



Every Breakthrough
BEGINS WITH BELIEF

**NGN-401 Phase 1/2 Interim
Data Update**

November 2025



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NGN-401: Setting the Standard for Rett Syndrome Gene Therapy

Best-in-Class Potential

- ✓ Multidomain improvements
- ✓ Progressive skill gains over time
- ✓ Durability of response
- ✓ Reproducibility across patients
- ✓ Improvements across full spectrum of disease severity
- ✓ 1E15 vg dose remains generally well-tolerated

First-in-Class Potential

- ✓ First participant dosed in Embolden trial
- ✓ 12 of 13 clinical trial sites initiated
- ✓ Enrollment expected to complete in 3-6 months
- ✓ Single trial design in ages ≥ 3 expected to enable most efficient path to market



A Best-in-Class Gene Therapy for Rett Syndrome Requires Durable, Multidomain Gains that Grow Over Time



Local Delivery into the Brain is a Demonstrated Strategy that Drives Efficacy

✓ *NGN-401 uses ICV Delivery*



Delivering Fully Functional Protein is the Optimal Strategy to Lead to Efficacy

✓ *NGN-401 uses Full-length MECP2*



Controlling for Overexpression is Required to Deliver Therapy Safely

✓ *NGN-401 uses EXACT™ Technology to Limit Expression*

Results in



NGN-401 Phase 1/2 Pediatric Data Update

8 Participants included



Multidomain Improvements



35 Skills Gained Overall



Durable, No Skills Lost

NGN-401 Phase 1/2 Interim Data Summary


Baseline Characteristics of Phase 1/2 Trial Pediatric Participants

Evaluating the Impact of NGN-401 Across Entire Spectrum of Disease Severity

Time Post Dosing	Pt:1 24 months	Pt:2 18 months	Pt:3 18 months	Pt:4 15 months	Pt:5 12 months	Pt:6 6 months	Pt:7 6 months	Pt:8 6 months
Age at Dosing	7	4	6	7	6	4	6	8
Baseline CGI-S Score	4 Moderately III	5 Markedly III	5 Markedly III	5 Markedly III	5 Markedly III	5 Markedly III	4 Moderately III	4 Moderately III
Genetic Variant Severity	Mild	Severe	Severe	Severe	Severe	Moderate	Mild-Moderate	Mild-Moderate

Responders in Phase 1/2 Trial Far Exceed Bar of Embolden Primary Endpoint at 12 Months with Increased Skill Gains Over Time

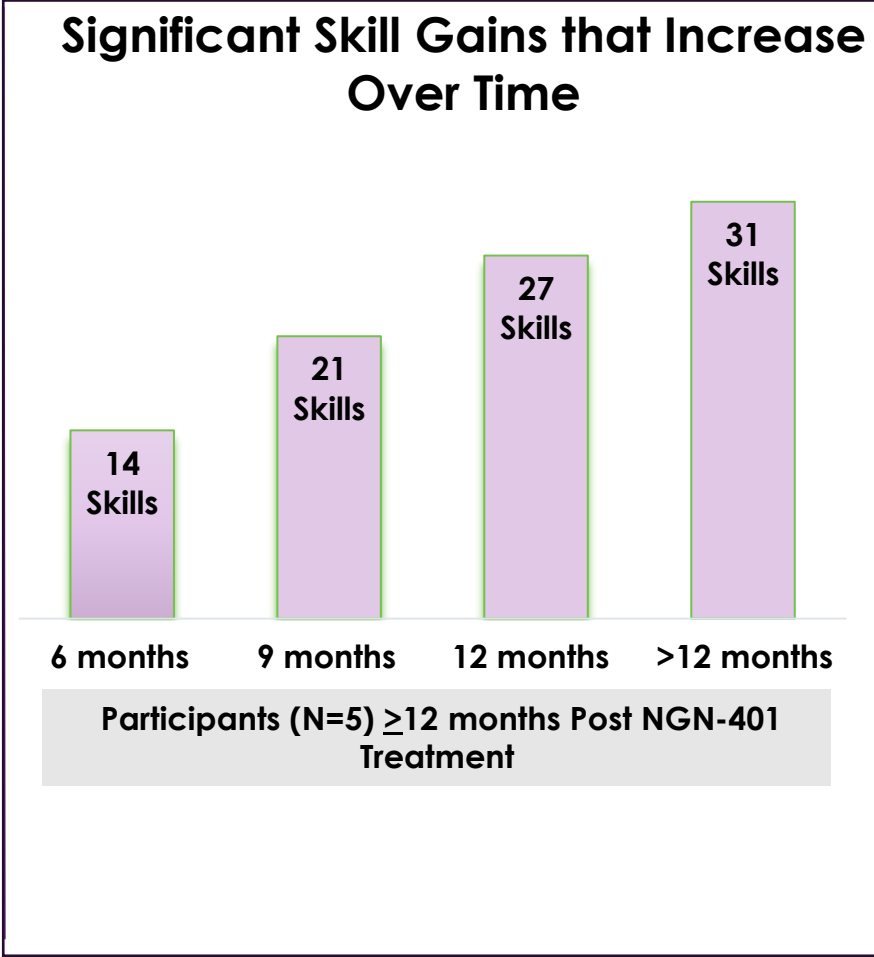
12 Months Post NGN-401 Treatment					
	Pt:1	Pt:2	Pt:3	Pt:4	Pt:5
5 of 5 with functional gains	✓	✓	✓	✓	✓
4 of 5 with CGI-I of ≤ 3, all durable	✓	✓	✓	✓	-
4 of 5 with > 1 skills	✓	✓	✓	✓	Gains in Hand Function & Communication


Embolden
A Clinical Study for Rett Syndrome

Embolden registrational trial primary endpoint:


- CGI-I of ≤ 3
- Gain of any 1 developmental milestone/skill at 12 months

Minimum Threshold for Success is 7 of 20 Participants (35%)



Participants Dosed in 1H'25 Show Efficacy Prior to 12-month Timepoint

6 Months Post NGN-401 Treatment			
	Pt:6	Pt:7	Pt:8
3 of 3 with functional gains	✓	✓	✓
3 of 3 with CGI-I of ≤ 3	✓	✓	✓
2 of 3 acquired skills	Gains in Hand Function, Communication, Gross Motor	✓	✓

**Embolden**
A Clinical Study for Rett Syndrome

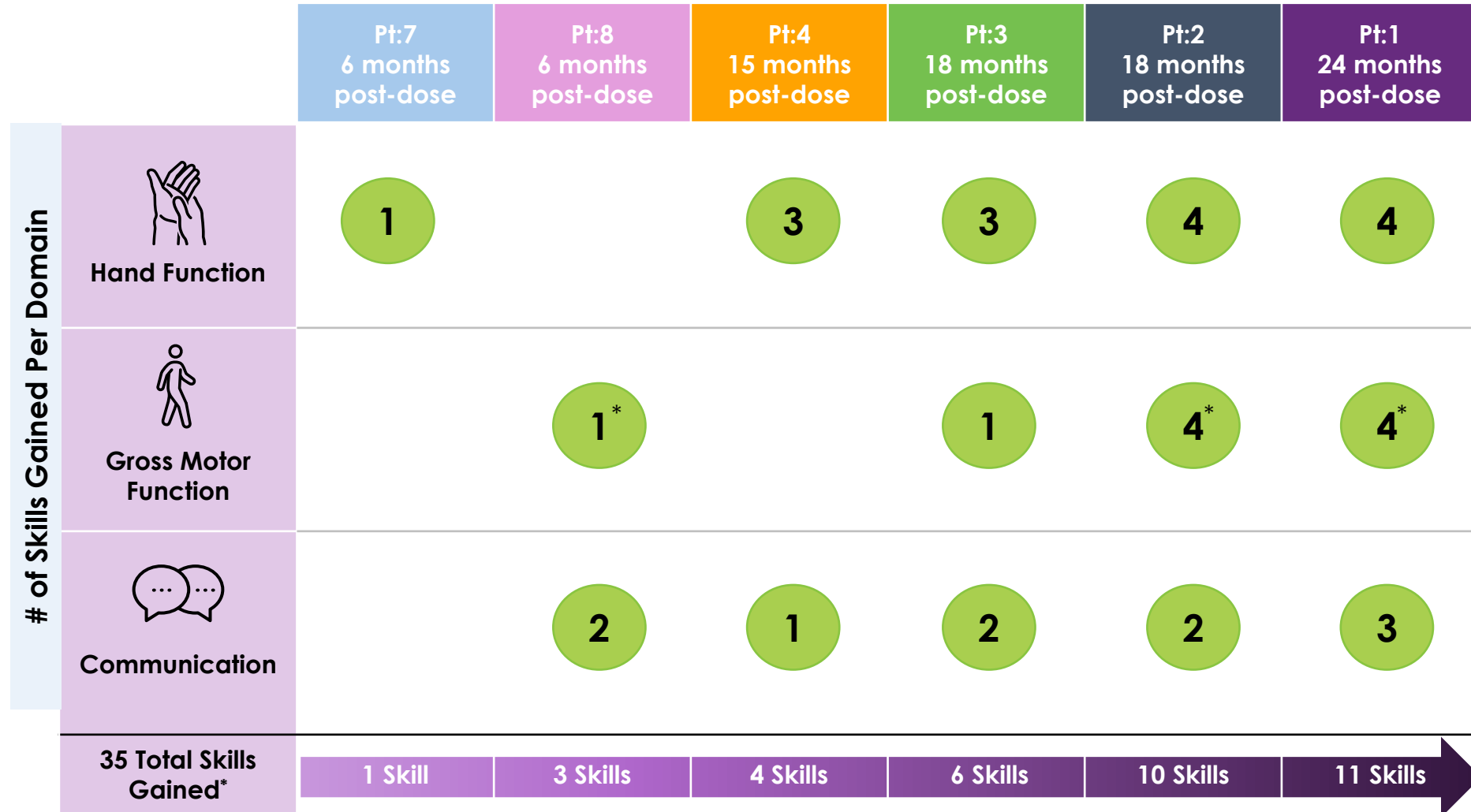
Embolden registrational trial primary endpoint:

- CGI-I of ≤ 3
- Gain of any 1 developmental milestone/skill at 12 months

Minimum Threshold for Success is 7 of 20 Participants (35%)

Early efficacy observed at 6 months is consistent with previously dosed participants

Early Multidomain Improvements with Skill Gains Increasing Over Time that Remain Durable



As of data cutoff date of October 30, 2025

*31 total skills acquired match Embolden developmental milestones/skills list; 35 total skills include previously reported skills from other validated scales

Pt:1 Gained 11 Developmental Milestones/Skills Across All Core Domains with Durability out to 24 Months

Baseline:
7 Yrs Old



Raking, no ability to hold objects

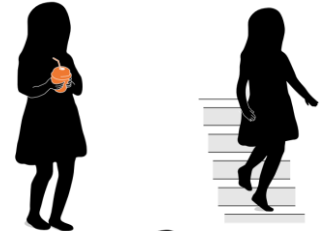
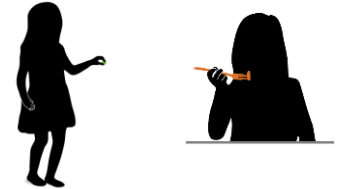
Walking, ataxic gait, no ability to climb stairs

Severe impairment, unable to follow commands, indicate wishes



		Pt:1 Developmental Milestones/Skills Post-NGN-401	Months Post-NGN-401							
			3	6	9	12	15	18	24	
Fine Motor	{	Used a pincer grasp (either refined or modified)		✓	✓	✓	✓	✓	✓	
		Taken a drink from a cup held without assistance		✓	✓	✓	✓	✓	✓	
		Used a spoon/fork to eat without assistance					✓	✓	✓	
		Transferred an object from one hand to the other					✓	✓	✓	
Gross Motor	{	Heel-to-toe walking*			✓	✓	✓	✓	✓	
		Climbed up stairs without help		✓	✓	✓	✓	✓	✓	
		Climbed down stairs without help				✓	✓	✓	✓	
		Come to sitting <i>New skill acquired since last update</i>							✓	
Communication	{	Followed a command without gesture		✓	✓	✓	✓	✓	✓	
		Waves bye bye				✓	✓	✓	✓	
		Pointed for something they want				✓	✓	✓	✓	

Post Treatment with NGN-401



As of data cutoff date of October 30, 2025

*Not included in Embolden developmental milestones/skills list; previously reported skill from other validated scale

Images are representative of skills

Pt:2 Gained 10 Developmental Milestones/Skills Across All Core Domains with Durability out to 18 Months

Baseline:
4 Yrs Old



Severe impairment,
unable to use hands

Fine Motor

Pt:2 Developmental Milestones/Skills Post-NGN-401	Months Post-NGN-401					
	3	6	9	12	15	18
Reached for toy	✓	✓	✓	✓	✓	✓
Used raking grasp to retrieve an object			✓	✓	✓	✓
Finger fed			✓	✓	✓	✓
Taken a drink from a cup held without assistance <i>New skill acquired since last update</i>			✓	✓	✓	✓
Pulled to standing	✓	✓	✓	✓	✓	✓
Bent down, touched floor, and recovered*			✓	✓	✓	✓
Stepped off curb with help*				✓	✓	✓
Climbed up stairs with help <i>New skill acquired since last update</i>					✓	✓
Followed a command without a gesture	✓	✓	✓	✓	✓	✓
Used words with meaning	✓	✓	✓	✓	✓	✓

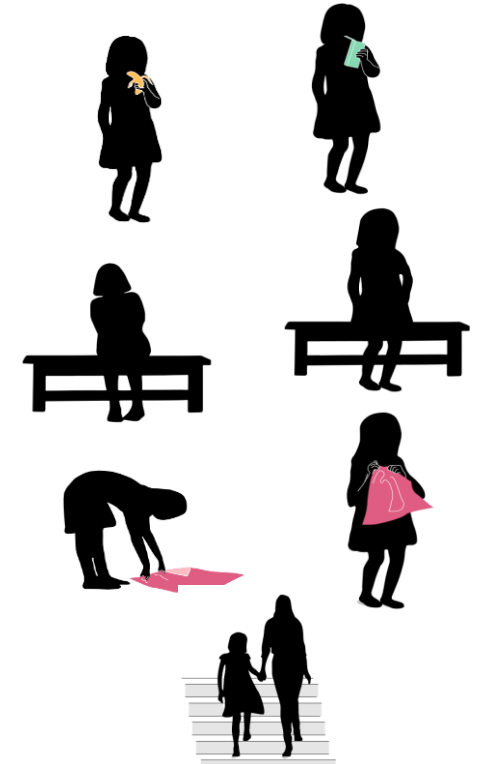
Impaired, ataxic,
help to stand

Gross Motor

Severe impairment,
unable to follow commands,
non-verbal

Communication

Post Treatment
with NGN-401



Pt:3 Gained 6 Developmental Milestones/Skills Across All Core Domains with Durability out to 18 Months

Baseline:
6 Yrs Old



Severe Dysphagia

Raking grasp

Cannot sit, stand
or walk
independently

Cannot follow
commands

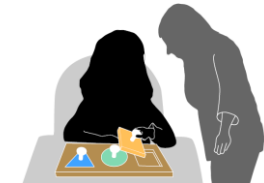
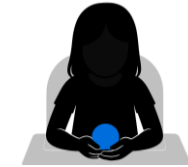
Fine Motor

Gross Motor

Communication

Pt:3 Developmental Milestones/Skills Post-NGN-401	Months Post-NGN-401					
	3	6	9	12	15	18
Used a pincer grasp (either refined or modified)		✓	✓	✓	✓	✓
Finger fed			✓	✓	✓	✓
Transferred an object from one hand to the other <i>New skill acquired since last update</i>			✓	✓	✓	✓
Sat without support when placed	✓	✓	✓	✓	✓	✓
Followed command without gesture <i>New skill acquired since last update</i>				✓	✓	✓
Followed command with gesture <i>New skill acquired since last update</i>						✓

Post Treatment
with NGN-401



Pt:4 Gained 4 Developmental Milestones/Skills Across 2 Core Domains with Durability out to 15 Months

Baseline:
7 Yrs Old



Raking grasp,
unable to
hold objects

Unable to
follow
commands

Fine Motor

Communication

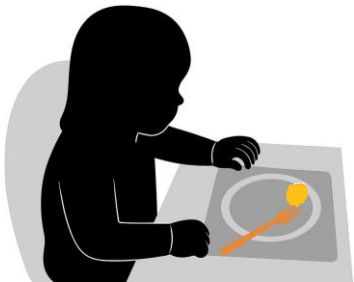
Pt:4 Developmental Milestones/Skills Post-NGN-401	Months Post-NGN-401				
	3	6	9	12	15
Used a pincer grasp (either refined or modified)	✓	✓	✓	✓	✓
Used a spoon/fork to eat without assistance	✓	✓	✓	✓	✓
Taken a drink from a cup held without assistance <i>New skill acquired since last update</i>	✓	✓	✓	✓	✓
Followed a command without a gesture <i>New skill acquired since last update</i>		✓	✓	✓	✓

Post Treatment
with NGN-401



Pt:7 Gained 1 Developmental Milestone/Skill at Early Timepoint

Baseline:
6 Yrs Old



Could not use
utensils

Fine Motor

Pt:7 Developmental Milestones/Skills Post-NGN-401	Months Post-NGN-401	
	3	6
Used a spoon/fork to eat without assistance		✓

Post Treatment
with NGN-401



Pt:8 Gained 3 Developmental Milestones/Skills Across 2 Core Domains at Early Timepoint

Baseline:
8 Yrs Old



Unable to bend
at waist

Unable to follow
commands,
cannot use words
with meaning

Gross Motor

Communication















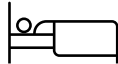


Pt:7 Developmental Milestones/Skills Post-NGN-401	Months Post-NGN-401	
	3	6
Bent down, touched floor, and recovered*	✓	✓
Followed a command with a gesture		✓
Used words with meaning		✓

Post Treatment
with NGN-401



NGN-401: Delivering What Matters to Families

New Functional Abilities and Improvements Post-Treatment with NGN-401

Fine Motor/Hand Function	Gross Motor/Ambulation	Communication	Autonomic
Less dependence on caregivers for basic needs	Reduced physical burden for caregivers for activities of daily living	Can communicate needs & wants, and foster greater social connections	Enhanced comfort and reduced distress
 Uses hands to self-feed, drink, play with toys, self-soothe	 Sits without support	 Says words with meaning	 Improvements in constipation
 Decreased to no stereotypies	 Walks up and down stairs unassisted	 Follows daily routines, e.g., getting ready for school	 Drinks clear liquids, eats solids for first time
 Uses utensils to self-feed	 Bends at waist and stands back up	 Communicates needs and wants; can ID colors	 Absent aspiration pneumonia events
	 Bears more weight for ease of transfer	 Engages with friends and family; shows affection	 Sleeps through the night
	 Can get on/off furniture, out of bathtub, into car unassisted	 Starting/ improved communication with use of assisted device	



Improvements in Key Domains Lead to:

Multidomain improvements

Participation in activities of daily living

Improvements in health-related quality of life



Phase 1/2 Caregiver Testimonials Following Treatment with NGN-401

Highlight Improvements Important to Families

"**Sleep improved significantly** as she is **able to sleep all through the night without any issue.**"

"Her **understanding has improved**, especially with me **when I ask her** to do small tasks, then **she will do it immediately almost every time...**"

"The other day she...**ran a couple steps** while out..."

"**She uses both hands to grab her blanket...She holds a banana and takes bites.**"

"She is **paying attention**, and even at school with decision-making...**she knows what we are asking of her.**"

"She reacts to...[the] puppy. We have never seen that...nothing going on before, nothing was worth her attention. **Now she is enjoying day-to-day.**"

"She is **happier.**"
"I **am grateful** [NGN-401] has seemed to **benefit [her] health and life...**"

"She is so happy all the time and calm."

"Before, she was really stuck a lot. Her **gait has improved a lot.**"

"**Walking and standing are so much better.** Before she would fall all the time and now she doesn't. **She is so much stronger and rarely falls.**"

"She **holds onto things longer...she is eating pieces of fruit using a fork, a new skill.**"

"She **kissed me** for the **first time ever.**"

NGN-401 Remains Generally Well Tolerated at the 1E15 vg Dose Level

	1E15 vg Dose Total N=10	
	N	Events
TEAEs related to NGN-401	9	59
Serious TEAEs Unrelated to NGN-401	3	4
Serious TEAEs Related to NGN-401	1	2

- All TEAEs related to NGN-401 have been Grade 1 (mild) or Grade 2 (moderate) in severity; the majority are known potential risks of AAV and have resolved or are resolving
 - Most participants experienced mild liver enzyme elevations
 - SAEs (Grade 2) related to abnormal nerve conduction findings occurred in Pt:5:
 - Areflexia and related elective inpatient diagnostic testing
 - Nerve conduction findings have returned to normal range
 - Unrelated to NGN-401, Pt:5 also experienced a leg fracture confounding her Month 12 gross motor assessment
- No evidence of hemophagocytic lymphohistiocytosis (HLH) in any participant
- Seizures have remained well controlled following NGN-401
- No intracerebroventricular (ICV) procedure-related AEs
- No signs or symptoms indicative of MeCP2 overexpression

Key Upcoming Anticipated Milestones

Rett Syndrome (NGN-401)

- ✓ Provide regulatory update in 1H:25 regarding Embolden registrational trial
- ✓ Initiate Embolden registrational trial activities
- ✓ Expand clinical trial footprint, more than doubling presence in U.S.
- ✓ Initiate dosing in Embolden registrational trial
- ✓ Announce additional Phase 1/2 clinical data in 2H:25
- Complete Embolden registrational trial enrollment in 3-6 months
- Announce additional Phase 1/2 clinical data in 2026

Cash Runway Expected to Fund Operations Through 1Q'28

Embolden™ Registrational Trial Overview



Key Elements of Embolden™ Registrational Clinical Trial of NGN-401 for Rett Syndrome

Design: Single-arm, open-label, baseline-controlled trial evaluating NGN-401 at 1E15 vg dose

Sample Size: 20 females with Classic Rett syndrome

13 Clinical Sites

Age Range: ≥ 3 years

Primary Endpoint: Responder-based composite endpoint

- Responder defined as attaining:
 - CGI-I of ≤ 3 and
 - Gain of any one developmental milestone/skill from Embolden list of 28 skills captured through standardized video recordings and rated by **independent, blinded central raters**
- 35% response rate, or 7 of 20 participants, needed for success
- Primary analysis at 12 months

Key Secondary Endpoints:

- CGI-I score of ≤ 2
- Gain of at least 2 developmental milestones/skills from Embolden list of 28 skills captured through standardized video recordings and rated by **independent, blinded central raters**

Immunosuppression:

Corticosteroids for 91 days, followed by taper

First Participant Dosed in Q4'25; Expect to Complete Enrollment in 3-6 months

28 Developmental Milestones/Skills from Rett Syndrome Natural History Study Being Evaluated in Embolden Trial



Fine Motor/Hand Function

- Reached for toy
- Taken a drink from a cup held without assistance
- Used raking grasp to retrieve an object
- Used a pincer grasp (either refined or modified)
- Finger fed
- Transferred an object from one hand to the other
- Used a spoon/fork to eat without assistance



Gross Motor/Ambulation

- Sat with support when placed
- Sat without support when placed
- Come to sitting
- Pulled to standing
- Stood while holding on
- Stood independently
- Cruised around furniture or holding on to someone
- Walked independently
- Climbed up stairs with help
- Climbed up stairs without help
- Climbed down stairs with help
- Climbed down stairs without help
- Ran 10 feet without falling



Communication

- Responded to familiar names/words
- Followed a command with a gesture
- Followed a command without a gesture
- Pointed for something they want
- Waved bye-bye
- Babbled
- Used words with meaning
- Spoken in phrases (2 words or more with meaning)

Skills Chosen Based on Meaningfulness to Caregivers and Rarely Learned/Relearned ≥ 3 Years*