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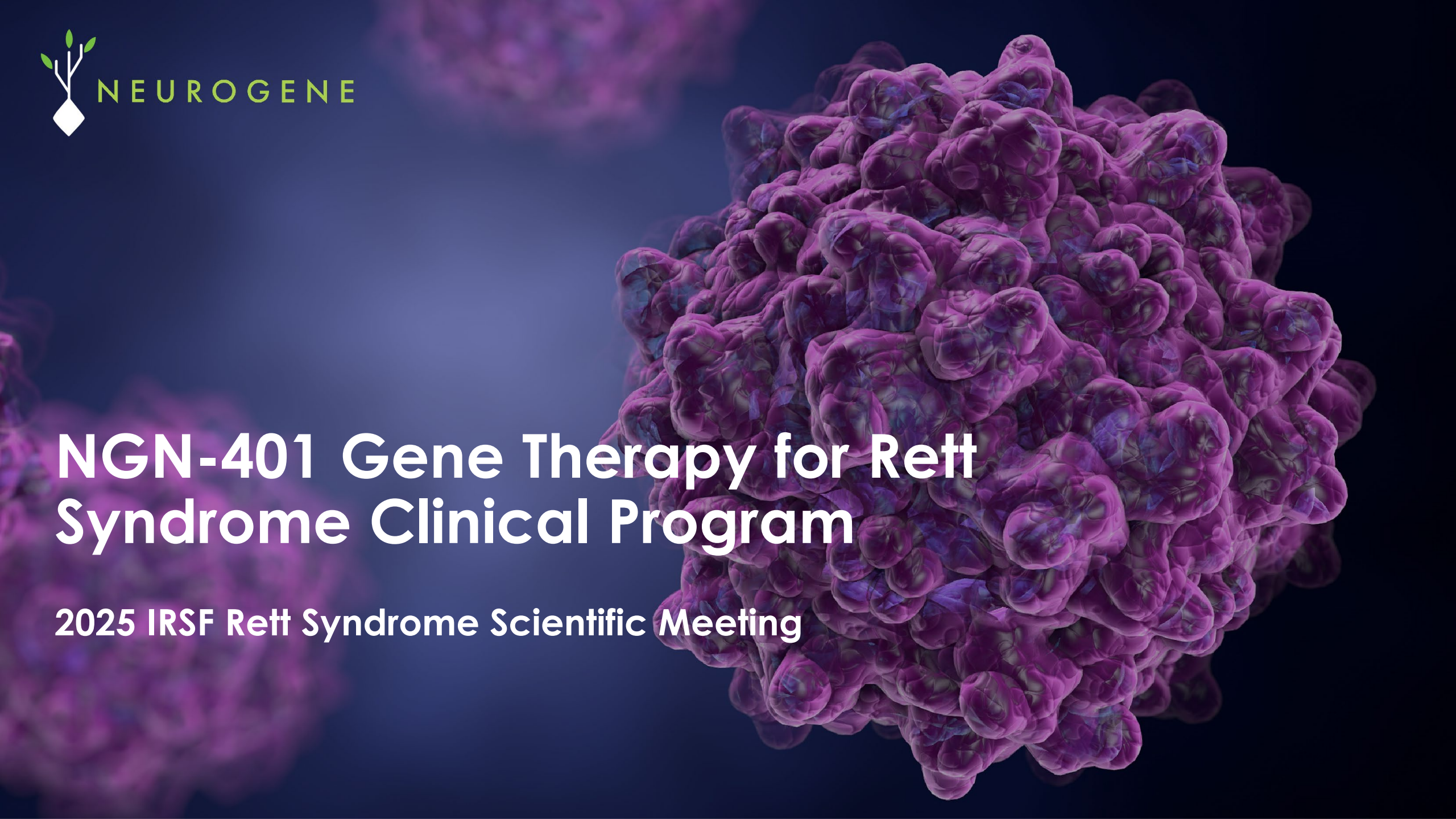

NGN-401 Gene Therapy for Rett Syndrome Clinical Program

2025 IRSF Rett Syndrome Scientific Meeting

Disclaimer

Forward Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may discuss goals, intentions and expectations as to future plans, trends, events, results of operations or financial condition, or otherwise, based on current expectations and beliefs of the management of Neurogene, as well as assumptions made by, and information currently available to, management of Neurogene, including, but not limited to, statements regarding: the therapeutic potential and utility, efficacy and clinical benefits of its programs, including its EXACT™ technology and NGN-401; market opportunities for Neurogene's product candidates; the safety and tolerability profile of NGN-401; trial designs, clinical development plans and timing for NGN-401, including enrollment and dosing in both the pediatric and adolescent/adult cohorts of the NGN-401 Phase 1/2 clinical trial for Rett syndrome, the expected durability and deepening of clinical data results from that trial, and potential impacts of adding an adolescent/adult cohort to the Phase 1/2 trial for NGN-401; the benefits of Neurogene's in-house manufacturing capabilities; and future interactions with U.S. or foreign regulatory authorities, including the timing and outcome of any such interaction and anticipated benefits of the FDA's RMAT designation as well as participation in the FDA's START program with respect to NGN-401. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as "may," "will," "should," "would," "expect," "anticipate," "plan," "likely," "believe," "estimate," "project," "intend," and other similar expressions or the negative or plural of these words, or other similar expressions that are predictions or indicate future events or prospects, although not all forward-looking statements contain these words. Statements that are not historical facts are forward-looking statements. Forward-looking statements are based on current beliefs and assumptions that are subject to risks and uncertainties and are not guarantees of future performance. Actual results could differ materially from those contained in any forward-looking statement as a result of various factors, including, without limitation: the ability of Neurogene to report its data on the predicted timeline; the ability of Neurogene to effectively use the START program to accelerate development of NGN-401; the potential for negative impacts to patients dosed in the ongoing clinical trials for NGN-401; the ability to advance NGN-401 through clinical development; the ability to obtain regulatory approval for, and ultimately commercialize, NGN-401; Neurogene's limited experience in designing and conducting clinical trials; expectations regarding the market and potential for NGN-401; expectations regarding the potential tolerability, safety or efficacy for NGN-401; the ability to attract, hire, and retain skilled executive officers and employees; reliance on third parties, contract manufacturers, and contract research organizations; the ability of Neurogene to protect its intellectual property and proprietary technologies; risks related to Neurogene's ability to correctly estimate its respective operating expenses, including its projected cash runway; and legislative, regulatory, political and economic developments and general market conditions.

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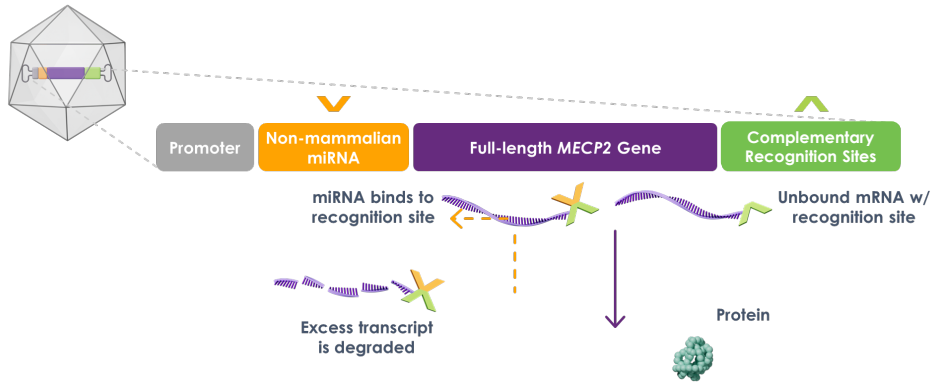
NGN-401: Positioned to be Best-in-Class Gene Therapy for Rett Syndrome

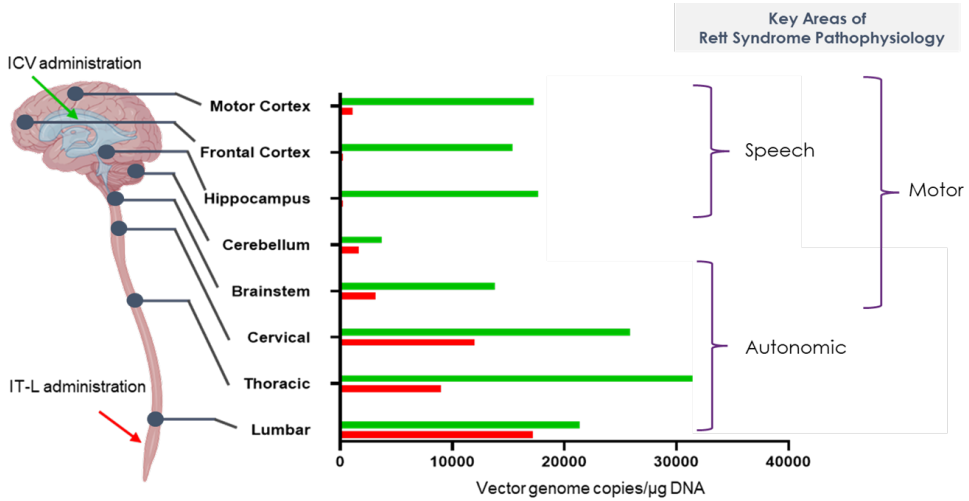
EXACT™ transgene regulation technology designed to deliver consistent and tightly controlled MeCP2 protein expression on a cell-by-cell basis.

NGN-401 includes the full-length human *MECP2* gene, which creates a fully functioning MeCP2 protein.

NGN-401's intracerebroventricular (ICV) route of delivery has been shown in preclinical models to have the broadest targeting of brain and nervous system regions underlying Rett syndrome pathophysiology.

An estimated 30,000 ICV procedures are performed by neurosurgeons annually in the U.S. and require minimal downtime/recovery.





NGN-401 Phase 1/2 Clinical Trial Design in Females with Rett Syndrome

Trial Design

Trial evaluating 1E15 vg dose of NGN-401*

Ages ≥ 11

N=3

2 Participants Dosed

Ages 4-10

N=8

Dosing Complete

Key Eligibility Criteria

- Females with Classic Rett syndrome in post regression stage of illness
- Clinical diagnosis and genetic confirmation of pathogenic *MECP2* mutation
- Pediatric: 4–10 years old; Adolescent/Adult: 11+ years old
- Clinical Global Impression-Severity (CGI-S) score of 4–6

Key Efficacy Assessments

- Clinician Global Impression-Improvement (CGI-I)
- Clinician Global Impression-Severity with Rett syndrome-specific anchors (CGI-S)
- Rett Syndrome Behavior Questionnaire (RSBQ)
- Autonomic function

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*In addition, three pediatric participants previously received 3E15 vg dose

Improvements in Clinician and Caregiver Assessments with 23 Skills Acquired Across 4 Participants

	CGI-I		CGI-S Total Score		RSBQ		Gain of Skills, Developmental Milestones and Symptom Improvement in RTT Clinical Domains				
	Improved?	How many points?*	Improved?	How many points?	Improved?	How many points? (% Change)	Hand Function	Gross Motor	Communi-cation	Autonomic	Attentive-ness
Pt:1 15 mos. post-NGN-401	✓	2 pts.			✓	10 pts. (-28%)	✓	✓	✓	✓	✓
Pt:2 12 mos. post-NGN-401	✓	2 pts.	✓	1 pt.	✓	32 pts. (-52%)	✓	✓	✓	✓	✓
Pt:3 9 mos. post-NGN-401	✓	2 pts.			✓	5 pts. (-29%)	✓	✓		✓	✓
Pt:4 3 mos. post-NGN-401	✓	2 pts.			✓	8 pts. (-28%)	✓			✓	✓

Consistent Improvement Across Key Rett Syndrome Scales, Bolstered by Functional Improvements in Core Clinical Domains

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As of data cut-off date of 17 October 2024
*Each participant achieved a 2-point improvement, or "much improved" from baseline

Pt:1 Multi-Domain Improvements Deepened Over Time, and Not Expected Based on Rett Syndrome Natural History

Baseline – 7 Yrs Old

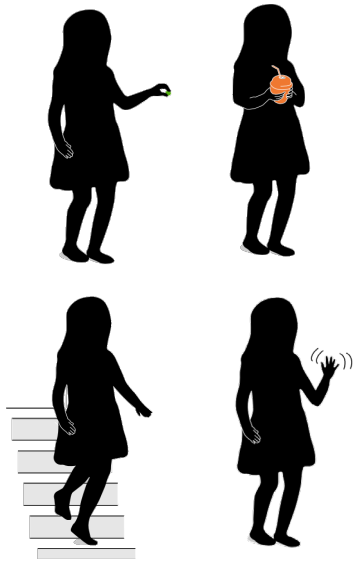
Mild Disease

Raking, no ability to hold objects

Walking, ataxic gait, no ability to climb stairs

Severe impairment, unable to follow commands

Select Pt:1 Developmental Skills Post-NGN-401		Months Post-NGN-401				
		3	6	9	12	15
Uses a pincer grasp	Fine Motor		✓	✓	✓	✓
Holds bottle or cup unpropped	Fine Motor		✓	✓	✓	✓
Uses spoon/fork to self-feed	Fine Motor					✓
Transfers objects between hands	Fine Motor					✓
Heel-to-toe walking	Gross Motor			✓	✓	✓
Climbs up stairs without help	Gross Motor		✓	✓	✓	✓
Climbs down stairs without help	Gross Motor				✓	✓
Follows a command without gesture	Communication		✓	✓	✓	✓
Waves hello*	Communication				✓	✓
Taps for wants	Communication				✓	✓



Post Treatment with NGN-401

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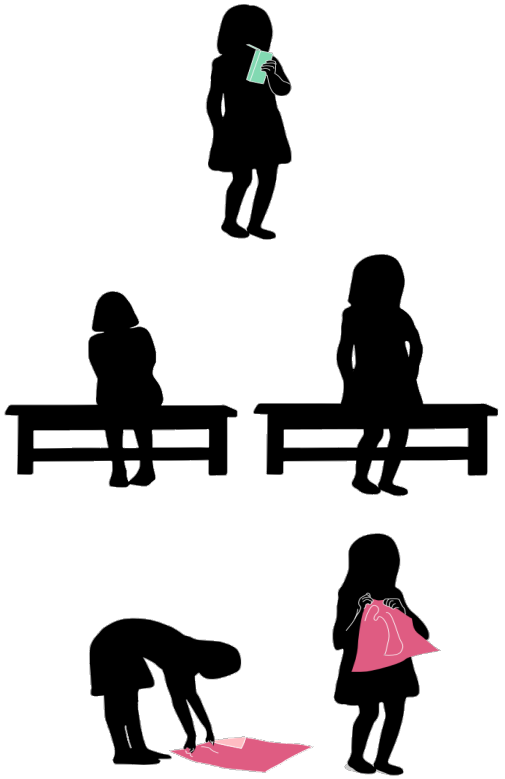
Data from the RNHS; N=200 female subjects with classic RTT, age 4-10 years, CGI-S score of 4 to 6 at baseline, confirmed genetic mutation
*Skill learned is "Wave hello;" however, RNHS tracked "Waves Bye Bye"
As of data cut-off of 17 October 2024
Images are representative of skills and are not photos of participants in the NGN-401 clinical trial

Pt:2 Multi-Domain Improvements from Severe Impairments at Baseline Deepened Over Time, and Not Expected Based on Rett Syndrome Natural History

Baseline - 4 Yrs Old

		Select Pt:2 Developmental Skills Post-NGN-401	Months Post-NGN-401			
			3	6	9	12
Severe impairment, unable to use hands	Fine Motor	Reaches for an object	✓	✓	✓	✓
		Uses raking grasp to retrieve an object			✓	✓
		Self-feeds			✓	✓
Impaired, ataxic, help to stand	Gross Motor	Stands independently from seated position	✓	✓	✓	✓
		Bends down, touches floor, and recovers			✓	✓
		Steps off curb with help				✓
Severe impairment, unable to follow commands, non-verbal	Communication	Follows a command without a gesture	✓	✓	✓	✓
		Uses words with meaning	✓	✓	✓	✓



Post Treatment with NGN-401

NEUROGENE

Data from the RNHS; N=200 female subjects with classic RTT, age 4-10 years, CGI-S score of 4 to 6 at baseline, confirmed genetic mutation
As of data cut-off date of 17 October 2024
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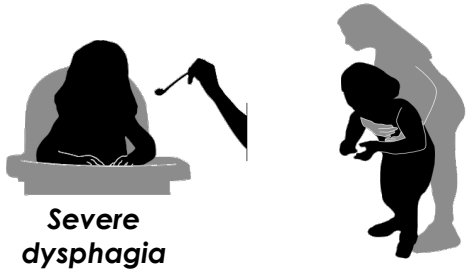
Pt:3 Multi-Domain Improvements Not Expected Based on Rett Syndrome Natural History



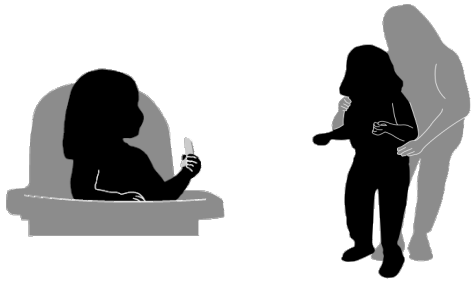
Severe dysphagia

Baseline – 6 Yrs Old

Select Pt:3 Developmental Skills		Months Post-NGN-401		
		3	6	9
Uses a pincer grasp	Fine Motor		✓	✓
Able to self-feed				✓
Sits independently	Gross Motor	✓	✓	✓

Raking grasp

Cannot sit, stand or walk



Post Treatment with NGN-401

Data from the RNHS; N=200 female subjects with classic RTT, age 4-10 years, CGI-S score of 4 to 6 at baseline, confirmed genetic mutation
As of data cut-off date of 17 October 2024
Images are representative of skills and are not photos of participants in the NGN-401 clinical trial

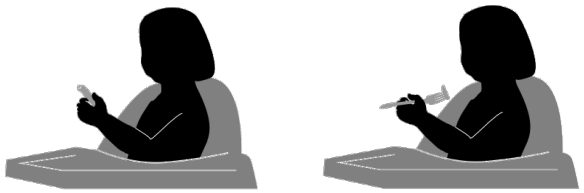
Pt:4 Early Improvements in Hand Function Not Expected Based on Rett Syndrome Natural History

Baseline – 7 Yrs Old

Raking grasp, unable to hold objects

Fine Motor

Select Pt:4 Developmental Skills	Months Post-NGN-401
	3
Uses a pincer grasp	✓
Can use utensils to self-feed (without assistance)	✓



Post Treatment with NGN-401

Data from the RNHS; N=200 female subjects with classic RTT, age 4-10 years, CGI-S score of 4 to 6 at baseline, confirmed genetic mutation
As of data cut-off date of 17 October 2024
Images are representative of skills and are not photos of participants in the NGN-401 clinical trial

Hemophagocytic Lymphohistiocytosis (HLH)/Hyperinflammatory Syndrome Following High Dose AAV9 Therapy

Aimee Donald[1], Simon Jones[1], Barry J. Byrne[2], Randy Q. Cron[3], Effie Albanis[4], Stuart Cobb[4], Julie Jordan[4]
1. UK; 2. Department of Pediatrics, College of Medicine, University of Florida, Gainesville, FL; Powell Gene Therapy Center, University of Florida, Gainesville, FL; 3. Division of Pediatric Rheumatology, University of Alabama at Birmingham, Birmingham, Alabama, USA; 4. Neurogene Inc., New York, NY

Hemophagocytic Lymphohistiocytosis (HLH)

- **HLH is a rare, life-threatening hyperinflammatory syndrome** characterized by immune dysregulation, cytokine storm, and multi-organ damage[1-3]
  - Most cases are triggered by infections, malignancy, autoimmune disease, or CAR-T (3.5% incidence)
- **Over 90% of patients present with the initial "three Fs" seen in the HLH-2004 study: Fever, elevated Ferritin, and Falling blood counts (cytopenia)[4]**

Monitoring for HLH is not part of standard monitoring in AAV therapy trials, and we believe should be implemented

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[1]Soy et al. Rheumatol Int. 2021;41(1):7-18. [2]Mérad et al., 2019; [3]Jordan et al. Blood. 2011;118(15):4041-52; [4]Henter J et al 2007 Feb; 48(2):124-31

HLH has been Rarely Reported Following High-dose AAV Gene Therapy

- Only one published case report[1] and mention of similar cases[2] reported HLH-like symptoms with high-dose systemic AAV treatment (1E14 vg/kg or higher)
- Symptoms: Elevated ferritin within the first few days, fever, pancytopenia, rash, hepatosplenomegaly[1]
- Cases treated successfully with early administration of either high dose steroids or anakinra (IL-1 receptor antagonist)
- No HLH events have been reported at AAV doses below 1E14 vg/kg

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[1]Galletta et al. J Clin Pharm Ther. 2022:47(9):1478-1481.; [2]Byrne et al Mol Ther. 2022;30(12):3503-3504.

FAERS Database Shows HLH/HLH-Like Symptoms Following High-Dose Systemic AAV (>1E14 vg/kg)

While HLH is extremely rare, emerging post-marketing data suggests that HLH-like immune responses may occur in a small subset of patients treated with high-dose systemic AAV gene therapy[1]

- HLH-Related Findings (N=15):
  - 1 confirmed case of HLH; 11 hyperferritinemia, 3 elevated blood iron
  - Common reported symptoms: fever (80%), ↑ALT and/or AST (100%), thrombocytopenia (60%)
- Incidence Estimates:
  - HLH-like: 1.3% of SAEs, ~0.3% of total exposures
  - For comparison: TMA: 3.1% of SAEs, ~0.8% of exposures
- HLH-like cases are separate from TMA: No overlap in ferritin elevation or diagnosis between the two

Data indicate standard monitoring for HLH after dosing with AAV should be implemented, similar to standard monitoring for TMA

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[1]Analysis based on 4,500 cases of Zolgensma treatment
Data cut-off date: December 31, 2024
FAERS = FDA Adverse Event Reporting System

HLH Risk Mitigation Strategy Implemented in RTT-200 Clinical Trial

- Dose level above 1E14 vg/kg not allowed
- In the first week post-dosing: employ daily monitoring of ferritin, fever, and falling blood counts (cytopenia)
- Exclude subjects with:
  - Any illness within 30 days of dosing, including EBV and CMV
  - COVID within 6 weeks of screening
- Prior to dosing, require sites to have anakinra available and encourage availability of a local HLH expert prior to dosing
- Include HLH treatment algorithm within protocol
  - 1st line of defense high-dose corticosteroids, 2nd line: anakinra

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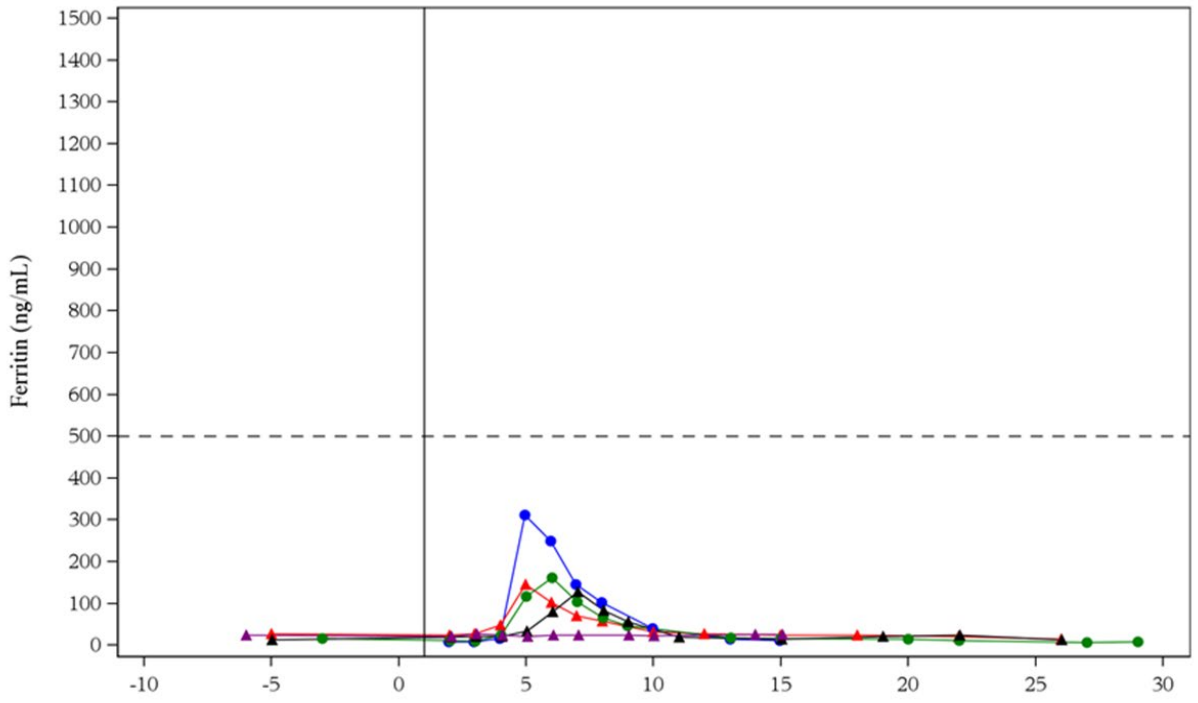
EBV = Epstein–Barr virus; CMV = Cytomegalovirus

No Evidence of HLH at the 1E15 vg Dose Level

- 5 additional participants dosed following new HLH monitoring protocol
  - 3 participants in the 4-10 years cohort
  - 2 participants in the 11 years and older cohort
- No participants have presented with the "three Fs" - **F**ever, elevated **F**erritin, and **F**alling blood counts (cytopenia)
- Transient ferritin elevations observed in 4 of 5 subjects recently dosed, peaking at Study Day 5-6 with recovery to Baseline by Day 10-12 with no intervention
- No ferritin levels above 500 ng/mL threshold and no clinical symptoms of HLH/ hyperinflammation have been observed

Ferritin Levels of Most Recently Dosed Participants – 1E15vg



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As of June 2, 2025

Thank You, and Acknowledgments

- Participants and caregivers/families in NGN-401 clinical trial
- Clinical investigators
- AAV and HLH specialists who consulted on the case

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