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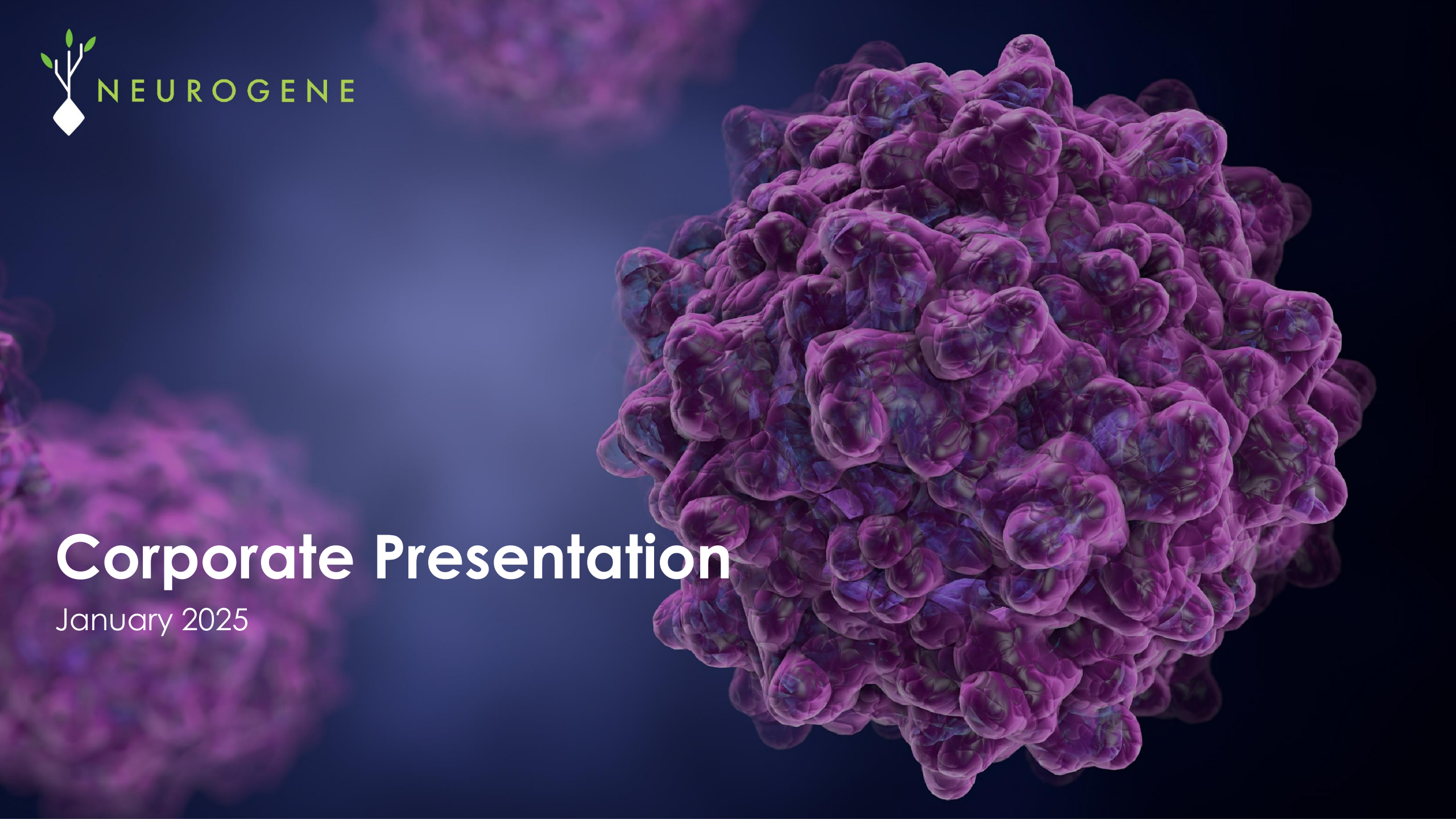

Corporate Presentation

January 2025

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Forward Looking Statements

This communication 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; the ability of Neurogene to identify future development plans for NGN-101; 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; anticipated early-stage discovery and expectations regarding the initiation of future clinical trials for programs in development; and Neurogene's cash runway. 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: Neurogene's limited operating history; the significant net losses incurred since inception of Neurogene; the ability to raise additional capital to finance operations; the ability of Neurogene to report its data on the predicted timeline; the ability of Neurogene to effectively used the RMAT designation or 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 product candidates through non-clinical and clinical development; the ability to obtain regulatory approval for, and ultimately commercialize, Neurogene's product candidates; Neurogene's limited experience in designing and conducting clinical trials; the ability to identify and pivot to other programs, product candidates, or indications that may be more profitable or successful than Neurogene's current product candidates; expectations regarding the market and potential for Neurogene's current product candidates; expectations regarding the potential tolerability, safety or efficacy for Neurogene's current product candidates; 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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Neurogene is a Differentiated Clinical-Stage Company Utilizing EXACT™ Technology to Treat Complex Neurological Diseases

- Novel EXACT technology designed to overcome key limitations of conventional gene therapy
- Pipeline addresses attractive market opportunities, including Rett syndrome
- Internal manufacturing provides financial and strategic pipeline flexibility
- 2H:27 cash runway enables operations beyond clinical inflection points

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EXACT: Expression Attenuation via Construct Tuning

Neurogene Clinical Stage Pipeline

Transgene Regulation CNS + Ocular Delivery

Product Candidate	Indication	IND* Enabling	Phase I/2	Pivotal	Near-Term Expected Milestones
NGN-401	Rett Syndrome				Registrational Trial Design Update 1H:25 Additional Interim Data 2H:25
NGN-101	CLN5 Batten Disease				Evaluating Opportunities for Program

*IND = investigational new drug

Multiple discovery stage assets in development with plans to advance one program into the clinic in 2025

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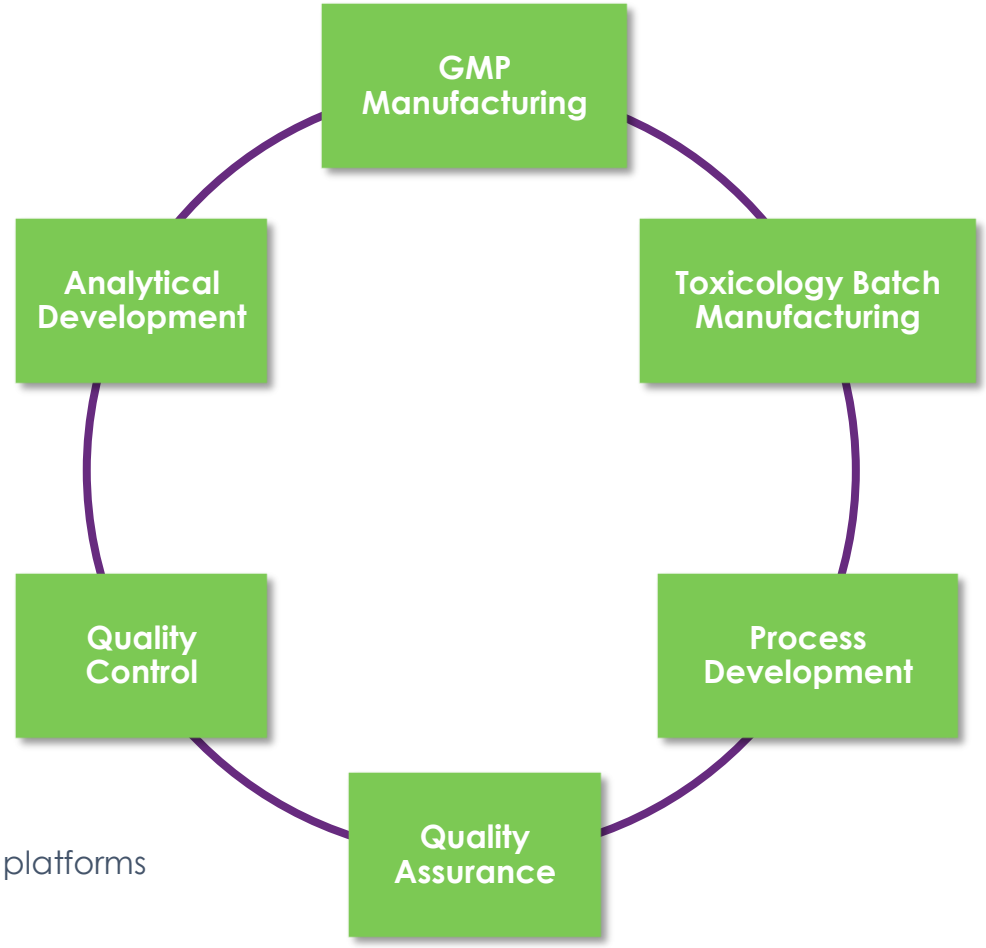
Wholly Owned and Fully Integrated In-House AAV Manufacturing



- Flexibility to manufacture AAV product at low cost
- Own product quality and development timelines
- Process development expertise supports both HEK293 and Sf9/rBV manufacturing platforms
- Flexibility to rapidly adapt CMC execution to program needs

Current research and clinical-grade manufacturing capabilities are designed for commercial-grade product to avoid potential future comparability challenges

NGN-401 for Rett Syndrome

Leveraging EXACT transgene regulation technology

Rett Syndrome – Devastating Disorder with High Unmet Need

Genetics

- X-Linked disorder causing mutations in the gene encoding for methyl-CpG binding protein 2 (MeCP2)
- Unknown incidence in boys, but typically lethal by ~3 years of age due to no healthy copy of MeCP2

Compelling Market Opportunity

- U.S. prevalence - ~6,000-9,000 patients
- WW incidence - 1:10,000 females

High Unmet Need

- There are no approved treatments that address root cause of disease
- Significant unmet need remains for new treatment options

U.S. prevalence estimate based on published incidence rates; Laurvick CL, et al. J Pediatr 2006;148(3):347–35.
WW incidence estimate based on published incidence rates; Pini G, et al. Orphanet Journal of Rare Diseases (2016) 11:132.

Rett Syndrome Treatment Requires Tight Transgene Regulation

Rett Syndrome*

Too little
gene expression drives disease

- ~50% of cells express WT levels of MeCP2
- ~50% are MeCP2 **deficient**

Balanced treatment goal

MeCP2 Duplication Disorder**

Too much
gene expression drives disease

- ~100% cells express **2x** MeCP2 levels

- Rett syndrome (RTT) is a severe neurological disorder caused by mosaic mutations in X-linked *MECP2* gene
- Mice modeling RTT recapitulate many neurological phenotypes observed clinically; disease reversibility has been demonstrated in both immature and mature adult animals

NGN-401 is designed to deliver therapeutic levels of MeCP2 to deficient cells while maintaining a non-toxic level in unaffected cells

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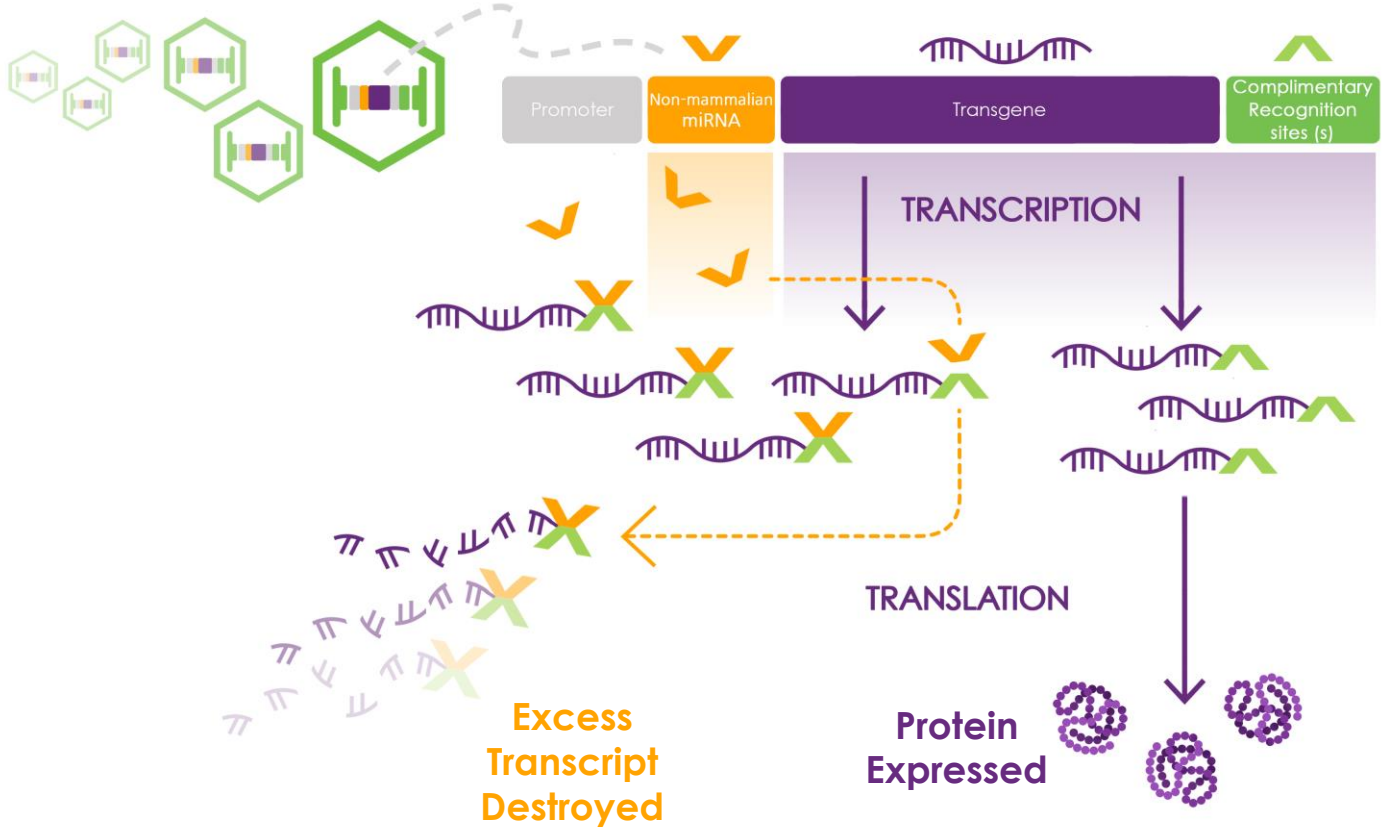
*Represents female Rett syndrome; **Represents male duplication disorder; WT = wildtype
Pini G, et al. Orphanet Journal of Rare Diseases (2016) 11:132.

EXACT Acts As a Genetic Thermostat, Limiting Transgene Expression

EXACT miRNA controls transgene levels to targeted range

Regulatory elements designed to avoid off-target effects

EXACT is expected to enable gene therapy for Rett syndrome and other complex disorders



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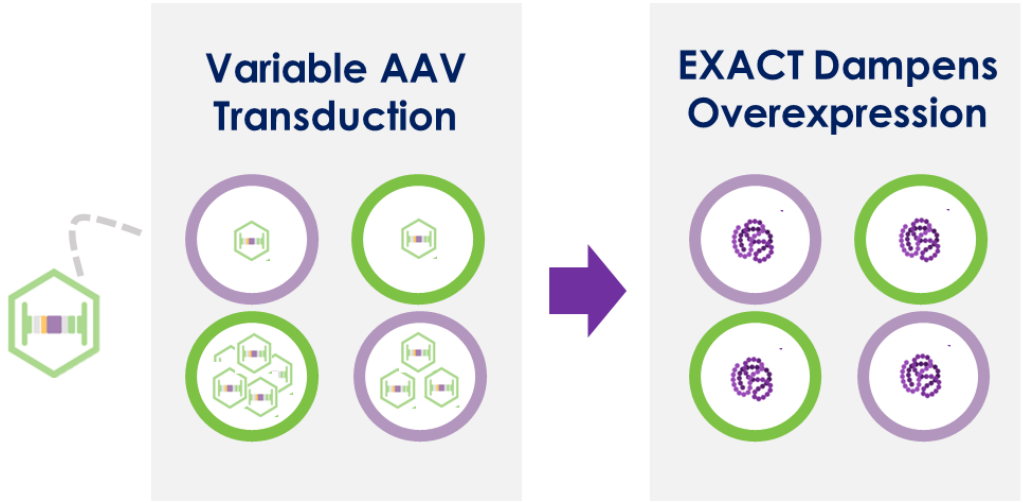
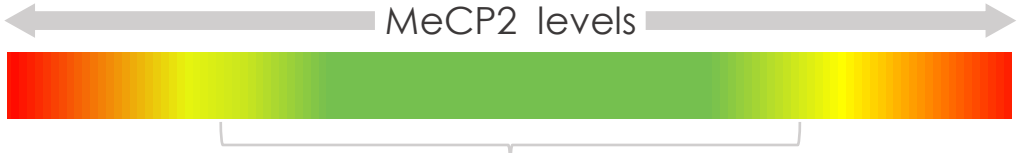
EXACT Designed to Widen Therapeutic Window and Enable Gene Therapy for Rett Syndrome



- ~50% of cells express WT levels of MeCP2
- ~50% are MeCP2 **deficient**

NGN-401 designed to provide therapeutic and tolerable levels of MeCP2 within this window



Too low
Rett Syndrome

Therapeutic and tolerable treatment window

Too high
MeCP2 Overexpression Toxicity

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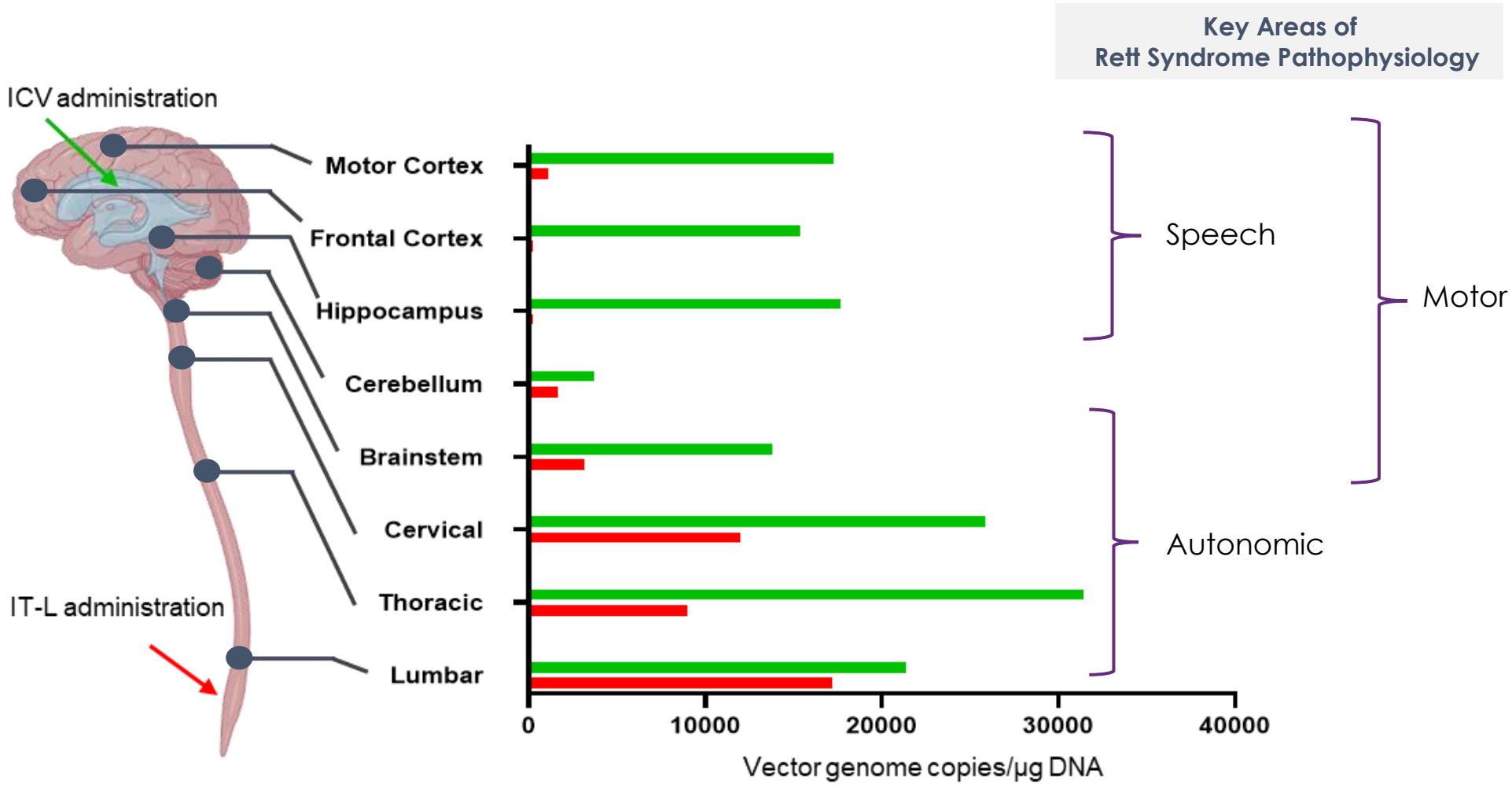
ICV Administration Resulted in Significantly Better Distribution Than IT-L To Key Areas of the Nervous System Underlying Rett Syndrome in NHPs



ASGCT 2021
ICV = Intracerebroventricular

Cardinal Clinical Features of Rett Syndrome

Inability to Communicate

- Loss of purposeful hand use & involuntary hand movements
- Loss of spoken language

Impaired Fine and Gross Motor Skills

- Loss of hand function
- Gait abnormalities
- Ambulation requiring assistance or non-ambulatory

Autonomic Dysfunction

- Severe apnea episodes
- Hyperventilation
- Constipation
- Difficulty swallowing
- Sleep disturbance

Additional Disease Manifestations

- Seizures
- Anxiety
- Scoliosis
- Muscle contractures

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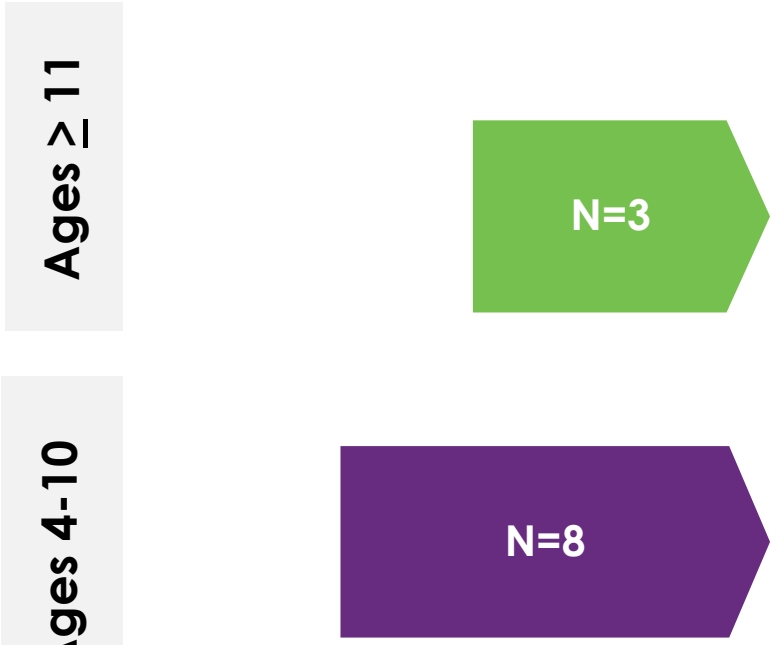
Pini G, et al. Orphanet Journal of Rare Diseases (2016) 11:132.

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

Trial Design

Trial evaluating 1E15 vg dose of NGN-401



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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Three pediatric participants previously received 3E15 vg dose; all future participants will receive 1E15 vg dose of NGN-401

Compelling Interim Clinical Data Show Gains of Function Across Core Domains and Improvements in Autonomic Function

Durable improvements observed across multiple scales, incl. two-point improvement in CGI-I in all participants, with concordance of benefit across scales

Consistent gains observed across core clinical domains of hand function, gross motor and communication, despite heterogeneous presentation

Clinically meaningful gain of skills and developmental milestones beyond those observed in natural history data

Objective improvements in autonomic domains of sleep and constipation

Rapid response post-treatment, with **deepening of response over time**

Favorable safety profile with 1E15 vg dose of NGN-401

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As of data cut-off date of 17 October 2024

Baseline Characteristics of Dosed Participants Range from Moderate to Severe Disease

	1E15 vg				
	Participant 1 (Pt:1)	**Participant 2 (Pt:2)**	**Participant 3 (Pt:3)**	**Participant 4 (Pt:4)**	**Participant 5 (Pt:5)**
Age at Dosing in Years	7	4	6	7	6
***MECP2* Mutation Severity**	Mild	Severe	Severe	Severe	Severe
Baseline Disease Severity as Indicated by CGI-S Score	4 (moderately ill)	5 (markedly ill)	5 (markedly ill)	5 (markedly ill)	5 (markedly ill)
Time Post Treatment with NGN-401 in Months	~15	~12	~9	<6	~1

Despite Similar CGI-S Scores, Individual Baseline Presentations Vary Widely Across Core Clinical Domains

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As of data cut-off date of 17 October 2024
As of 11 November 2024, Neurogene discontinued use of 3E15 vg dose and updated Phase 1/2 protocol to use 1E15 vg dose for all future participants

1E15 vg Dose of NGN-401 Has Shown a Favorable Safety and Tolerability Profile

- No treatment-related serious adverse events (SAEs)
- Most AEs are known potential risks of AAV, have been responsive to corticosteroid treatment and have resolved or are resolving
- No signs or symptoms indicative of MeCP2 overexpression, consistent with preclinical data
- No ICV procedure-related AEs
- No seizures reported in any participant after treatment with NGN-401

	1E15 vg Number of Events [Number of Participants]
Related TEAE	21 [4]
Grade 1	21 [4]
Grade 2	0
Grade 3	0
Related SAE	0
Unrelated SAE	1 [1]

- Unrelated SAE was urinary tract infection

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As of data cut-off date of 17 October 2024

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

	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%)	✓			✓	✓

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

Understanding the CGI-I with Rett Syndrome-Specific Anchors

- Clinician-rated scale assessing improvement from baseline
- 1-point improvement considered clinically meaningful (score ≤ 3)*
- 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
- CGI-I is more sensitive to change than CGI-S

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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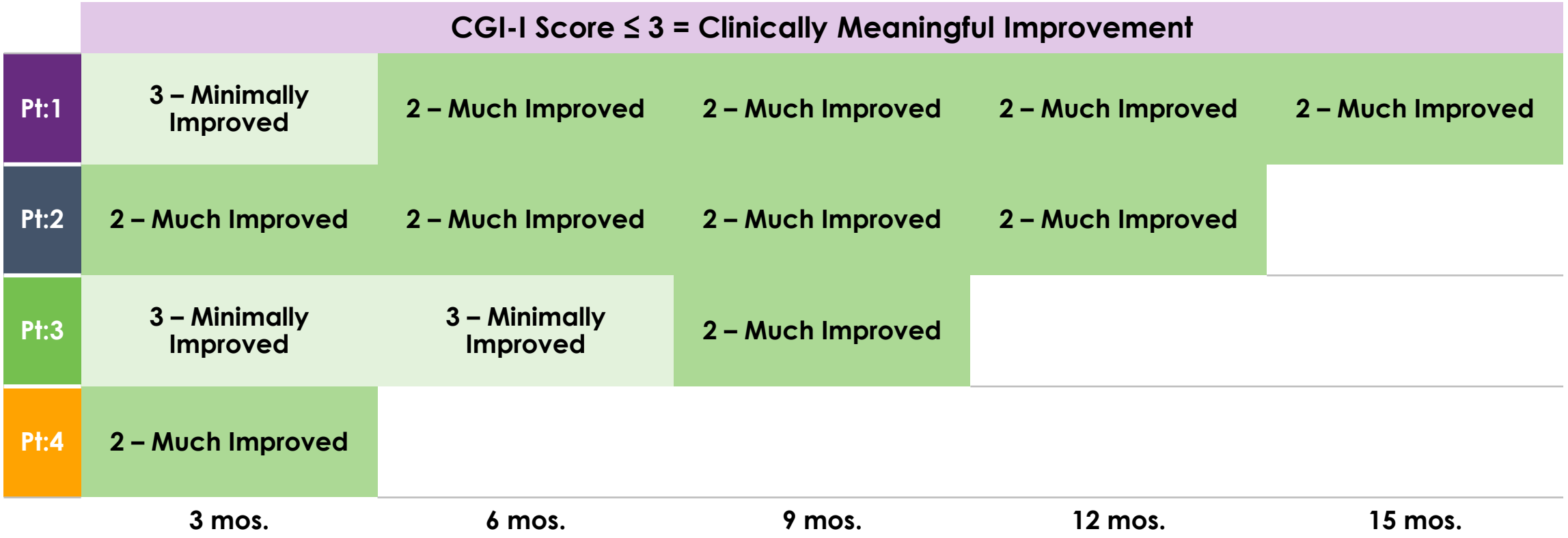
*Clinical Review Report: Brexpiprazole (Rexulti), 2017.
Neul J, et al. *J Child Neurol* (2015) 30(13):1743–1748

All Participants Achieved CGI-I Rating of "Much Improved"

Clinically Meaningful Improvement Observed Early After Treatment, with Deepening Response and Durability Over Time



Post Treatment with NGN-401

As of data cut-off date of 17 October 2024

Understanding the CGI-S with Rett Syndrome-Specific Anchors

- Clinician-rated scale of disease severity across 7 clinical domains
- Communication, ambulation, and hand function, have the greatest weighting on total score
- The majority of patients with Classic Rett Syndrome have a CGI-S of 4-6
- Scale not designed to be sensitive to change; substantial gains across core domains required to improve scale by 1 point

Score	CGI-S	
1	Normal, not at all ill	
2	Borderline ill	
3	Mildly ill	
4	Moderately ill	NGN-401 Clinical Trial Inclusion Criteria
5	Markedly ill	
6	Severely ill	
7	Extremely ill	

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Neul J, et al. *J Child Neurol* (2015) 30(13):1743–1748

CGI-S Clinical Domains Provide Insights Into Core Functional Areas; Scale Was Not Designed as Clinical Outcome Measure

Core functional domains

Key clinical focus is breathing abnormalities

Following commands clinically meaningful

Clinical Domains	CGI-S 3	CGI-S 4	CGI-S 5	CGI-S 6
Language/ Communication	Phrases-sentences. May have conversations or echolalia	<5 words Babbles Makes choices 25%-50%	No words Babbles Makes choices ≤25%	Vocalizations Occasionally screams Rarely or makes no choices
Ambulation	Walks, able to use stairs/run May ride tricycle or climb	Walks independently Unable to use stairs or run	Walks with assistance	Stands with support or independently May walk with support Sits independently or with support
Hand use	Bilateral pincer grasp. May use pen to write but has fine motor issues like tremor	Reaches for objects, raking grasp or unilateral pincer May use utensils/cup	Reaches No grasps	Rarely-occasionally reaches out No grasp
Social (eye contact)	Appropriate eye contact, >30s	Eye contact <20s	Eye contact <10s	Eye contact, inconsistent 5s
Autonomic	No or minimal breathing abnormalities (<5%) warm, pink extremities	Breathing dysrhythmia <50% No cynanosis Cool UE, Pink LE	Breathing dysrhythmia 50% No cynanosis Cold UE, Pink LE	Breathing dysrhythmia 50-100% May have cynanosis Cool UE or LE, may be blue
Seizures*	None, with or without meds	Monthly-weekly	Weekly	Weekly-daily
Attentiveness	Attentive to conversation, follows commands	50-100%	50%	<50%

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*Treated participants to date have been stable with no seizures on study
Neul J, et al. *J Child Neurol* (2015) 30(13):1743–1748

Hand Function: All Participants Gained Meaningful Improvements and Gained Skills that Deepened Over Time

All Participants Gained Higher-level Grasping and Improvements in Self-feeding

		Baseline	3 mos.	6 mos.	9 mos.	12 mos.	15 mos.
Pt:1 7 yrs. at dosing	CGI-S Domain Score	4	4	4	4	4	4
		Raking grasp; Limited self-feeding	• More consistent self-feeding, able to take multiple bites of foods without dropping	• Modified pincer grasp to self-feed	• Drinks with two hands • Able to place ball in basket on command	• Pincer grasp	• Uses fork to self-feed • Transfers objects between hands
Pt:2 4 yrs. at dosing	CGI-S Domain Score	6	4	4	4	4	
		No functional hand use	• Palmer grasp	• Engages both hands	• Beginning to self-feed • Picks up and grasps blanket with both hands • Raking grasp	• Can place pacifier in own mouth	
Pt:3 6 yrs. at dosing	CGI-S Domain Score	4	4	4	4		
		Raking grasp	• Modified pincer grasp	• Modified pincer grasp	• Beginning to self-feed		
Pt:4 7 yrs. at dosing	CGI-S Domain Score	4	4				
		Raking grasp; Self-feeds with adaptive utensils	• Modified pincer grasp; • Uses utensils to self-feed				

Time Post Treatment with NGN-401

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As of data cut-off date of 17 October 2024

Gross Motor Function: Gains are Faster in Participants Who Walked Independently at Baseline

First Three Participants Experienced Improvements in Gross Motor Function that Led to Greater Physical Independence From Caregivers

		Baseline	3 mos.	6 mos.	9 mos.	12 mos.	15 mos.
Pt:1 7 yrs. at dosing	CGI-S Domain Score	4	4	3	3	4	3
		Impaired, ataxic, unstable gait; Freezes often and walks on tip-toes; Unable to ascend or descend stairs independently	• More fluid gait, more heel-to toe	• Able to ascend stairs independently	• Can get on and off bed independently • Ascends stairs independently • Consistent heel-to-toe walking	• Able to ascend and descend stairs independently	• Able to climb out of bathtub independently • Gets down from carseat and exits car independently
Pt:2 4 yrs. at dosing	CGI-S Domain Score	4	4	4	4	4	
		Impaired, ataxic unstable gait ; Frequent falls; Needs assistance to stand up from seated position	• Able to get up from seated position independently • More fluid, faster gait	• Able to get off of couch independently • Steps over objects more easily	• More stable, fluid gait • Falls reduced by ~75% • Bends over at hip to pick up blanket from floor, returns to standing	• Can step off a curb with one hand held	
Pt:3 6yrs. at dosing	CGI-S Domain Score	6	6	6	6		
		Cannot sit, stand or walk independently	• Sits independently	• Sits independently	• Needs less support to get up from seated position and stand		
Pt:4 7 yrs. at dosing	CGI-S Domain Score	5	5				
		Cannot sit, stand or walk independently	• Cannot sit, stand or walk independently				

Time Post Treatment with NGN-401

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As of data cut-off date of 17 October 2024

Communication: All Participants Demonstrated Improvement in Ability to Convey Choices (Slide 1 of 2)

Ability to Follow Caregiver Commands Demonstrated in Patients With Longest Follow Up

		Baseline	3 mos.	6 mos.	9 mos.	12 mos.	15 mos.
Pt:1 7 yrs. at dosing	CGI-S Domain Score	6	6	5	5	4	4
		Makes choices 50% of time; Unable to follow commands	• Some choice-making	• Makes choices most of time; food 80–90% of time • Intermittently follows commands	• Makes choices nearly 100% of time for food • Follows multiple commands	• Makes choices 100% of time for food • Taps food items she wants • Follows >10 commands, many without gesture	• Consistently makes choices for food • Follows >10 commands, many without gesture • Actively seeks attention from others
Pt:2 4 yrs. at dosing	CGI-S Domain Score	6	5	4	4	4	
		Rarely makes choices; Unable to follow commands	• Makes choices 25–50% of time	• Makes choices 25–50% of time	• Makes food choices 50–75% of time • Follows simple commands	• Makes choices 50% of time • Follows simple commands	
Pt:3 6yrs. at dosing	CGI-S Domain Score	6	6	6	6		
		Rarely makes choices; Unable to follow commands	• Makes choices 50% of time	• Makes choices 25% of time	• Makes choices <25% of the time		
Pt:4 7 yrs. at dosing	CGI-S Domain Score	4	5				
		Makes choices with eye gaze device; Unable to follow commands	• Makes choices ~25% of time				

Time Post Treatment with NGN-401

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As of data cut-off date of 17 October 2024

Communication: All Participants Experiencing Improvements in Ability to Express Themselves (Slide 2 of 2)

		Baseline	3 mos.	6 mos.	9 mos.	12 mos.	15 mos.
Pt:1 7 yrs. at dosing	CGI-S Domain Score	6	6	5	5	4	4
	Vocalizations		• Vocalizations	• Vocalizations	• Vocalizations	• Babbles • Consistently waves "hello" on command	• Shouts or yells to express emotions when unhappy or uncomfortable
Pt:2 4 yrs. at dosing	CGI-S Domain Score	6	5	4	4	4	
	Vocalizations		• Occasional babbling, "dada" for Daddy	• Says "mama" and "dada" clearly	• Says "mama," "dada" and "nana" purposefully and in context	• Says "mama," "dada" and "nana" purposefully and in context	
Pt:3 6yrs. at dosing	CGI-S Domain Score	6	6	6	6		
	Vocalizations		• Increased Vocalizations	• Increased Vocalizations	• Laughs when caregiver makes jokes playing with toys		
Pt:4 7 yrs. at dosing	CGI-S Domain Score	4	5				
	Vocalizations		• Laughs at jokes when watching a movie • Vocalizations to express discomfort or protest				

Time Post Treatment with NGN-401

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As of data cut-off date of 17 October 2024

Autonomic Function: Breathing Dysrhythmias Are Variable, Difficult to Assess Clinically Meaningful Improvements at Clinic Visits

		Baseline	3 mos.	6 mos.	9 mos.	12 mos.	15 mos.
Pt:1 7 yrs. at dosing	CGI-S Domain Score	5	5	3	4	4	5
	Breathing dysrhythmias 50% of the time		• Breathing dysrhythmias 50% of the time	• No or minimal breathing abnormalities, <5% of time	• Breathing dysrhythmias <50% of the time	• Much less breath holding but still hyperventilating 50% of the time	• Much less breath holding but still hyperventilating 50% of the time
Pt:2 4 yrs. at dosing	CGI-S Domain Score	6	4	4	3	5	
	Significant dysrhythmias, breath holding and hyperventilation episodes >50% of the time		• Reduced breath holding and hyperventilation	• Breathing dysrhythmias are much less than 50% of the day	• Breathing dysrhythmias < 5% of the day	• 50% huffing and puffing, more with anxiety	
Pt:3 6yrs. at dosing	CGI-S Domain Score	3	3	3	3		
	No or minimal breathing abnormalities		• No breath holding, hyperventilation	• No breath holding, hyperventilation	• No breath holding, hyperventilation		
Pt:4 7 yrs. at dosing	CGI-S Domain Score	4	4				
	No breathing dysrhythmias		• Breath holding 25% of the time				

Time Post Treatment with NGN-401

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As of data cut-off date of 17 October 2024

Understanding the Rett Syndrome Behavior Questionnaire (RSBQ)

- Caregiver-completed scale consisting of 45 items measuring behavior in females with RTT
- Developed as a diagnostic tool to differentiate females with Rett syndrome from those with severe intellectual disability
- Scale is limited due to no questions on communication and very limited number of questions on gross motor function
- Higher score indicates greater behavioral symptoms; scale does not correlate with disease severity

Subscales	Total Possible Points (90)
General mood	16
Breathing problems	10
Hand behaviors	12
Repetitive face movements	8
Body rocking and expressionless face	12
Nighttime behaviors	6
Fear/anxiety	8
Walking/standing	4
Other	14

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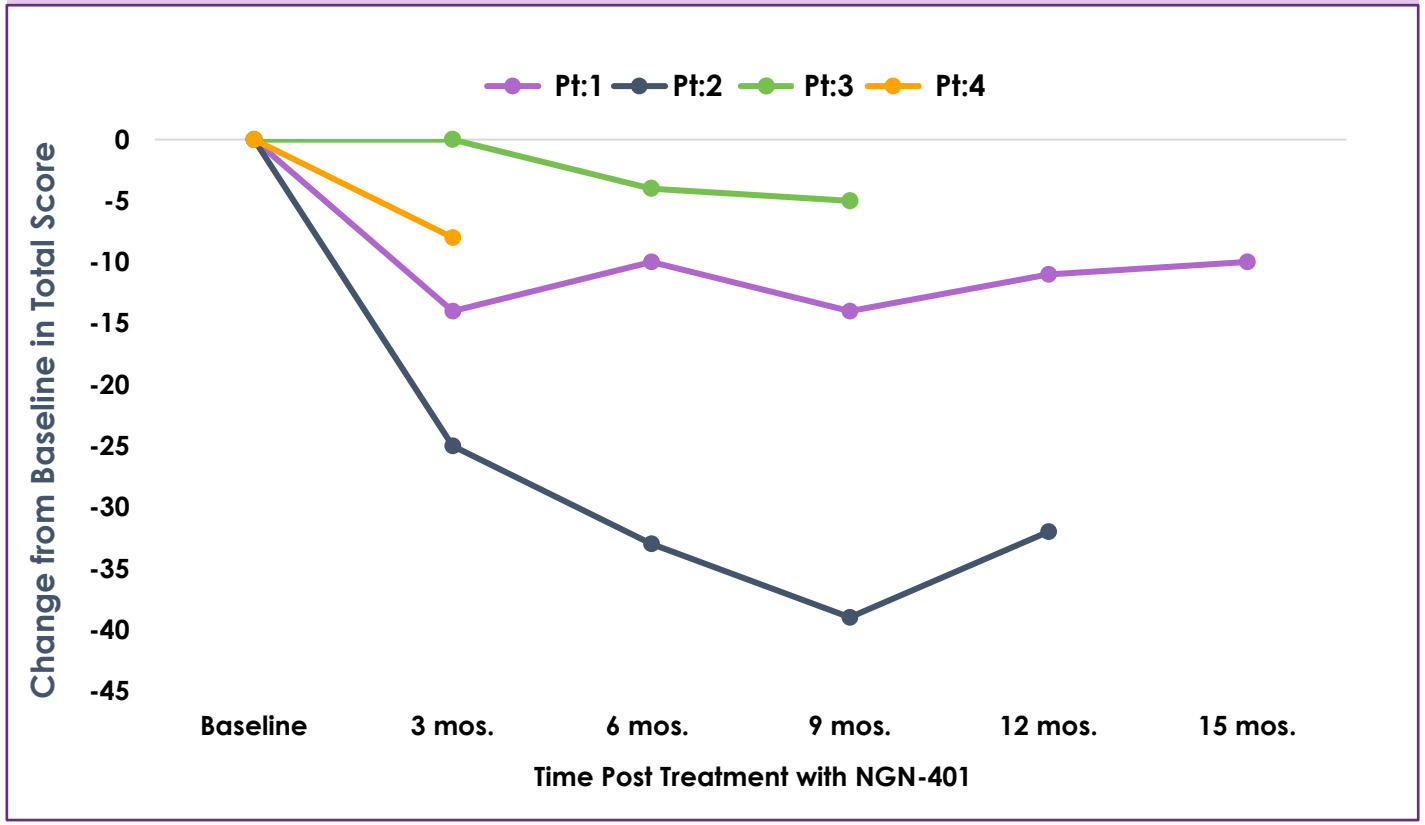
Percy A, et al. *Front Pediatr* (2023)

All Participants Have Experienced Improvement in RSBQ Score

RSBQ: Change from Baseline
Reduction in Score = Improvement



Participant	Baseline CGI-S Score	Baseline RSBQ Score	Change from Baseline	% Change
Pt:1	4	39	-10	-28%
Pt:2	5	62	-32	-52%
Pt:3	5	17	-5	-29%
Pt:4	5	29	-8	-28%

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As of data cut-off date of 17 October 2024

All Participants Experienced Improvements in Autonomic Function, as Measured by Objective Assessments

- **Pt:1** and **Pt:2**, who had sleep deficits at Baseline, experienced improvements in sleep parameters, as measured by a wearable device
  - Pt:1 sleep efficiency increased from 83% to 90% at 6 months
  - Pt:2 sleep efficiency increased from 90% to >95% at 6 months, considered ideal

- **Pt:1**, **Pt:2** and **Pt:4** had constipation at Baseline, and experienced improvements over time as measured by the caregiver-reported modified Bristol Stool Form Scale

- **Pt:3** had dysphagia, or difficulty swallowing, at Baseline, requiring a pureed diet and had to be spoon-fed by caregiver due to aspiration; she is now able to swallow liquids from a cup and chew and swallow food items

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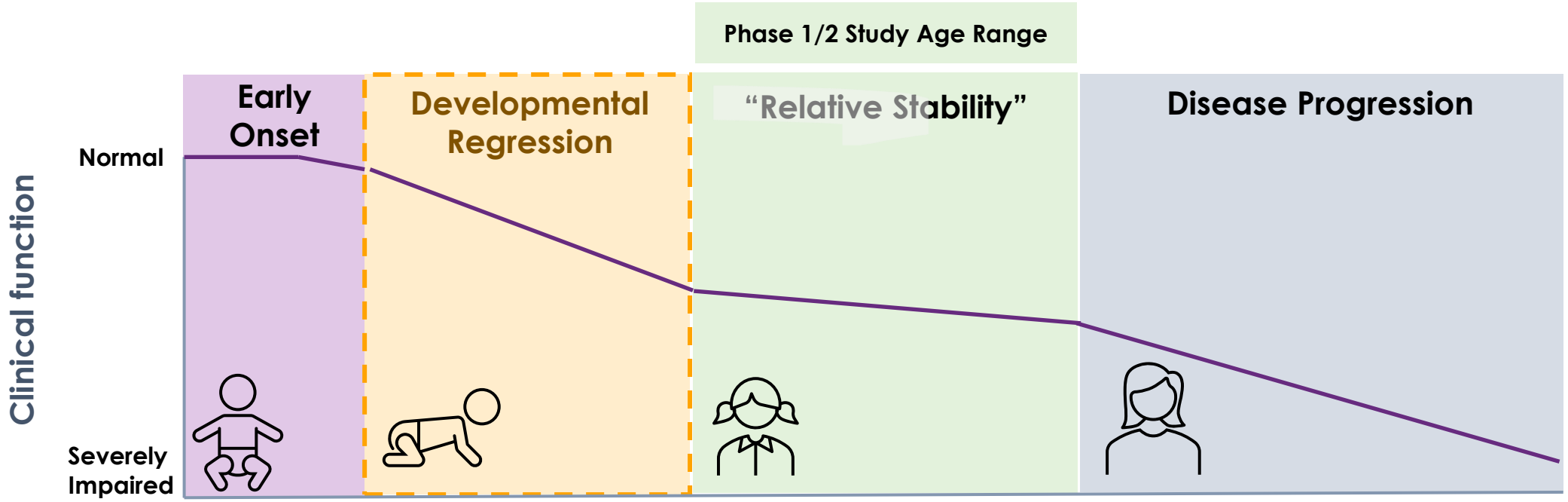
As of data cut-off date of 17 October 2024
Detailed data provided in Appendix

Participant Vignettes

Rett Syndrome is Defined By Regression Period in Early Development



Pini G, et al. *Orphanet Journal of Rare Diseases* (2016) 11:132.
Neul J, et al. *Journal of Neurodevelopmental Disorders* (2014) 6:20
U.S. Natural History Study of Rett Syndrome (RNHS) Clinicaltrials.gov identifier: NCT02738281. Accessed 2022 from International Rett Syndrome Foundation (IRSF).

Simple Skills Are Generally Acquired but Majority Are Lost During Regression; More Complex Skills are Generally Not Acquired

Natural History of Rett Syndrome

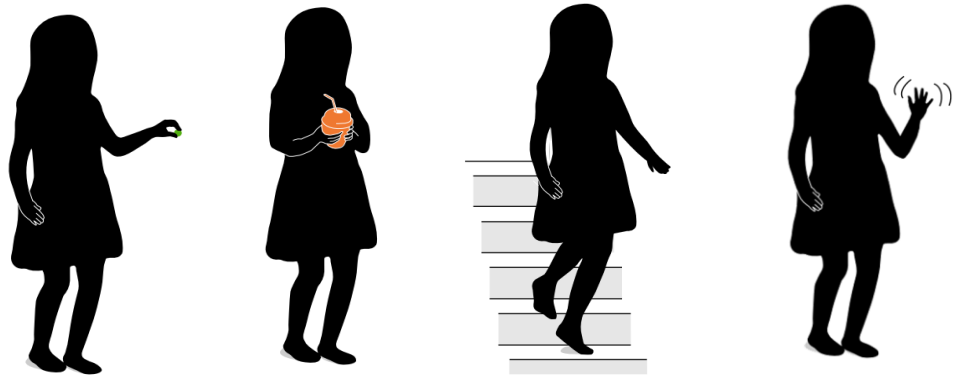
	Early Onset	Developmental Regression +	
	Simple Skills Generally Acquired	**Simple Skills Generally Lost***	**Complex Skills Not Generally Acquired**
	% Learned	**% Lost**	**% Never Learned**
Hand Function Fine motor more likely to be lost than gross motor	Raking Grasp (~85%) Transferred Objects (~80%) Hold Bottle (~80%) Pincer Grasp (70%)	Loss → Raking grasp (~50%) Transferred Objects (~60%) Hold Bottle (~60%) Pincer Grasp (~50%)	Spoon/Fork Without Assist - (~80%)
Gross Motor Advanced skills less likely ever acquired	Sitting (>~90%) Walking (~60%)	*If gross motor skills acquired, not generally lost Sitting - ~80% retain Walking - ~50% retain	Run (~75%) Climb Up Stairs Without Help (82%) Climb Down Stairs Without Help (86%)
Communication Expressive more likely to be lost/never learned than receptive	Babbling (~90%) Single Words (66%)	Loss → Babbling (~45%) Single Words (~60%)	Waved Bye (~50%) Points When Wants (~80%) Spoken Phrases (~80%)

U.S. Natural History Study of Rett Syndrome (RNHS) Clinicaltrials.gov identifier: NCT02738281. Accessed 2022 from International Rett Syndrome Foundation (IRSF).
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
Neul J, et al. *Journal of Neurodevelopmental Disorders* (2014) 6:20

Pt:1 From Pre-Treatment to 15 Months Post NGN-401

Hand Function / Fine Motor	• Had a raking grasp, briefly held objects, dropping items quickly, with limited ability to self-feed	• Developed a pincer grasp, able to self-feed, has begun using a fork to eat; uses both hands to drink on her own
Ambulation / Gross Motor	• Walked independently, but would stay on her tip-toes, freeze often and required a parent to help her go up/down stairs or get on/off a bed	• More fluid gait with heel to toe walking, and does the following on her own: goes up/down the stairs, climbs out of high rimmed bathtub, gets on/off furniture, climbs out of her car seat to exit the car
Language / Communication	• Unable to indicate her wishes, follow simple commands from her parents, or express emotion	• Without being told, navigates her house to the car to go to school, waves hello to her grandfather on daily video calls, taps on food items to express choices, frowns/shouts to show displeasure • Follows >10 commands such as "give a kiss," "sit down," "give it to me," "put item in trash," "open/close door," "flush toilet"

Baseline (7 years old)



Post Treatment with NGN-401

Images are representative of skills and are not photos of participants in the NGN-401 clinical trial
As of data cut-off date of 17 October 2024

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

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

Pt:1 Complex Developmental Skills Learned/Re-Learned Well Outside RNHS	
Pt:1 Newly Learned Complex Skills Post-NGN-401	% Never Learned in RNHS
Climbs up stairs without help	82%
Climbs down stairs without help	86%

Pt:1 Re-Learned Complex Skill Post-NGN-401	% Re-Learned in RNHS
Waves hello*	4%

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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

Pt:2 From Pre-Treatment to 12 Months Post NGN-401

	Baseline (4 years old)	Post Treatment with NGN-401
Hand Function / Fine Motor	• Had no functional hand use, clenched hands, could not grab, reach, hold objects	• Holds juice box and drinks, starting to self feed, frequently grabs and holds her security blanket, places pacifier in her mouth to self-soothe, turns on videos by tapping tablet
Ambulation / Gross Motor	• Walked independently, but fell frequently, couldn't stand up from seated position without being pulled up, couldn't bend over	• Faster, steadier gait with infrequent falls; on her own she can: stand from seated position, bend over and pick up her blanket from the floor, step off a curb with one hand held
Language / Communication	• No babbling, no ability to make choices, not able to follow commands	• Says "mama," "dada," and "nana" clearly and in context • Follows commands such as "come here" and "give a kiss" and more regularly choosing preferred foods

Images are representative of skills and are not photos of participants in the NGN-401 clinical trial
As of data cut-off date of 17 October 2024

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

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

Pt:2 Developmental Skills Learned/Re-Learned Well Outside RNHS	
Pt:2 Newly Learned Complex Skills Post-NGN-401	% Never Learned in RNHS
Follows a command without a gesture	64%
Pt:2 Re-Learned Skills Post-NGN-401	**% Re-Learned in RNHS**
Uses raking grasp to retrieve an object	3%
Reaches for an object	13%
Uses words with meaning	8%

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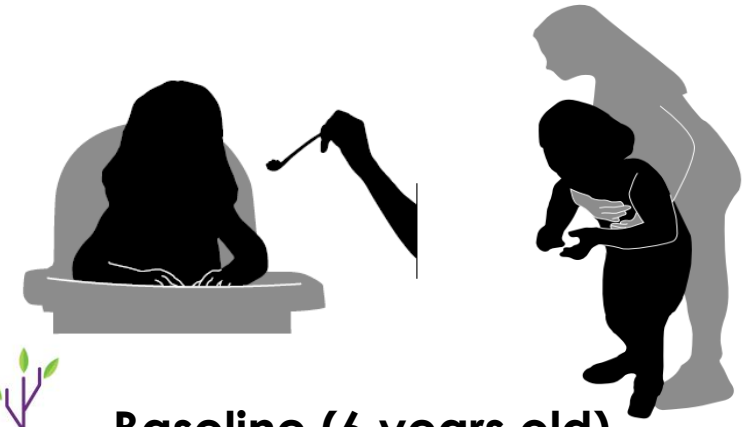
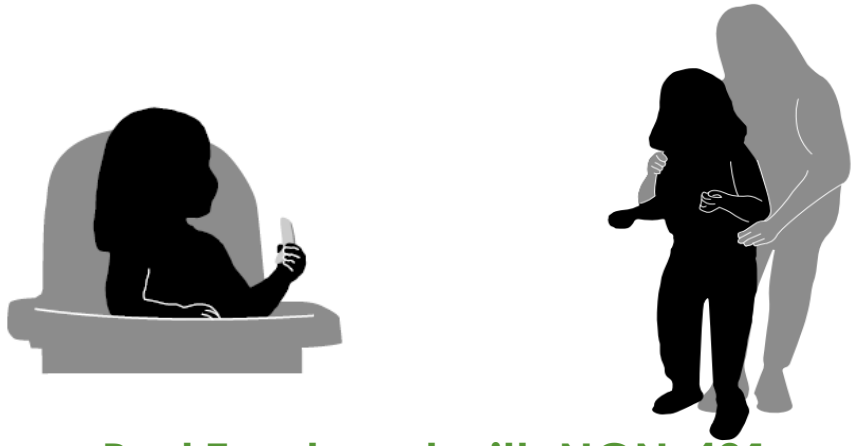
Data from the RNHS; N=200 female subjects with classic RTT, age 4-10 years, CGI-S score of 4 to 6 at baseline, confirmed genetic mutation
As of data cut-off date of 17 October 2024

Pt:3 From Pre-Treatment to 9 Months Post NGN-401

	Baseline (6 years old)	Post Treatment with NGN-401
Hand Function / Fine Motor	• Raking grasp, required caregiver to spoon feed all meals due to inability to swallow anything safely other than pureed food	• Able to self-feed solid foods, swallow liquids
Ambulation / Gross Motor	• Could not sit, stand, or walk independently due to poor core strength and lower extremity weakness	• Sits independently, improved posture, able to stand with less support, able to advance feet forward better with support
Language / Communication	• No choice making, babbling; not able to follow commands	• Laughs at jokes made by caregiver • Makes some choices





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Images are representative of skills and are not photos of participants in the NGN-401 clinical trial
As of data cut-off date of 17 October 2024

Pt:3 Multi-Domain Improvements Not Expected Based on Rett Syndrome Natural History

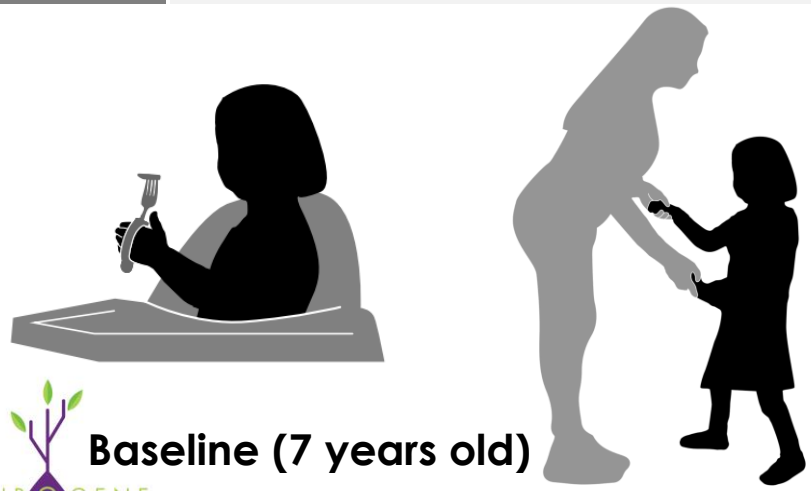
	Select Pt:3 Developmental Skills	Months Post-NGN-401		
		3	6	9
Fine Motor	Uses a pincer grasp		✓	✓
Fine Motor	Able to self-feed			✓
Gross Motor	Sits independently	✓	✓	✓

Pt:3 Developmental Re-Learned Well Outside RNHS	
Pt:3 Re-Learned Skills Post-NGN-401	% Re-Learned in RNHS
Uses a pincer grasp	6%
Able to self-feed	8%
Sits independently	7%

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

Pt:4 From Pre-Treatment to 3 Months Post NGN-401

Hand Function / Fine Motor	• Raking grasp, able to use adaptive utensils to self-feed, unable to hold or use regular utensils	• Able to use regular utensils to self-feed, reaches with more precision
Ambulation / Gross Motor	• Could not stand or walk independently	• No substantial improvement observed yet at 3 months post treatment with NGN-401
Language / Communication	• No babbling, unable to follow commands, laughed out of context	• Laughs at appropriate moments while watching favorite movie or listening to an audio program • Vocalizes to express discomfort or show emotion



Baseline (7 years old)

Post Treatment with NGN-401

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Images are representative of skills and are not photos of participants in the NGN-401 clinical trial
As of data cut-off date of 17 October 2024

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

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

Pt:4 Developmental Skills Learned Well Outside RNHS	
Pt:4 Newly Learned Complex Skill Post-NGN-401	% Never Learned in RNHS
Can use utensils to self-feed (without assistance)	80%

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

Leveraging START and RMAT to Accelerate Program to Registration

Multiple Touch Points with FDA Intended to Accelerate Registration

- START Program participation provides clear channel of communication with FDA intended to accelerate registrational planning
- RMAT designation provides eligibility for an Accelerated Approval pathway and rolling BLA and potential for Priority Review
- FDA alignment on potency assay strategy to support future registrational trial and manufacturing scale-up plans at Neurogene Houston facility expected to support commercial launch plans
- Initiated ages ≥ 11 cohort to support potential for a broad label to capture higher portion of prevalent population

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Key Anticipated Milestone Events

Key Upcoming Anticipated Milestones and Pipeline Developments

Rett syndrome (NGN-401)

- ❑ Provide regulatory update in 1H:25 regarding pivotal trial design
- ❑ Announce additional Phase 1/2 clinical data in 2H:25

CLN5 Batten disease (NGN-101)

- ❑ Evaluate opportunities for the program

Early-stage discovery

- ❑ Advance one program into the clinic (2025)

Cash runway expected to fund operations into 2H:27

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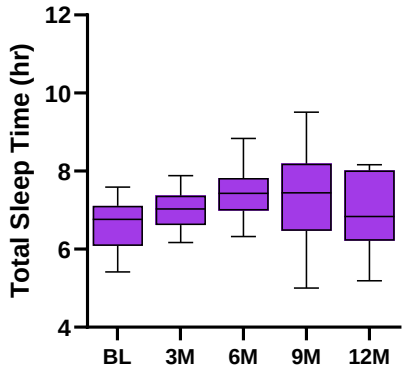
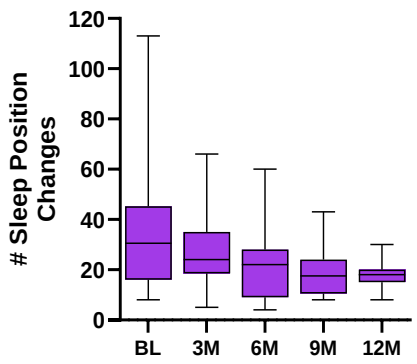
Appendix

Pt:1 Autonomic Function: Objective Improvements Observed in Sleep Parameters and Constipation

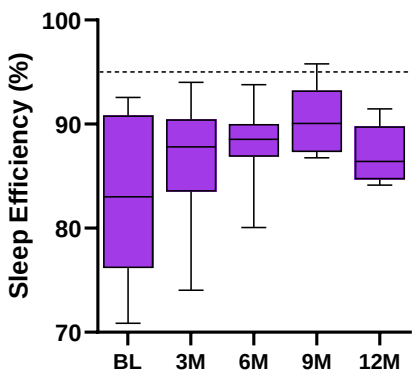
Improvements in All Sleep Parameters, as Assessed by Wearable Device



Total sleep time **increased from 6.6 to 7 hrs./night**

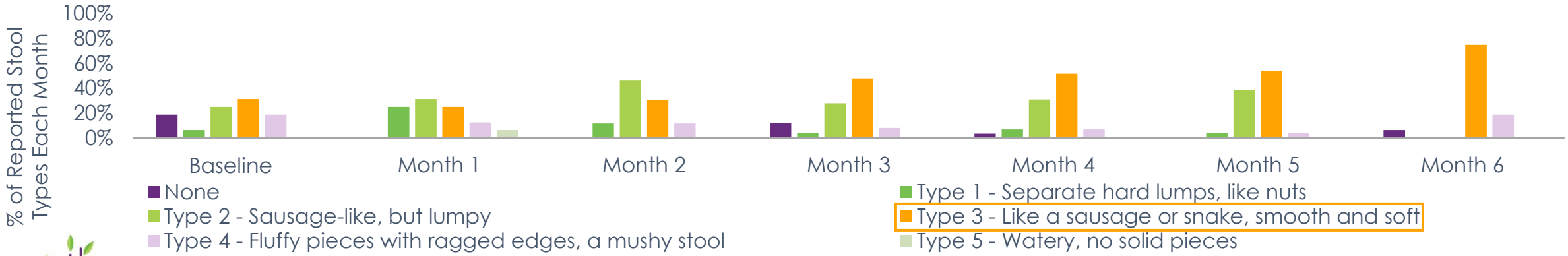


Number of position changes **decreased from 37 to 18** per night



Sleep efficiency* **increased from 83% to ~90%** (95% is ideal)

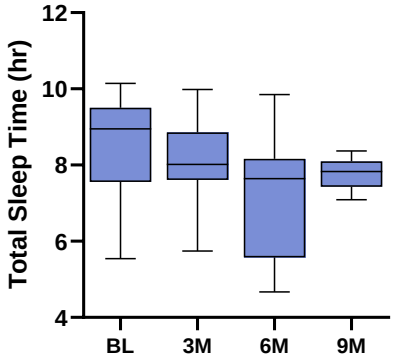
Constipation Improved Over Time, as Measured by Stool Consistency and Frequency**



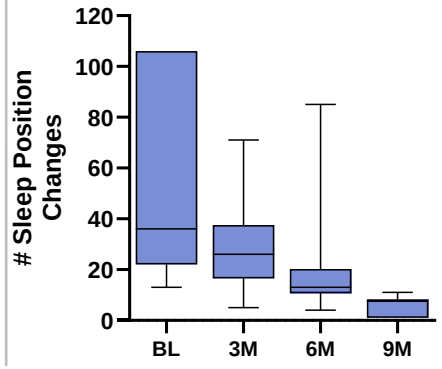
*Sleep efficiency defined as time spent asleep vs. total time spent in bed
**As measured by Caregiver on modified Bristol Stool Form Scale
As of data cut-off date of 17 October 2024

Pt:2 Autonomic Function: Objective Improvements Observed in Sleep Parameters and Constipation

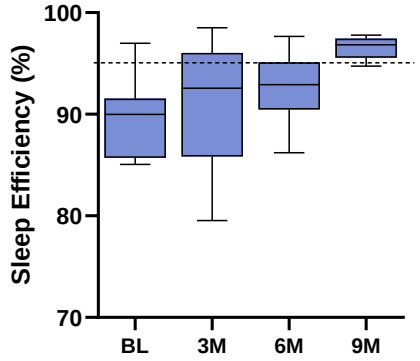
Transition to More Restful Sleep, as Assessed by Wearable Device



Total sleep time decreased; however, **more restful sleep occurring**

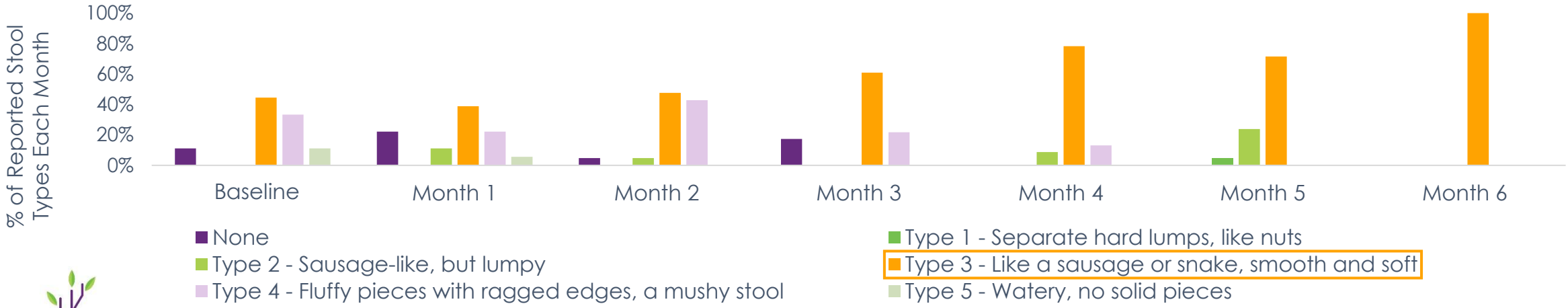


Number of position changes **decreased from 37 to 8** per night



Sleep efficiency* **increased to >95%**, which is ideal

Constipation Improved Over Time, as Measured by Stool Consistency and Frequency**



*Sleep efficiency defined as time spent asleep vs. total time spent in bed
**As measured by Caregiver on modified Bristol Stool Form Scale
As of data cut-off date of 17 October 2024

Pt:3 Autonomic Function: Experienced Clinically Meaningful Improvement in Swallowing and Gained Ability to Self-feed

At Baseline, Pt:3 had dysphagia requiring a pureed diet and had to be spoon-fed by caregiver due to aspiration

Beginning 3 months post-NGN-401, Pt:3 could swallow liquids, such as clear soup and water from a sippy cup, and chew and swallow soft items, such as meatballs and cooked carrots, without choking

At 9 months post-NGN-401, she is now able to grasp food such as apple slices and self-feed

Pt:3 did not have Baseline deficits in autonomic categories of sleep or constipation

- Sleep duration and quality maintained post-treatment
- No change in Modified Bristol Stool Form Scale scores post-treatment

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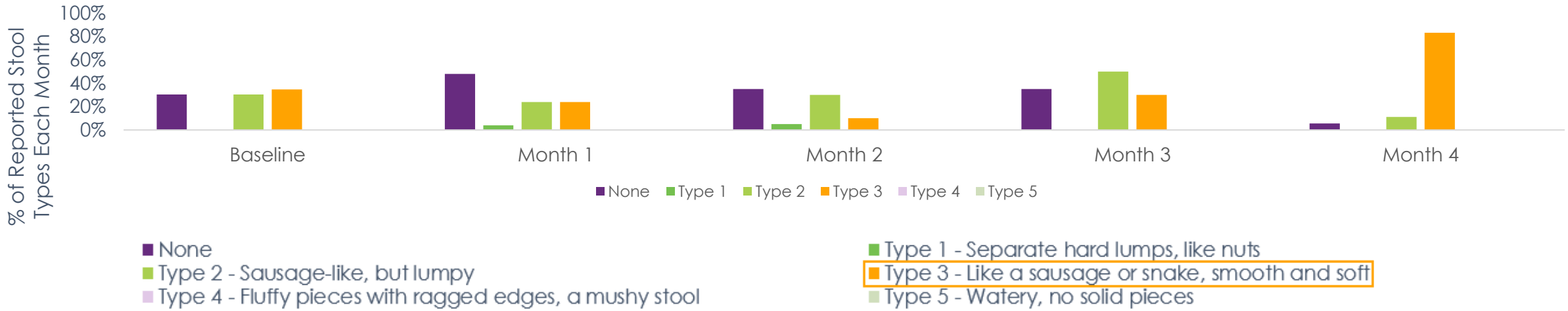
As of data cut-off date of 17 October 2024

Pt:4 Autonomic Function: Objective Improvement Observed in Constipation

Constipation Improved in Month 4, as Measured by Stool Consistency and Frequency*



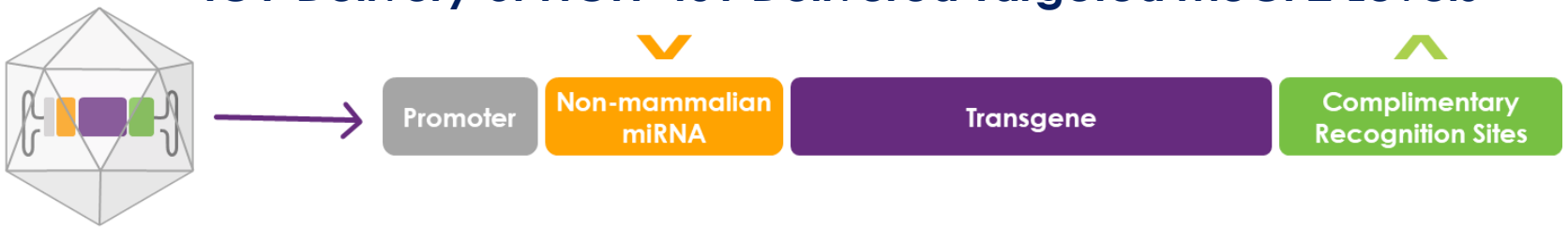
Pt:4 did not have Baseline deficits in autonomic category of sleep

Sleep quality maintained post-treatment

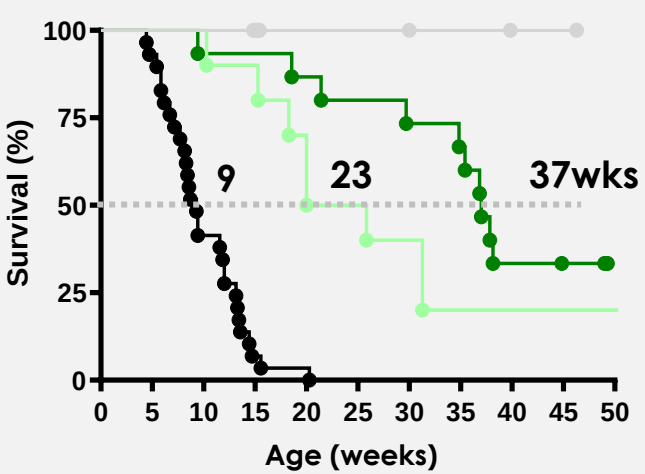
*As measured by Caregiver on modified Bristol Stool Form Scale
As of data cut-off date of 17 October 2024

NGN-401 Demonstrated Efficacy and Safety in *Mecp2* Mouse Models

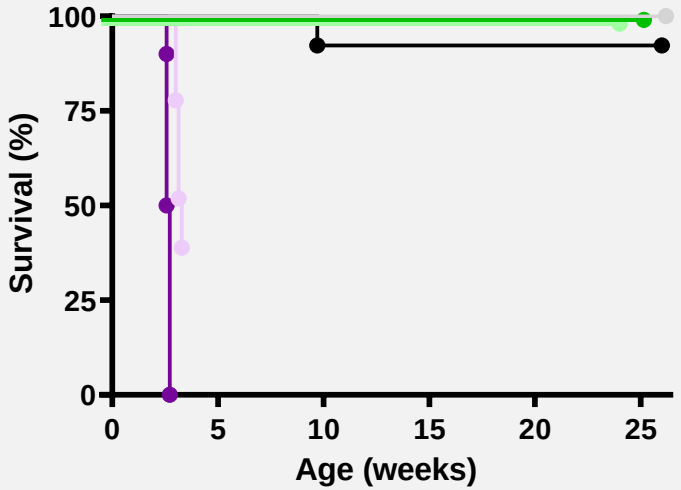
ICV Delivery of NGN-401 Delivered Targeted MeCP2 Levels

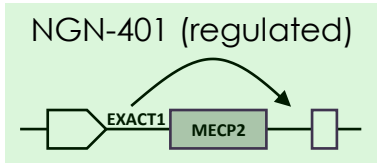


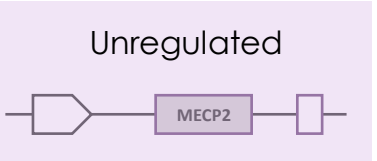
Survival in Male Knockout



Survival in Female Het







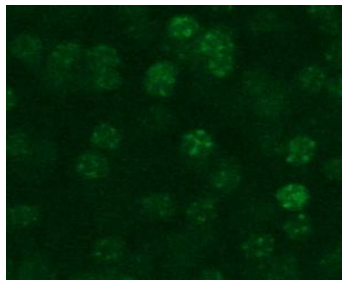
NGN-401 1E11 vg
NGN-401 3E11 vg
Unregulated 1E11 vg
Unregulated 3E11 vg

WT + Vehicle
Male or female + Vehicle

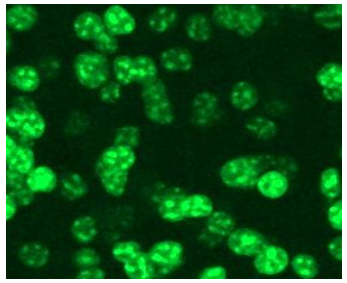
Het=heterozygous for Mecp2, mirroring genetic makeup of human females with Rett syndrome

EXACT Delivers Consistent Levels of *MECP2* Expression on Cell-by-Cell Basis

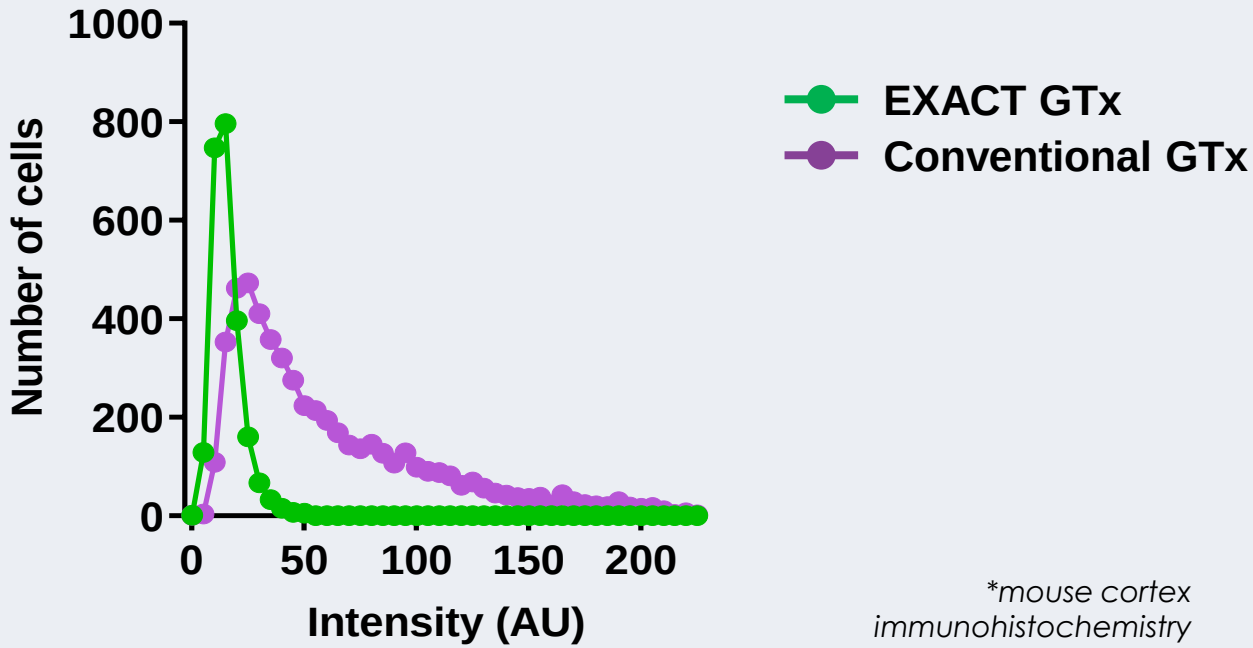
EXACT



Conventional



NGN-MECP2 Achieves Narrow Expression of *MECP2**



*mouse cortex immunohistochemistry

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