain and spinal cord following lumbar intrathecal infusion" *Front. Med.* 13:1819594. doi:10.3389/fmed.2026.1819594

ICM=Intra-cisterna magna; NHP=Non-human primate; HED=Human equivalent dose; SC=Spinal cord; ns=Not significant

FDA-aligned pathway supports potential 6-month interim registrational strategy

PART A: REVEAL Phase 1/2 Trials
DOSING COMPLETE

Adolescent and Adult (females ≥12 years)

- **Low dose cohort** *5.7x10^{14} total vg* **N=2**
- **High dose cohort** *1x10^{15} total vg* **N=4**

Pediatric (females 5-8 years)

- **Low dose cohort** *5.7x10^{14} total vg* **N=2**
- **High dose cohort** *1x10^{15} total vg* **N=4**

PART B: REVEAL Pivotal Trial
DOSING COMPLETE

Developmental Plateau Population
(females 6 to <22 years)

- Evaluate efficacy and safety

N=17
1x10^{15} total vg

ASPIRE Trial
DOSING COMPLETE

Pre-developmental Plateau Population
(females 2 to <4 years)

- Evaluate safety and preliminary efficacy; efficacy data to be extrapolated from pivotal trial

N=4
1x10^{15} total vg[1]

Potential Registrational Path

Patients with Rett syndrome Age 2+

Written FDA alignment on:

- Potential to submit BLA based on REVEAL pivotal trial 6-month interim analysis
- Inclusion of ≥3 months of ASPIRE safety data in BLA submission to support a broad label in patients aged ≥2 years

[1]The 1x10^{15} total vg dose administered in ASPIRE will be scaled to account for the lower brain volume in 2 to <4-year-olds

Completed dosing in REVEAL pivotal trial for TSHA-102 to support BLA submission – on track to complete 6-month interim analysis

REVEAL
RETT SYNDROME PIVOTAL STUDY

Single-arm, open-label trial, using each patient as own control evaluating TSHA-102 in Rett syndrome

- TSHA-102 administered intrathecally at $1x10^{15}$ total vg (high dose)
- Dosed 17 females, ages 6 to <22 years (developmental plateau population)
  - Generally well tolerated; no severe treatment-related SAEs or DLTs[1] with all patients having cleared the acute post-dosing safety monitoring period
- **Primary Endpoint:** Response rate, defined as the % of patients who gain or regain ≥1 developmental milestone from a validated list of 28
  - Video-based determination of milestone gain/regain is performed by independent, blinded central raters

- **SAP:** 33% response rate is the minimum threshold for success sufficient to reject the null hypothesis of 6.7%[2]
  - 12-month primary analysis
  - FDA alignment on potential to submit BLA based on 6-month interim analysis
- **Key Secondary Endpoints:**
  - Average number of developmental milestones gained/regained per patient
  - R-MBA
  - CGI-I

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[1]Based on August 2026 safety data cutoff (N=17). [2]Based on Taysha's natural history data analysis, the null hypothesis is that one out of 15 patients aged ≥6 years may gain/regain one of the 28 natural history defined developmental milestone without treatment, corresponding to a response rate of 6.7%.
vg=Vector genomes; SAE=Serious adverse event; DLT=Dose-limiting toxicity; SAP=Statistical analysis plan; BLA=Biologics license application; R-MBA=Revised Motor Behavior Assessment; CGI-I=Clinician Global Impression–Improvement

Key findings that supported alignment with FDA on the REVEAL pivotal trial

1

Rett Syndrome Caregiver Research

achievement of a developmental milestone would be a meaningful therapeutic outcome

2

Rett Syndrome Natural History Data Analysis

by age ≥ 6 years, there is ~0% likelihood of gaining or regaining developmental milestones[1]

3

Part A Clinical Data

100% of patients gained/regained ≥ one developmental milestone post-TSHA-102[2]

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[1]Montgomery et al. "*The Developmental Plateau in Rett Syndrome: New Insights from the Natural History Study to Inform Novel Interventional Study Designs.*" 2026 IRSF Rett Syndrome Scientific Meeting, June 29-July 1, 2026, Prior Lake, MN. Poster Presentation.
[2]Based on May 2026 data cutoff (N=12).

Rett syndrome caregiver research indicates improved function or achievement of developmental milestones would significantly improve quality of life



Communication

Gained or improved communication of basic needs—through eye gaze, gestures, or words—would enable self-advocacy and strengthen social connections

- Ex: follow a command without a gesture, pointed for something they wanted, use word(s) with meaning, identify body parts (pointed with eyes or fingers)

Fine Motor Function

Gained or improved hand function would restore a sense of control and purpose, and enable play and social engagement

- Ex: finger feed, use fork or spoon to eat without assistance, reached for a toy, drank from a cup held without assistance

Gross Motor Function

Gained or improved gross motor function would foster independence and reduce the physical burden of caregiving

- Ex: walked independently or with support, stood while holding on, sat without support, climbed up stairs without help

"If she can actually tell me what she wants, or make a choice between two things, even if it's just looking at something purposefully…because now I don't know what's going on."
– Caregiver of 20-year-old

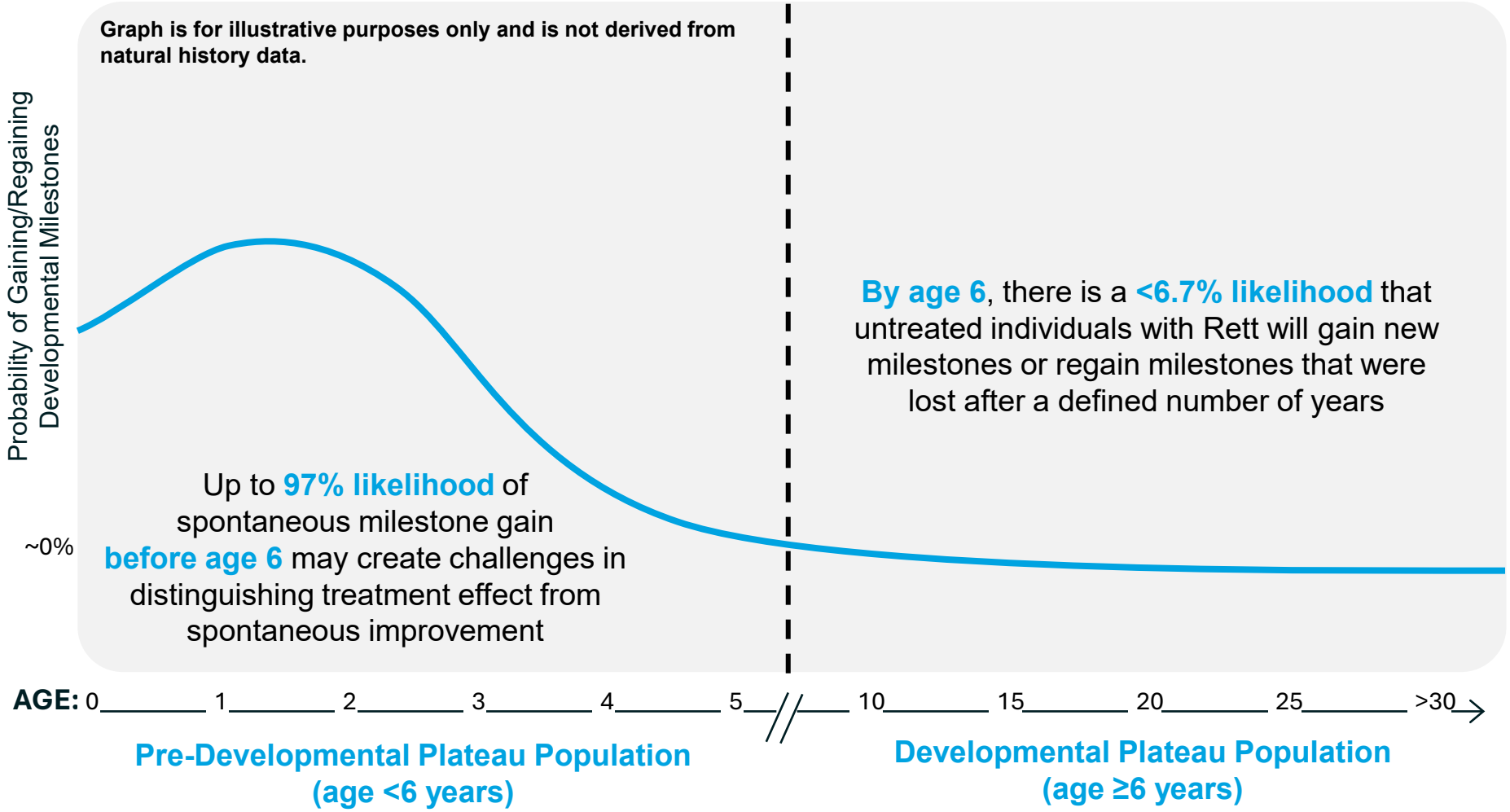
"Feeding herself, entertaining herself…being able to flip pages or purposefully hold a book, change the channel on a remote...would be a game changer for us."
– Caregiver of 8-year-old

"If we got a safe and secure sitting position from her, that would be a win. We would be able to have her sitting and not have to be right next to her. We could have her at the dining table with us."
– Caregiver of 5-year-old

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Keeley, Jessica et al. "*Every Gain, Expanding Possibilities: Caregiver Insights on Meaningful Improvement in Rett Syndrome Gene Therapy*." 2025 IRSF Rett Syndrome Scientific Meeting, 9-11 June 2025, Boston. Poster Presentation.

Rigorous analysis of the NHS informed the inclusion criteria and endpoint design for the REVEAL pivotal trial[1]



Results support minimum inclusion age of 6 years in a **well-controlled, single-arm interventional trial** evaluating gain and regain of developmental milestones

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[1]Montgomery et al. "*The Developmental Plateau in Rett Syndrome: New Insights from the Natural History Study to Inform Novel Interventional Study Designs*." 2026 IRSF Rett Syndrome Scientific Meeting, June 29-July 1, 2026, Prior Lake, MN. Poster Presentation.

28 developmental milestones from the natural history dataset included in the pivotal trial primary endpoint

Communication

- Pointed for something they wanted
- Waved “Bye-Bye”
- Followed a command with a gesture
- Identified body parts (pointed with eyes or fingers)
- Followed a command without a gesture
- Used word(s) with meaning
- Spoke in phrases (2 words or more) with meaning

Fine Motor

- Reached for toy
- Holds bottle unpropped
- Used raking grasp to retrieve an object
- Used pincer grasp (refined or modified)
- Transferred an object from one hand to another
- Finger fed
- Drank from a cup held without assistance
- Used a fork or spoon to eat with assistance
- Used a fork or spoon to eat without assistance

Gross Motor

- Come to sitting
- Sat without support
- Stood while holding on
- Pulled to standing
- Stood independently
- Walked with support
- Walked independently
- Climbed up stairs with help
- Climbed down stairs with help
- Climbed up stairs without help
- Climbed down stairs without help
- Ran 10 feet without falling

Selection criteria:

- ✓ **Meaningful functional gains based on caregiver research**
- ✓ **Represent activities of daily living**
- ✓ **0% to <6.7% likelihood gained/regained in patients age ≥ 6 years with untreated Rett syndrome[1]**

[1]Montgomery et al. "*The Developmental Plateau in Rett Syndrome: New Insights from the Natural History Study to Inform Novel Interventional Study Designs*." 2026 IRSF Rett Syndrome Scientific Meeting, June 29-July 1, 2026, Prior Lake, MN. Poster Presentation.
NHS=Natural history study

Longer-term REVEAL Part A data demonstrated broad, consistent functional gains that deepened over time regardless of patient age, disease severity or genotype[1]

- **100% of patients (N=12, 6-21 years) in the developmental plateau population of Rett gained/regained ≥1 developmental milestone**
- **Longer-term follow-up demonstrated a durable and deepening treatment effect across all patients, with additional functional gains accumulating over time ≥12 months post-TSHA-102**
  - Developmental milestone gains increased by 69% from 6 to 12 months and by 94% from 6 to ≥12 months
  - Patients with longest follow-up at 30 months continued to demonstrate functional gains/improvements
- **Broad functional impact consistently demonstrated across core disease domains regardless of age, disease severity or genotype**
  - At ≥12 months post-TSHA-102, a total of 310 functional gains were observed (~26 per patient), comprising 31 developmental milestones and 279 additional skill gains/improvements
  - Durable, multi-domain gains enable independent engagement in daily activities, reduce caregiver burden and enhanced social engagement
- **Robust, clinically meaningful responses at 6 and ≥12 months exceed FDA-aligned minimum threshold for efficacy, supporting the potential for a BLA submission based on REVEAL pivotal trial 6-month interim analysis**
  - FDA alignment on product comparability enables REVEAL Part A data to be included in the BLA, which further supports the potential for a BLA submission based on the pivotal trial interim analysis
- **No treatment-related SAEs or DLTs observed in any patients, with all patients having ≥12 months of follow-up**

Based on May 2026 data cutoff (N=12).

Rigorous evaluation criteria applied to Part A data enabled reliable, objective assessment of TSHA-102 efficacy

Evaluation of Functional Gains

Primary evidence of efficacy

Developmental Milestones (DM)

The functional gain of ≥1 of the **28 DMs defined in the natural history study** assessed via rigorous video-evidenced evaluation

Evaluation Criteria:

- ✓ **Baseline**: Video data/medical history confirming milestone was either never gained or lost sufficiently long ago, such that the likelihood of spontaneous gain/regain is <6.7%[1]
- ✓ **Post-treatment**: Video evidence of milestone demonstration
- ✓ **Evaluation method**: Determined by multiple independent central raters based on prespecified definitions of achievement for each milestone

Additional evidence of functional gain

Additional Skills and Improvements

Functional gain or improvement in a core disease characteristic **beyond the 28 natural history defined DMs** assessed via rigorous video-evidenced evaluation and validated scales

Evaluation Criteria:

- ✓ **Adapted Mullen Scales of Early Learning (MSEL-A)**: Centrally rated video-recorded evaluation assessing expressive and receptive language skills
- ✓ **Observer-Reported Communication Ability (ORCA)**: Caregiver-reported structured evaluation assessing communication skills
- ✓ **Revised Motor Behavior Assessment (R-MBA):** Clinician-reported video evaluation assessing frequency, severity or independence of Rett syndrome characteristics

n=8 patients with ORCA data, n=7 with MSEL-A data, and n=12 with R-MBA data

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[1]Accessed from IRSF. ClinicalTrials.gov: NCT02738281: a prospective cohort of individuals with a pathologic mutation in the MECP2 gene, commonly associated with RTT. Incidence models of NHS data conducted by third-party statistical partners.

All 12 pediatric, adolescent and adult patients across a broad range of disease severity gained/regained ≥one **developmental milestone** post-TSHA-102

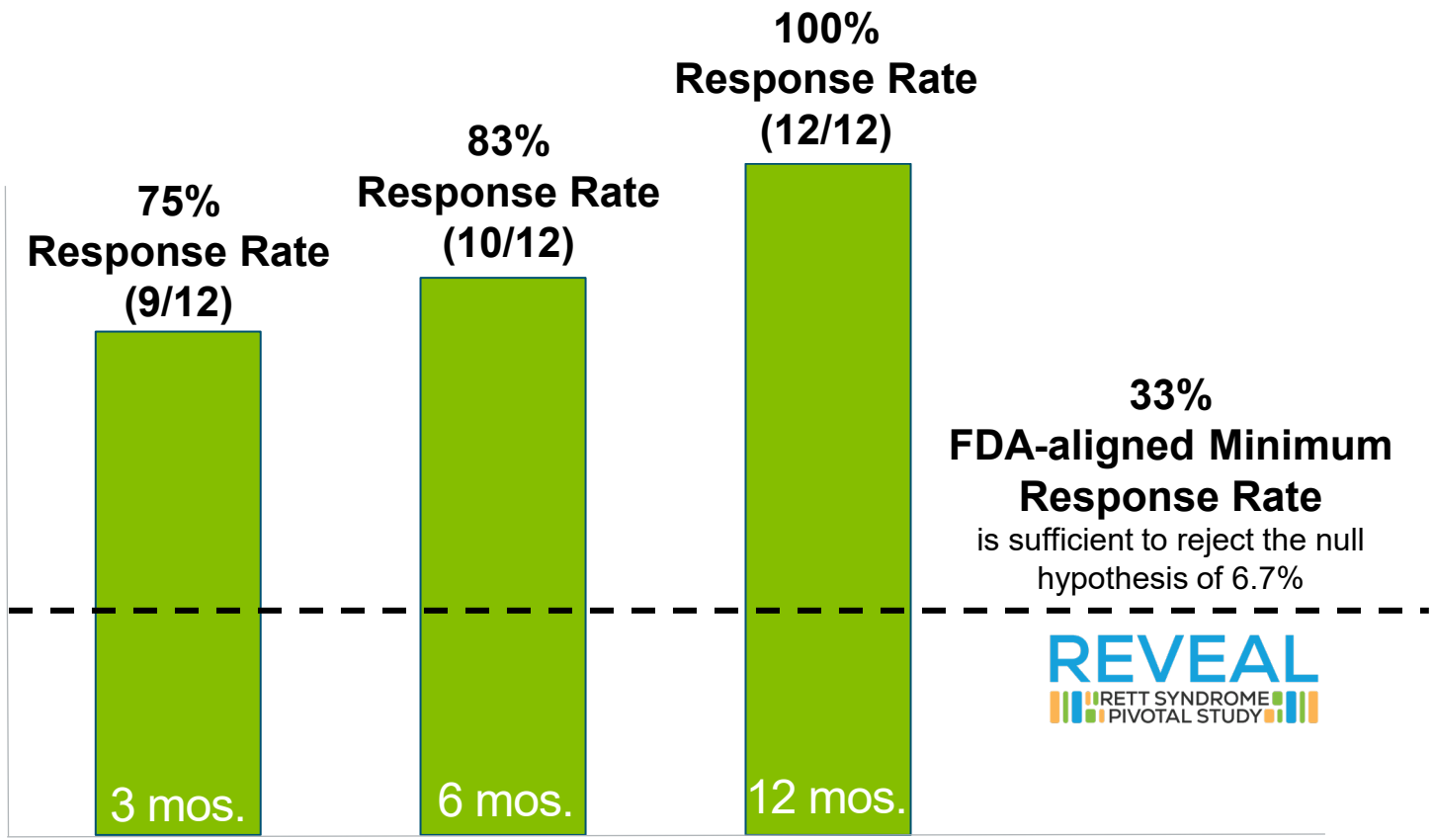
with a **<6.7% likelihood** of being achieved without treatment based on NHS data[1]

	Cohort 1: Low Dose 5.7x10^{14} total vg				Cohort 2: High Dose 1x10^{15} total vg							
	LD:P1	LD:P2	LD:P3	LD:P4	HD:P1	HD:P2	HD:P3	HD:P4	HD:P5	HD:P6	HD:P7	HD:P8
Age at Dosing:	20 yrs	21 yrs	6 yrs	7 yrs	15 yrs	21 yrs	8 yrs	15 yrs	16 yrs	6 yrs	7 yrs	6 yrs
Baseline CGI-S Score:	6	4	5	4	5	5	5	5	5	4	6	5
Time Post-Dosing	30 mos.	30 mos.	24 mos.	24 mos.	18 mos.	18 mos.	18 mos.	12 mos.	12 mos.	12 mos.	12 mos.	12 mos.
	≥1 Milestone Gained Post-TSHA-102				≥1 Milestone Gained Post-TSHA-102							
	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

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Based on May 2026 data cutoff (N=12). Developmental milestone gains and regains were assessed by multiple independent central raters through video evidence.[1]Incidence models derived from NHS data; accessed from IRSF. ClinicalTrials.gov: NCT02738281: a prospective cohort of individuals with a pathologic mutation in the MECP2 gene, commonly associated with RTT. Cumulative incidence models of NHS data conducted by third-party statistical partners.
NHS=Natural history study; vg=Vector genomes; CGI-S=Clinical Global Impression-Severity (4=moderately ill, 5=markedly ill, 6=severely ill)

Rapid and robust response rate in REVEAL Part A supports the pivotal trial is well-powered to establish efficacy



REVEAL Phase 1/2 Part A Data

REVEAL Part A data exceeded FDA-aligned response rate threshold for pivotal trial success

Supports potential for 6-month REVEAL pivotal trial interim analysis to enable BLA submission

Response Rate = the % of patients who gain or regain ≥1 developmental milestone from a list of 28

Based on May 2026 data cutoff (N=12). Developmental milestone gains and regains were assessed by multiple independent central raters through video evidence.

31 total developmental milestones achieved across core disease domains post-TSHA-102 reflect meaningful improvements in daily living



Communication

- Spoke in phrases with meaning
- Used word(s) with meaning
- Followed a command without a gesture
- Followed a command with a gesture
- Pointed for something they wanted
- Identified body parts

Enable **expression of needs**, preferences, emotions, and foster **social connections**



Fine Motor

- Used utensils to eat without assistance
- Used utensils to eat with assistance
- Finger fed
- Holds bottle unpropped
- Used a pincer grasp
- Reached for a toy
- Transferred an object from one hand to another

Reflect self-care skills and purposeful hand use that **enable independence**



Gross Motor

- Walked with support
- Climbed down stairs with support
- Stood while holding on
- Pulled to standing
- Sat without support

Enhance mobility and independence, and **reduce the physical burden of caregiving**

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Based on May 2026 data cutoff (N=12). Developmental milestone gains and regains were assessed by multiple independent central raters through video evidence.

TSHA-102 delivered consistent and clinically meaningful treatment benefit across pediatric and adolescent/adult patients with Rett syndrome

Results support the broad treatment potential of TSHA-102

16

Total Developmental Milestones Achieved Across 6 **PEDIATRIC** Patients



15

Total Developmental Milestones Achieved Across 6 **ADOLESCENT & ADULT** Patients



"Her hands are more relaxed, and she tries to grab everything. She can follow directions in a snap, like if we say, 'let's go,' she gets up, heads to the door. She's babbling now, which she didn't do before, and is definitely trying to tell us something.**"**

– Caregiver of pediatric participant

"She's a lot easier to care for. She can point a lot more deliberately to make choices and show us what she wants, and she will keep gesturing until we get it for her. And she pushes away what she doesn't want.**"**

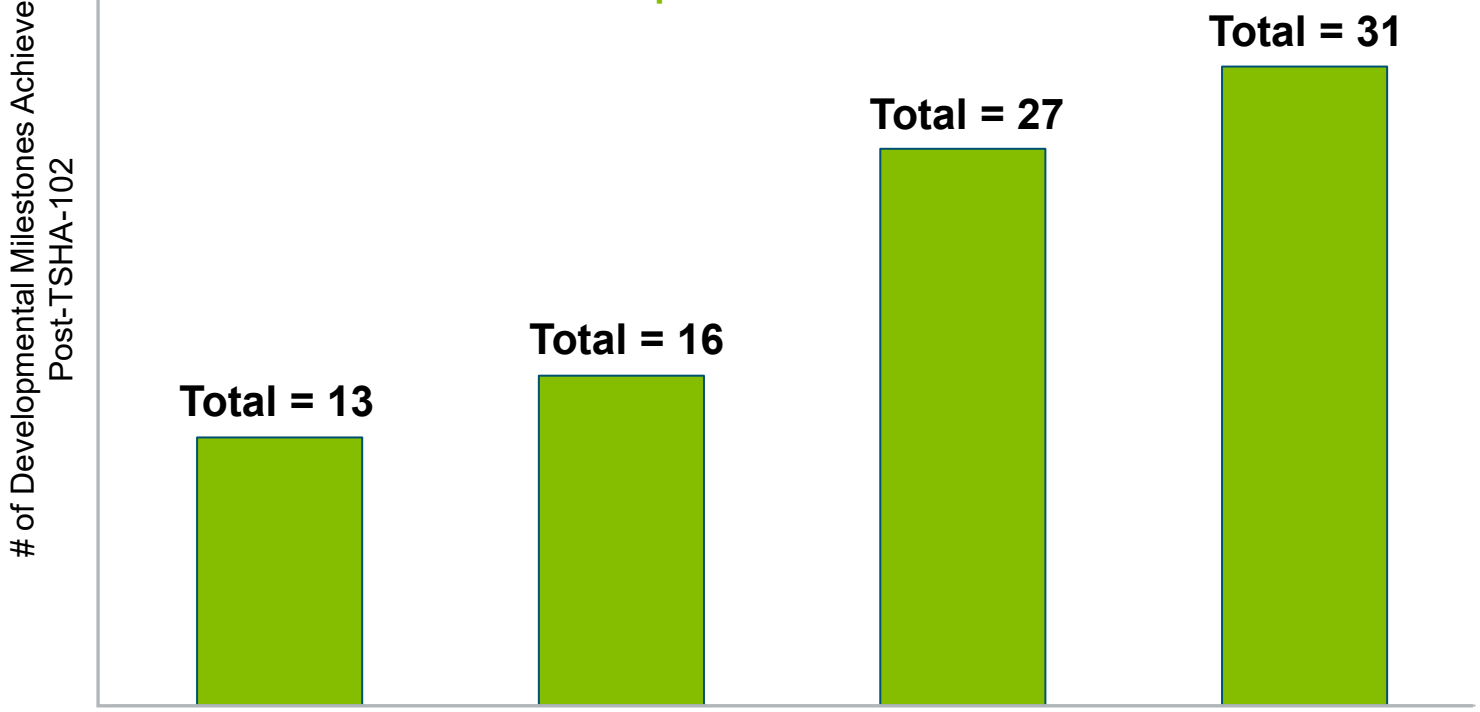
– Caregiver of adolescent/adult participant

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Based on May 2026 data cutoff (N=12). Developmental milestone gains and regains were assessed by multiple independent central raters through video evidence.

TSHA-102 drove early and sustained **developmental milestone gains** with additional gains over time across the three core disease domains

Assessed by multiple independent central raters using video-evidenced review in accordance with the pivotal trial criteria

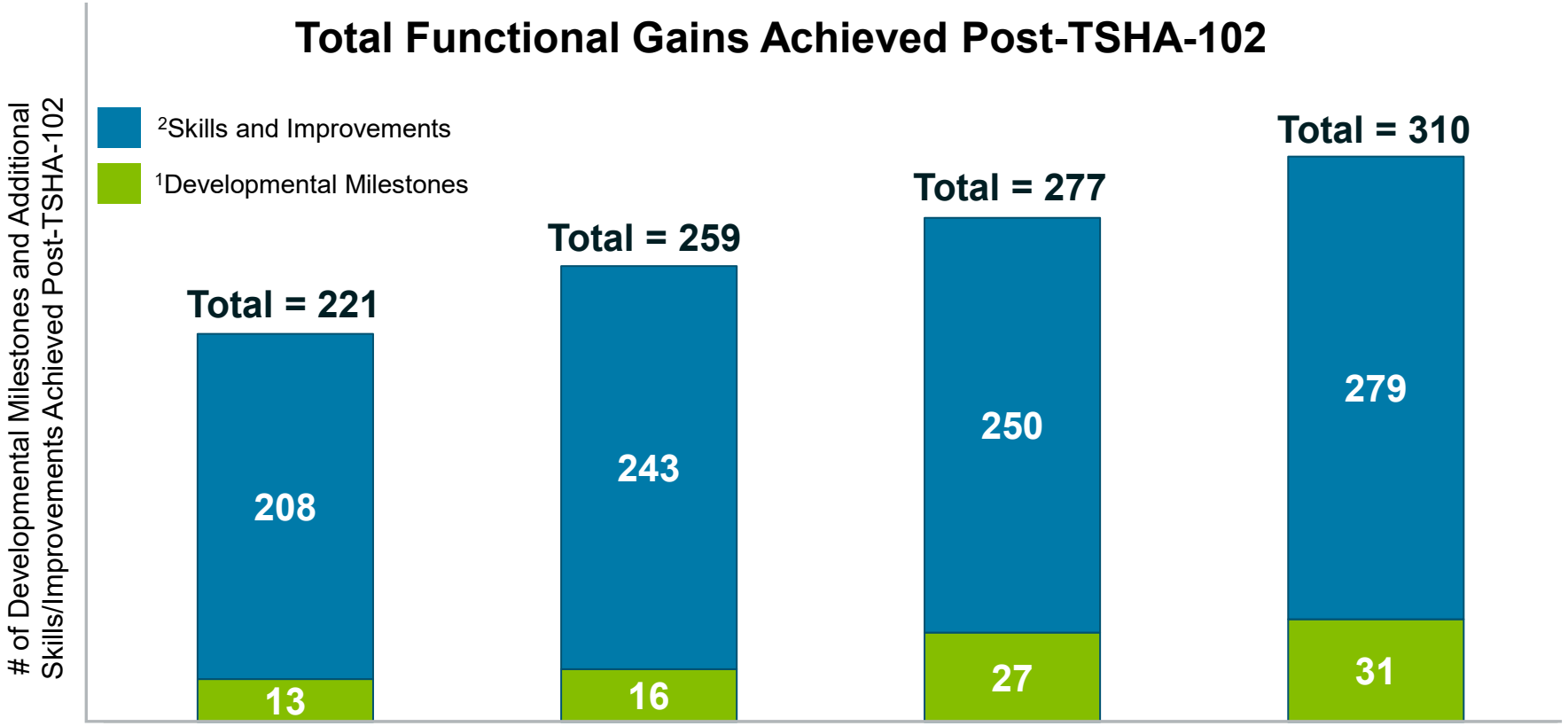


3 mos	6 mos	12 mos	≥12 mos
N=12	N=12	N=12	N=12*
1.1 average gains per patient	**1.3 average gains per patient**	**2.3 average gains per patient**	**2.6 average gains per patient**

- Milestones increased by 69% from 6 to 12 months and by 94% from 6 to ≥12 months post-TSHA-102
- 75% of patients in the high dose cohort achieved ≥2 milestones post-TSHA-102

Based on May 2026 data cutoff (N=12). Developmental milestone gains and regains were assessed by multiple independent central raters through video evidence. *N=7 patients with data >12 months post-TSHA-102 and N=5 patients with 12-month data.

Patients achieved durable, clinically meaningful **skill gains and improvements** that accumulated over time in addition to developmental milestones



~26 functional gains per patient across core disease domains reflect the broad functional impact demonstrated post-TSHA-102

Based on May 2026 data cutoff (N=12). [1]Gain/regain of ≥1 of the 28 natural history-defined developmental milestones from the REVEAL pivotal trial primary endpoint.
[2]Skill gains/improvements derived from MSEL-A, R-MBA and ORCA: N=8 patients with ORCA data, N=7 with MSEL-A data, and N=12 with R-MBA data.
*N=7 patients with data >12 months post-TSHA-102, N=5 patients with 12-month data.

REVEAL caregiver testimonials post-TSHA-102 highlight the impact of functional gains on quality of life

"She has lots of interest in the world around her. She **says what she wants**, and we know what she doesn't! **We can negotiate with her** – if I ask her if she wants this or that, **she'll respond, 'no way'** and she will argue."

"She's **gained multiple words** – 'no,' 'yeah,' 'mom,' 'dad' – and even says some phrases – 'ok, bye' and 'no more.'"

"She can **feed herself finger foods**. She can **bring the fork up to her face**, she will get it to mouth – she's never done before!"

"Now, when I am brushing her teeth, she will **reach for the toothbrush**. So, I am working on **teaching her to brush by herself**."

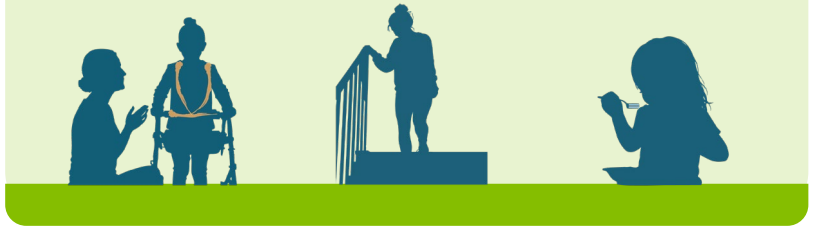
"**Huge quality of life gain – standing with support.** It has been a godsend when it comes to toileting while out in the community because now, **I can have her stand and hang on to my arm** to toilet or wipe her."

"She's **walking well in gait trainer**. I've never seen her initiate steps with such intent. At baseline she would just drag her feet. School staff was super impressed!"

310 total functional gains achieved post-TSHA-102 highlight its broad functional impact

31 developmental milestones, including:[1]

- Walked with support
- Climbed down stairs with support
- Used utensils to eat without assistance
- Pulled to standing
- Finger fed
- Used word(s) with meaning
- Spoke in phrases with meaning
- Pointed for something they wanted



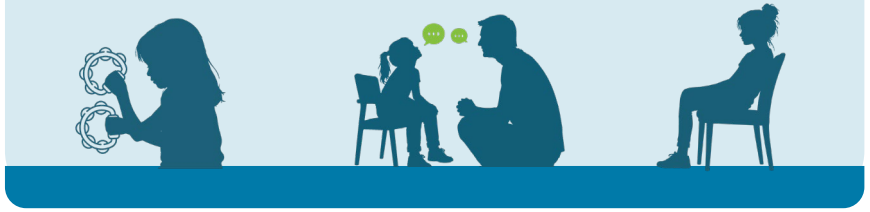
310

Functional Gains

demonstrated across the 12 patients post-TSHA-102

279 skill gains and improvements, including:[2]

- Improved motor skills and hand use
- Understood and responded to questions
- Reduced/no seizure episodes
- Reduced/no hand stereotypies
- Reduced/no breath holding/hyperventilation
- Followed directions related to daily routine(s)
- Identified body parts (to indicate pain/discomfort)
- Engaged in play with others



Functional gains listed are not inclusive of all that were observed in the study

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Based on May 2026 data cutoff (N=12). [1]According to gain/regain of ≥1 of the 28 natural history-defined developmental milestones from the REVEAL pivotal trial primary endpoint. [2]According to the MSEL-A (53 skill gains), ORCA (128 skill gains) and R-MBA (98 improvements).

Meet Jane, a 21-year-old woman living with Rett syndrome

BASELINE



Non-verbal

Low interest in social interactions



Unable to express her wants and needs and rarely made choices

Unable to follow commands



No purposeful hand use and very rarely finger fed



Walked independently with slow, unsteady movements, requiring close supervision

Unable to use stairs



Daily to weekly seizures

Took more than 30 minutes to feed

Based on May 2026 data cutoff. The name shown is a pseudonym used to protect the patient's identity.

Jane, 21-years-old at dosing, achieved sustained, meaningful functional gains

18 MONTHS POST-TSHA-102 (HIGH DOSE)



Speaks in phrases with meaning

Consistently engaged and socially interactive



Points to what she wants and consistently makes choices

Follows commands without a gesture



Consistently uses her fingers to self-feed and holds a juice box in her hands



Improved gait and mobility with reduced bradykinesia

Climbs the stairs with minimal support



Monthly seizures

No feeding difficulties

"All of our days are better. Her improvements are much beyond anything we had expected or hoped for."
— JANE'S MOM

"She has benefited strongly from this therapy. She has gained more autonomy, and her quality of life has improved. She is now able to interact purposefully with her environment and with her loved ones."
— PRINCIPAL INVESTIGATOR

"We would never go back to the way things were before. This has been a miracle!"
— JANE'S MOM

Based on May 2026 data cutoff. The name shown is a pseudonym used to protect the patient's identity.

Meet Sarah, a 6-year-old girl living with Rett syndrome

BASELINE



Used one word with meaning

Rarely responded to spoken words



Constant hand stereotypies with limited hand function



Unable to use eating utensils



Takes a few steps with assistance

Required assistance for positional transfers



Frequent breath-holding and hyperventilation with cyanosis and cold, blue extremities

Based on May 2026 data cutoff. The name shown is a pseudonym used to protect the patient's identity.

Sarah, 6-years-old at dosing, achieved sustained, meaningful functional gains

12 MONTHS POST-TSHA-102 (HIGH DOSE)



Can use multiple words with meaning

Uses an AAC device to communicate, express her needs, and make requests

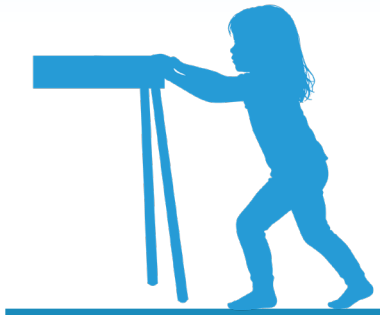


Reduced frequency of hand stereotypies

Uses her hands to play with toys



Uses utensils to eat without assistance



Pulls herself to a standing position and maintains a standing position with support



Reduced frequency of breath-holding and hyperventilation

Improved cyanosis with warm extremities, normal in color

"…if we were given the choice to receive this therapy again, we would definitely do it again. This was all worth it!"
— SARAH'S DAD

"Her ability to communicate and to interact with her environment has improved notably since therapy. Her attention, eye gaze and engagement with others have significantly improved. Her hand function is also improved."
— PRINCIPAL INVESTIGATOR

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Based on May 2026 data cutoff. The name shown is a pseudonym used to protect the patient's identity.
AAC=Augmentative and Alternative Communication

TSHA-102 delivered durable, multi-domain functional gains that enable activities of daily living

REVEAL
RETT SYNDROME PHASE 1/2 STUDY

Examples of functional gains observed across the 12 patients post-TSHA-102



Communication improvements

Pre-TSHA-102	Post-TSHA-102
Non-verbal	**Speaks in phrases / sentences with meaning**
Understood simple words	**Engages in conversations and play/activity with others**
Made choices <10% of time using eye gaze	**Consistently makes choices by pointing**
Rarely responds to spoken words	**Follows directions and responds to questions**



Fine motor improvements

Pre-TSHA-102	Post-TSHA-102
Required caregiver-assisted feeding	**Finger feeds and uses utensils to eat independently**
No purposeful hand use	**Plays with toys and self-feeds**
Stereotypies 76-100% of time	**Stereotypies 1-25% of time**
Limited hand function	**Holds a bottle unpropped**



Gross motor improvements

Pre-TSHA-102	Post-TSHA-102
Non-ambulatory	**Walks with support**
Unable to use stairs	**Climbs down stairs with support**
Required caregiver support for positional transfers and to stand	**Pulls self to standing position and stands while holding on**
Most severe dystonia (fixed positional deformity)	**No dystonia**



Autonomic/other improvements

Pre-TSHA-102	Post-TSHA-102
Unable to eat by mouth and required a g-tube	**Eats/drinks by mouth**
Weekly to monthly seizure episodes	**Seizure-free ≥6 months**
Hyperventilating/ breath holding 26-50% of time	**Absent or reduced hyperventilating/ breath holding**
Feeding took >30 minutes	**No feeding difficulties**

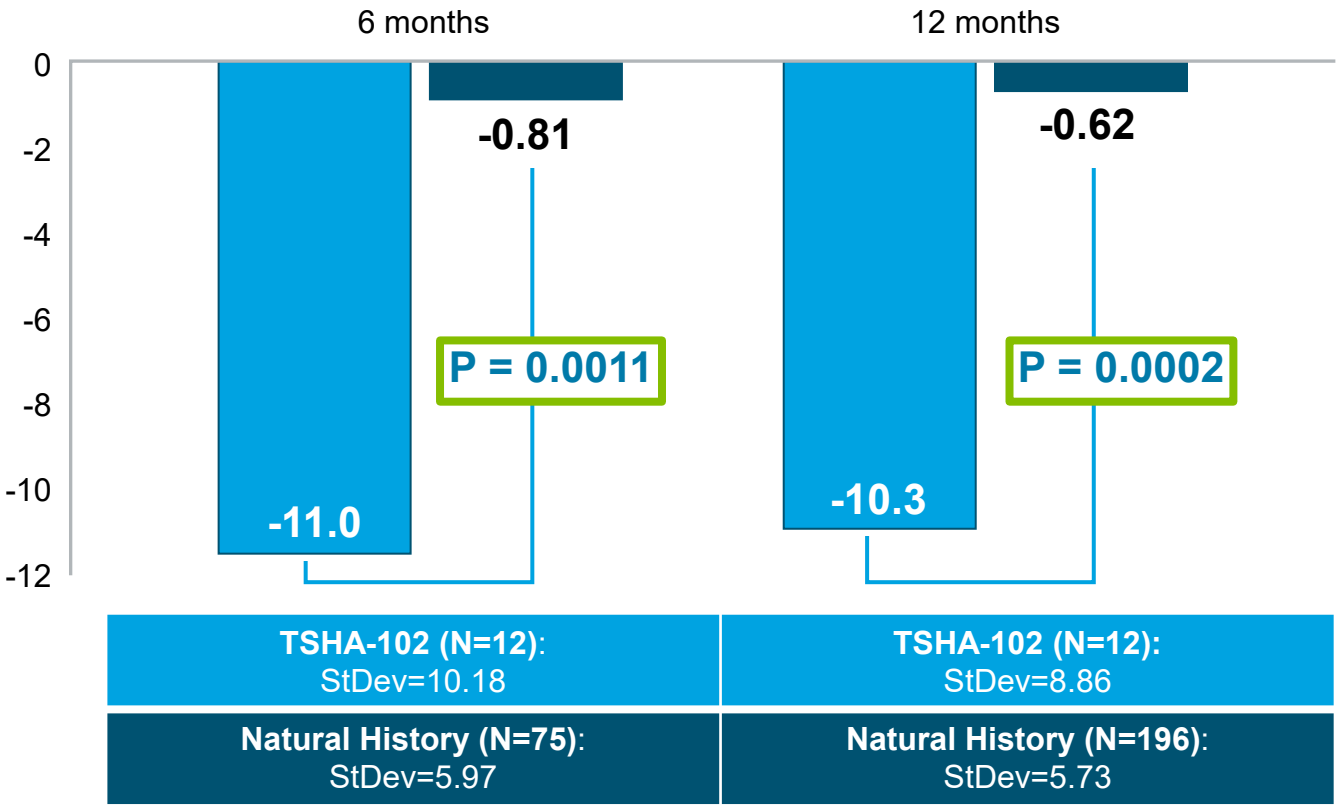
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Based on May 2026 data cutoff (N=12).

TSHA-102 demonstrated a **statistically significant** mean R-MBA score improvement indicating a reversal in the disease trajectory

Lower R-MBA score is associated with developmental milestone acquisition and quality of life improvement

R-MBA Score Mean Change From Baseline in Patients ≥6 Years: REVEAL low and high-dose patients vs natural history[1]



- **Average score ≥18 months post-TSHA-102:**
  - -15.7 in high dose cohort
  - -7.8 in low dose cohort

Based on May 2026 data cutoff (N=12 at 6 and 12 months, N=7 at ≥18 months post-TSHA-102). Statistical analyses are based on May 2026 data cutoff (N=12). [1]R-MBA assessed in Rett syndrome NHS at ~6 and ~12 months; MBA natural history data converted to R-MBA; mean scores reported were calculated from baseline to 6 and 12 months: Accessed from International Rett Syndrome Foundation (IRSF). ClinicalTrials.gov: NCT02738281: a prospective cohort of individuals with a pathologic mutation in the MECP2 gene, commonly associated with RTT.
R-MBA=Revised Motor Behavior Assessment

TSHA-102 demonstrated early global improvement, with dose-dependent effects that deepened over time in CGI-I

100% of Patients Demonstrated an Improved CGI-I Score of ≤3 at Multiple Post-treatment Visits

CGI-I assesses clinician's impression of improvement from baseline
(1 = Very much improved | 7 = Very much worse)

	3 months	6 months	9 months	12 months	≥18 months
Low Dose: Average CGI-I Score	**3.0** N=4	**2.3** N=4	**3.0** N=2	**3.3** N=4	**2.3** N=4
High Dose: Average CGI-I Score	**2.7** N=7	**2.5** N=8	**2.5** N=8	**2.6** N=8	**1.7** N=3

Time Post TSHA-102:

Based on May 2026 data cutoff (N=12). CGI-I average scores based on latest assessment for each patient.
CGI-I=Clinical Global Impression-Improvement

Robust and clinically meaningful responses at 6 and ≥12 months support potential for BLA submission based on the 6-month interim analysis from REVEAL pivotal trial

Endpoint		6 Months Post-TSHA-102 *n=12*	12 Months Post-TSHA-102 *n=12*	≥18 Months Post TSHA-102 *n=7*
Functional Gains	% of Patients Gained/Regained ≥1 Developmental Milestone	83%	100%	100%
	Average Functional Gains Per Patient	22 gains per patient	23 gains per patient	26 gains per patient
R-MBA[1]	Statistically Significant Mean Score Improvement vs Natural History	-11.0 P = 0.0011	-10.3 P = 0.0002	-11.0 P = 0.0046
CGI-I	% of Patients with CGI-I Score ≤3 at Multiple Post-treatment Assessments	100%	100%	100%
CGI-S[2]	% of Patients with CGI-S Total Score Improvement	25%	25%	57%

FDA alignment on product comparability enables REVEAL Part A data to be included in the BLA, which further supports the potential for a BLA submission based on the pivotal trial interim analysis

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Based on May 2026 data cutoff (N=12).
[1]R-MBA mean score change post-TSHA-102 is relative to baseline; lower score=improvement from baseline.
[2]CGI-S=Clinical Global Impression-Severity: a clinician-assessed scale ranging from 1 to 7, assessing severity of illness.

TSHA-102 was generally well-tolerated at low and high doses with no severe treatment-related SAEs or DLTs

Events Across the 12 Pediatric, Adolescent and Adult Patients Dosed in Part A of REVEAL Phase 1/2 Trials[1]

	Low Dose $5.7x10^{14}$ vg (n=4)		High Dose $1x10^{15}$ vg (n=8)		Total (n=12)	
	N	E	N	E	N	E
TEAE Related to TSHA-102:	4	17	5	20	9	37
Serious TEAE Unrelated to TSHA-102:	3	9	4	8	7	17
Serious TEAE Related to TSHA-102:	0	0	0	0	0	0

N=Number of participants; E=Number of events

- All TEAEs considered related to TSHA-102 were mild-moderate in severity, with the most common being:
  - Elevated liver enzymes* (n=4, 33%)
  - CSF protein increased (n=3, 25%) (clinically insignificant)
  - Pyrexia (n=3, 25%)
- Seizures have generally been well controlled following TSHA-102

*Includes PTs: Gamma-glutamyltransferase increased, Hypertransaminasaemia, Liver function test increased, Transaminases increased

No severe treatment-related SAEs or DLTs across the REVEAL Phase 1/2, Pivotal and ASPIRE trials (N=33)[2]

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[1]REVEAL Part A data cut May 2026 (N=12).[2]REVEAL Part A, REVEAL pivotal trial, and ASPIRE safety data cut August 2026 (N=33)
SAE=Serious adverse event; DLT=Dose-limiting toxicity; TEAE=Treatment-emergent AE; NfL=Neurofilament light chain; CSF=Cerebrospinal fluid; ULN=Upper limit normal

Anticipated milestones

Q1 2027	FDA feedback following CMC Type B meeting
1H 2027	Topline data from REVEAL pivotal trial 6-month interim analysis and FDA feedback on BLA submission pathway
1H 2027	Nominate additional gene therapy development candidate targeting a CNS disorder and commence preclinical development activities

Well-capitalized through key milestones:

- Cash and cash equivalents of $422.8 million as of September 30, 2026
- Cash runway expected to fund operating expenses and capital requirements into 2H 2028

Appendix

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Overview of Clinical Global Impression-Improvement (CGI-I) rating with Rett syndrome-specific anchors[1]

CGI-I: Clinician-rated scale
assessing improvement from baseline

- Designed as a global clinical assessment
- Factors considered to determine change included duration, onset, durability of change and the context of sign/symptom change across the Rett syndrome specific domains of the CGI

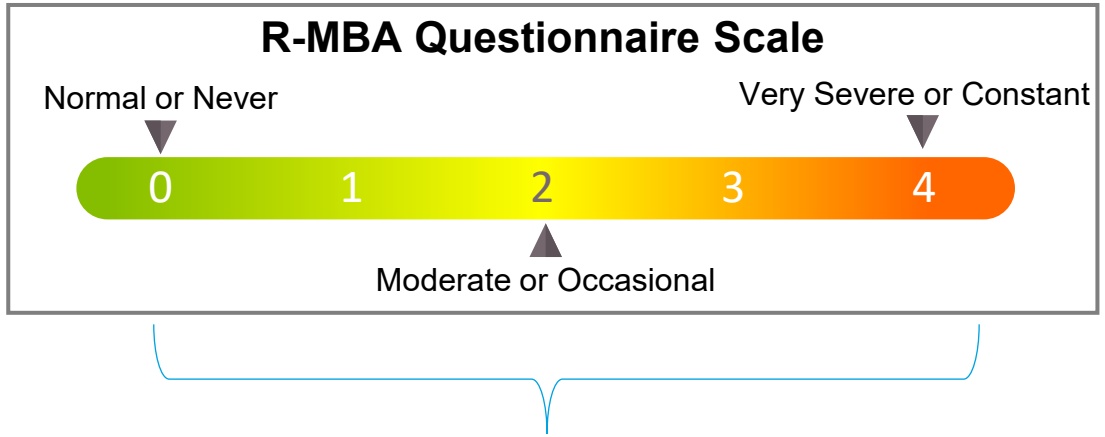
Score	CGI-I
1	**Very much improved**
2	**Much improved**
3	**Minimally improved**
4	No change
5	Minimally worse
6	Much worse
7	Very much worse

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[1]Neul, Jeffrey L et al. "Improving Treatment Trial Outcomes for Rett Syndrome: The Development of Rett-specific Anchors for the Clinical Global Impression Scale." Journal of child neurology vol. 30,13 (2015): 1743-8. doi:10.1177/0883073815579707

Overview of Revised Motor Behavior Assessment (R-MBA)

- Clinician-reported assessment that measures the onset of disease regression, growth, motor and communication skills, and disease behaviors for individuals with Rett syndrome[1]
- **Associated with developmental milestone acquisition and function impacting quality of life**
- Measures the severity or frequency of a diverse set of symptoms to capture phenotypic variability
- Assessed in Rett syndrome natural history study[2]



24-item questionnaire across five domains:

1. Motor Dysfunction
2. Functional Skills
3. Social Skills
4. Aberrant Behavior
5. Rett-specific Behavior (i.e. Respiratory)

[1]Raspa, M. et al. A Psychometric Evaluation of the Motor-Behavioral Assessment Scale for Use as an Outcome Measure in Rett Syndrome. Nov 2020. [2]MBA natural history data converted to R-MBA; Accessed from International Rett Syndrome Foundation (IRSF). ClinicalTrials.gov: NCT02738281: a prospective cohort of individuals with a pathologic mutation in the MECP2 gene, commonly associated with RTT.

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

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



TSHA-102 was well tolerated up to 2x10^{15} vg
in NHPs and rats



Broad biodistribution to brain and spinal cord
demonstrated in NHPs, rats and mice



WT animals treated with TSHA-102 and vehicle demonstrated similar levels of *MECP2,* supporting the mechanism of miRARE
by 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



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Source: Company data
KO=Knockout; WT=wild-type; NHP=Non-human primate; vg=Vector genome

Robust preclinical data for TSHA-102 demonstrated **across age ranges**

Species	Animal Model	Age	Study Size	HED (vg/participant)	Route of Administration	Findings:
Mouse	Wild-type and *Mecp2*$^{-/Y}$	Neonates (P2)	n=45	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	2.9x10^{14} 7.1x10^{14} 1.4 x 10^{15} 2.9x10^{15}	IT	○ **Significant improvement in survival, body weight, motor function and respiratory health** across treatment ages in KO Rett mice ○ No signs of overexpression in WT treated mice
Mouse	Wild-type and *Mecp2*$^{-/Y}$	P28 - P35	n=137	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	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
Non-human primate	Wild-type	Juvenile (~2 yrs)	n=24	2.5×10^{14} 5.0×10^{14} 2.0×10^{15}	IT	○ TSHA-102 was **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	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