TSHA-102 Rett Syndrome program Update: Longer-term Results from REVEAL Phase 1/2 trials

June 2026

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Legal disclosure

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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.

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Agenda

Rett Syndrome Overview & REVEAL Pivotal Trial Update

TSHA-102 Clinical Data from Part A of REVEAL Phase 1/2 Trials

Next Steps & Concluding Remarks

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

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

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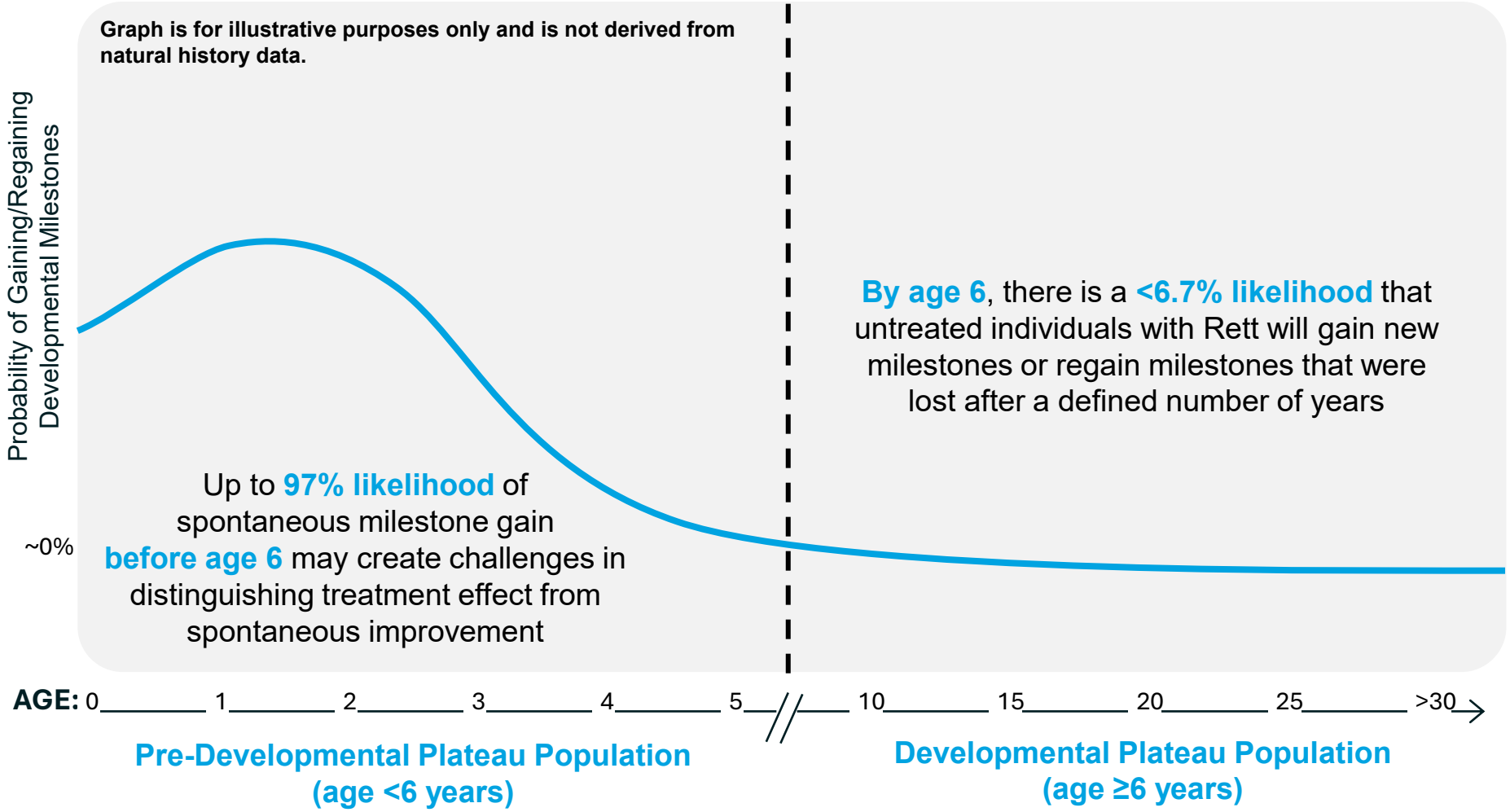
[1]Fu, Cary et al. "Consensus guidelines on managing Rett syndrome across the lifespan." *BMJ paediatrics* open vol. 4,1 e000717. 13 Sep. 2020, doi:10.1136/bmjpo-2020-000717. [2]Coenraads, Monica et al. "Voice of the Patient Report: *Rett Syndrome Externally-Led Patient-Focused Drug Development Meeting*." 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]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. [5]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).

Rigorous analysis of the Rett Syndrome Natural History Study 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

[1]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.

Completed dosing in REVEAL pivotal trial for TSHA-102 to support BLA submission – on track to complete six-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)
  - No treatment-related SAEs or DLTs[1]
- **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 June 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

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

[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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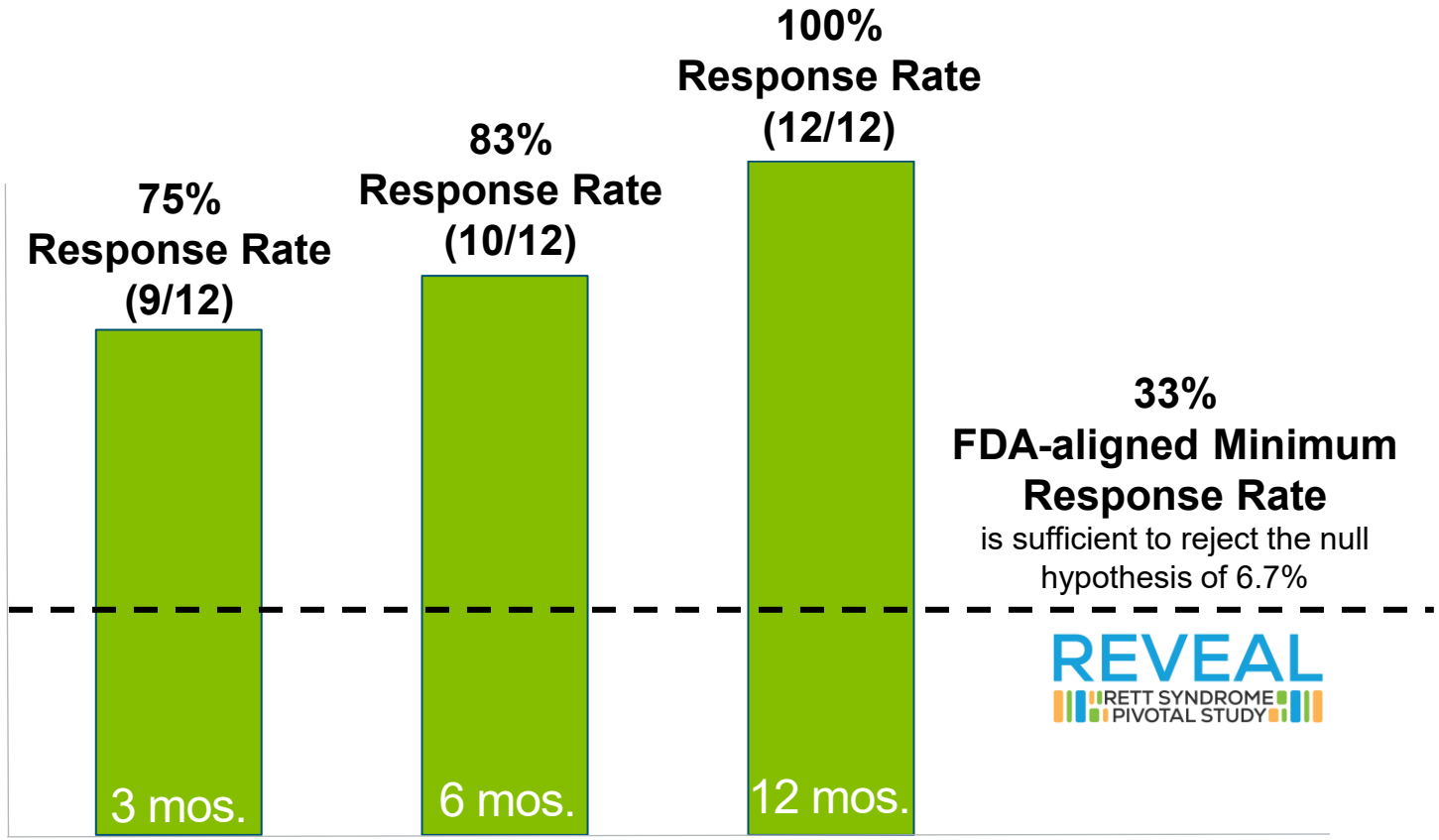
Based on May 2026 data cutoff (N=12). Developmental milestone gains and regains were assessed by multiple independent central raters through video evidence.[1]Incidence models derived from NHS data; accessed from IRSF. ClinicalTrials.gov: NCT02738281: a prospective cohort of individuals with a pathologic 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**

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

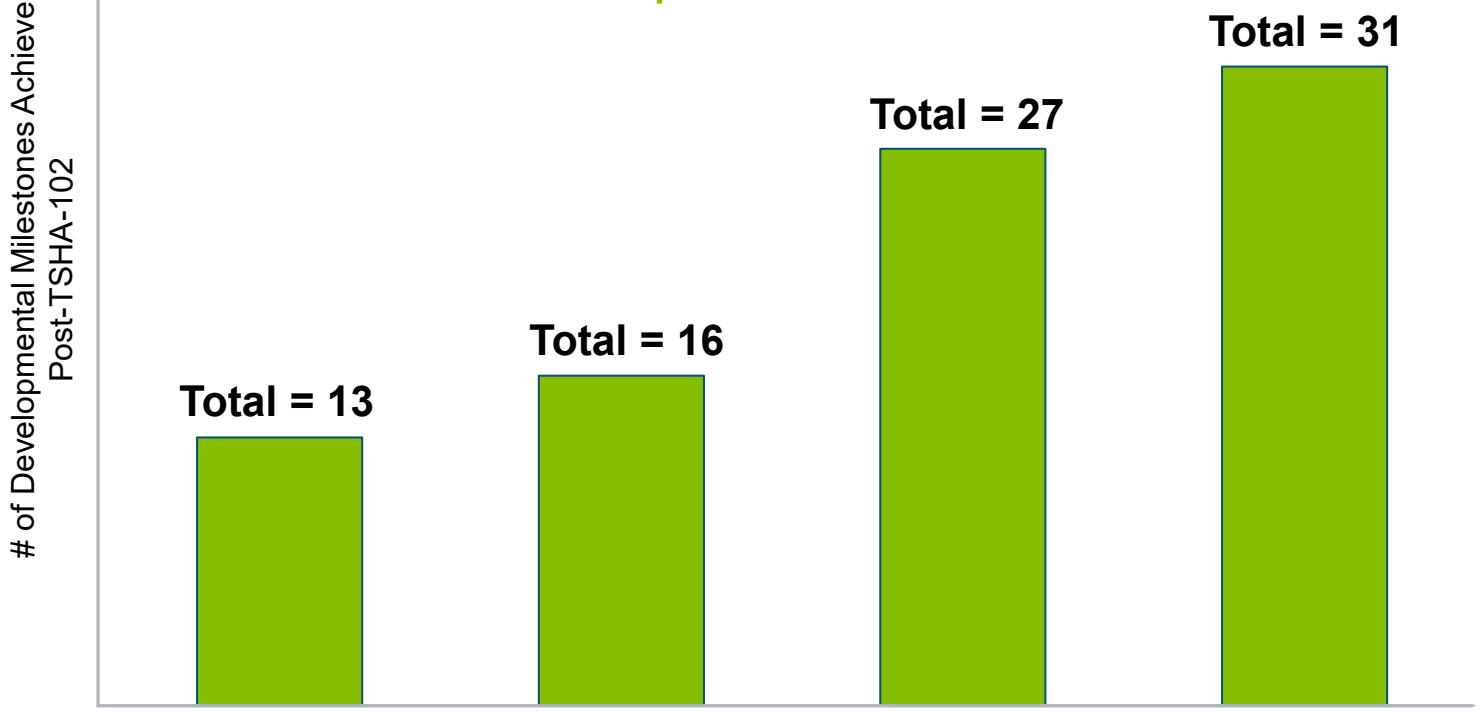
"She's a lot easier to care for. She can point a lot more deliberately to make choices and show us what she wants, and she will keep gesturing until we get it for her. And she pushes away what she doesn't want.**"**

– Caregiver of adolescent/adult participant

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

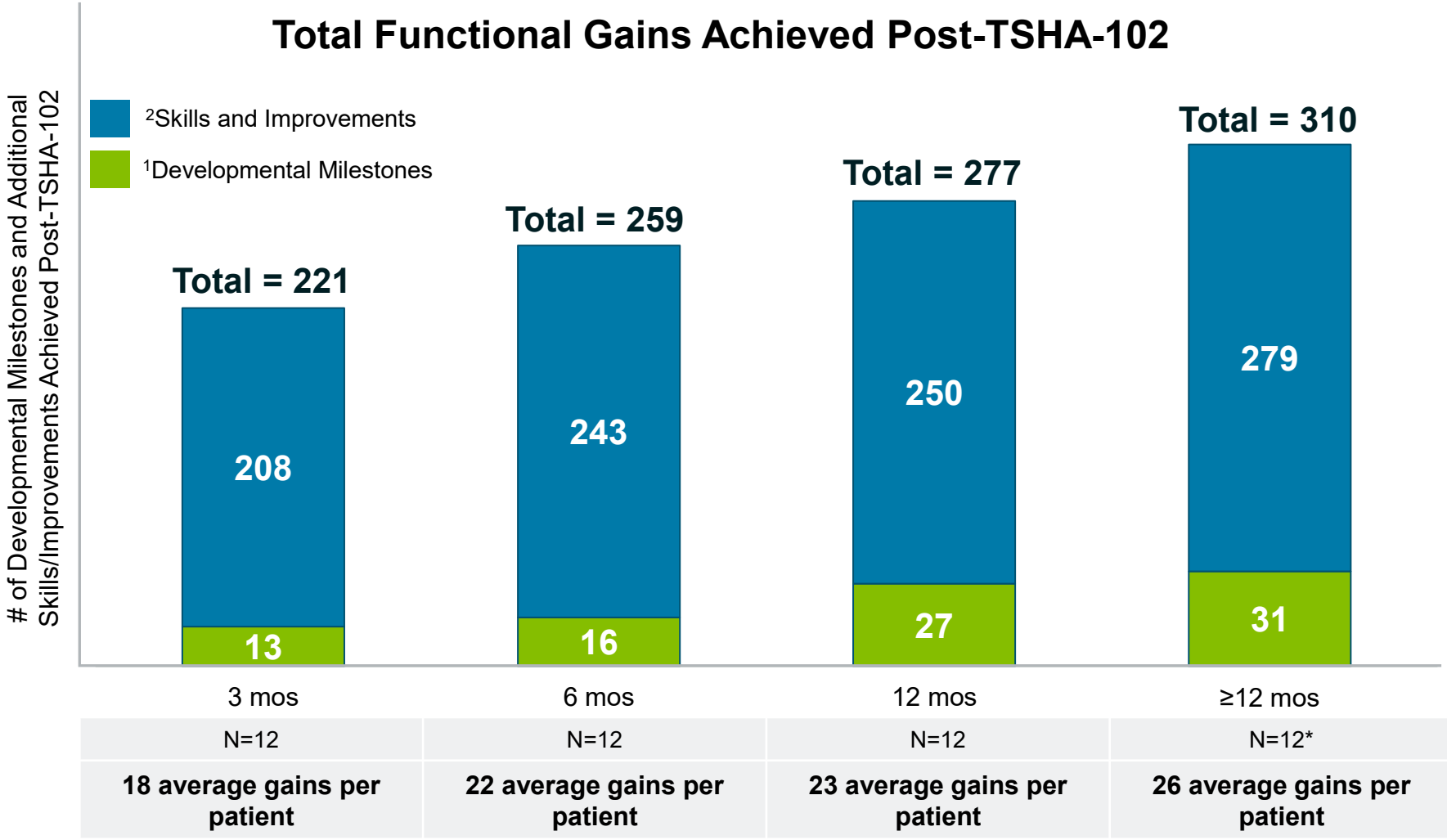


3 mos	6 mos	12 mos	≥12 mos
N=12	N=12	N=12	N=12*
1.1 average gains per patient	**1.3 average gains per patient**	**2.3 average gains per patient**	**2.6 average gains per patient**

- 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.

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).

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!"

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)

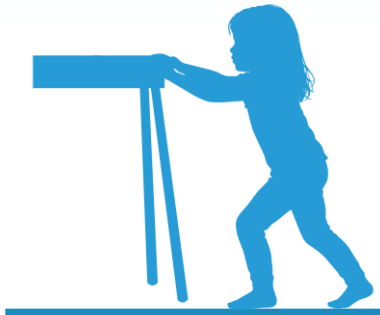
Can use multiple words with meaning

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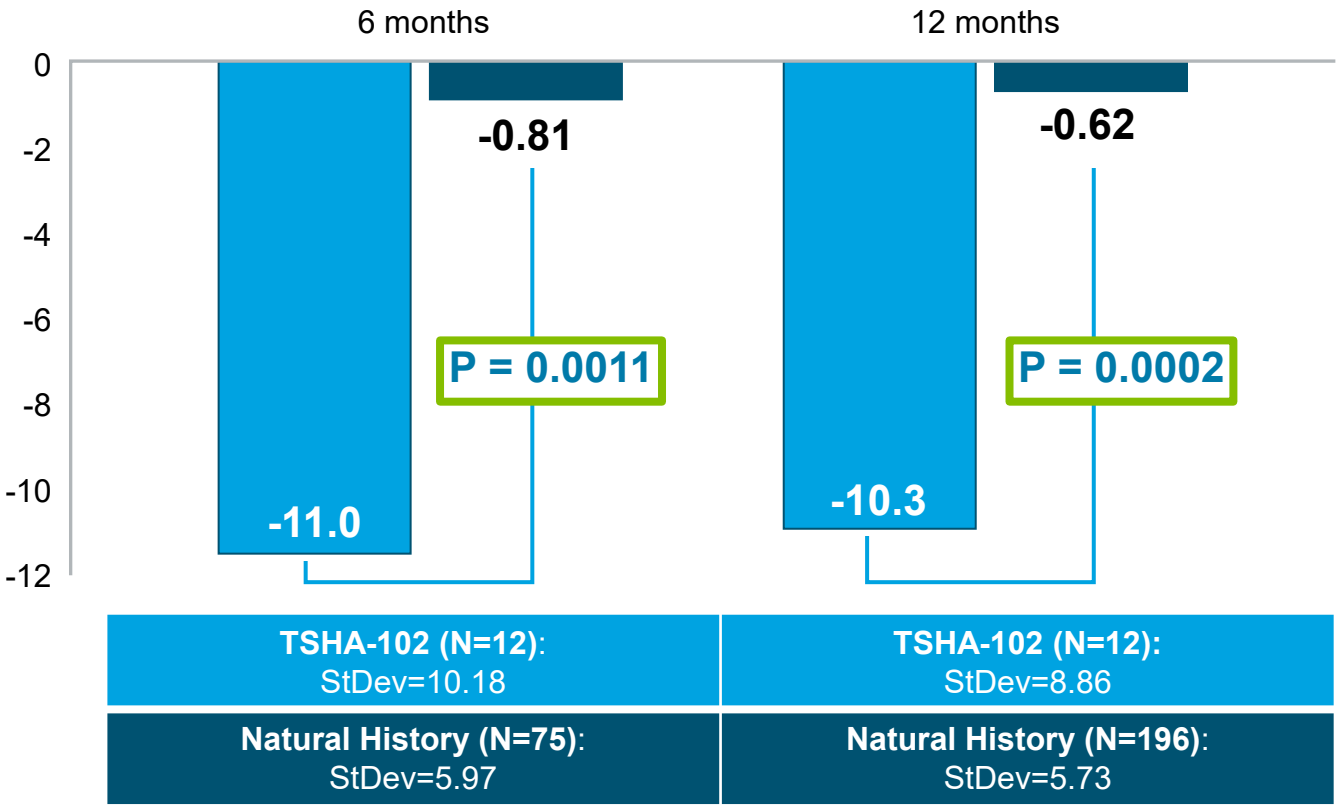
Based on May 2026 data cutoff (N=12).

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

TSHA-102 was generally well-tolerated at low and high doses with no 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 treatment-related SAEs or DLTs across the REVEAL Phase 1/2 and Pivotal trials (N=29)[2]

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[1]REVEAL Part A data cut May 2026 (N=12).[2]REVEAL Part A and pivotal trial safety data cut June 2026 (N=29)
SAE=Serious adverse event; DLT=Dose-limiting toxicity; TEAE=Treatment-emergent AE; NfL=Neurofilament light chain; CSF=Cerebrospinal fluid; ULN=Upper limit normal

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 ONGOING

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

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 is a 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] ○ TSHA-102 delivered intrathecally, a 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 ○ 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 ○ ASPIRE trial ongoing (N=4, 2 to <4 years); FDA alignment to include ≥3 months of safety data in BLA to support broad ≥2 years label

Next Steps

Completion of dosing in ASPIRE trial (N=4) expected **July 2026**

Completion of BLA-enabling PPQ campaign expected **Q4 2026**

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

[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

Thank you

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