UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 OR 15(d) of The Securities Exchange Act of 1934

Date of Report (date of earliest event reported): August 11, 2025

Neurogene Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-36327**	**98-0542593**
(State or other jurisdiction of incorporation or organization)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

535 W 24th Street, 5th Floor
New York, NY 10011
(Address of principal executive offices, including zip code)

Registrant's telephone number, including area code: (877) 237-5020

N/A
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.000001 par value	**NGNE**	**The Nasdaq Global Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition

On August 11, 2025, Neurogene Inc. (the "Company") issued a press release announcing financial results for the quarter ended June 30, 2025. A copy of the press release announcing such results is attached as Exhibit 99.1 to this Current Report on Form 8-K. Also on August 11, 2025, the Company posted an updated corporate presentation on its website. A copy of the corporate presentation is furnished as Exhibit 99.2 to this Current Report on Form 8-K.

The information in this Item 2.02 and Exhibits 99.1 and 99.2 attached hereto are being furnished and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall such information or Exhibits 99.1 and 99.2 be deemed incorporated by reference into any filing under the Exchange Act or the Securities Act of 1933, as amended, except as expressly set forth by specific reference to such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Press Release dated August 11, 2025
99.2	Corporate Presentation (August 11, 2025)
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

NEUROGENE INC.

Date: August 11, 2025

By: /s/ Christine Mikail
Name: Christine Mikail
Title: President, Chief Financial Officer

Neurogene Reports Second Quarter 2025 Financial Results and Highlights Recent Updates

Announced design of Embolden™ registrational clinical trial of NGN-401 gene therapy for Rett syndrome; trial initiation activities underway

Completed dosing in Phase 1/2 NGN-401 trial, and remains on track to report updated clinical efficacy and safety data in the second half of 2025

Cash runway into early 2028

NEW YORK – August 11, 2025 – Neurogene Inc. (Nasdaq: NGNE), a clinical-stage company founded to bring life-changing genetic medicines to patients and families affected by rare neurological diseases, today announced second quarter 2025 financial results and highlighted recent corporate updates.

"In the first half of 2025, we made significant progress in our NGN-401 program for Rett syndrome. We completed dosing of the last five participants in the Phase 1/2 trial and received written agreement from the U.S. FDA on the key elements of the Embolden™ registrational trial, in which we have already begun initiation activities," stated Rachel McMinn, Ph.D., Founder and Chief Executive Officer of Neurogene. "We are pleased to be moving forward with Embolden, which was purposefully and rigorously designed to differentiate NGN-401 by evaluating participants as young as three years of age with a primary endpoint that incorporates measures that KOLs, caregivers and payors believe to be clinically meaningful. Our previously announced reallocation of capital provides us runway into early 2028, enabling us to focus our resources on advancement of this potential therapy for the patients and families who urgently need new treatment options."

Dr. McMinn continued, "In leveraging the continual dialogue under the START program, the FDA encouraged the analysis of the Embolden primary endpoint to remain at 12 months as the basis for full approval, noting that a 6-month endpoint may not be considered clinically meaningful. In further maintaining the rigorous design of the Embolden trial, we are electing to dose the last planned participant from the Phase 1/2 trial as part of the registrational Embolden trial and add one more participant to complete the proposed sample size at 20 patients."

Second Quarter 2025 and Recent Highlights, and Anticipated Milestones

NGN-401 Gene Therapy for Treatment of Rett Syndrome

- Received written agreement from the U.S. Food and Drug Administration (FDA) on key elements of the Embolden registrational trial of NGN-401 and refined the sample size to propose 20 participants
- Initiated Embolden clinical trial activities to support the conversion of the Phase 1/2 trial to a registrational trial
- Completed enrollment in the Phase 1/2 trial, with the last 5 additional participants dosed in the first half of 2025
- Remains on track to report updated clinical efficacy and safety data from the Phase 1/2 trial in the second half of 2025
- Presented at scientific conferences the hemophagocytic lymphohistiocytosis (HLH) monitoring and treatment algorithm incorporated into the NGN-401 clinical trial, which has been acknowledged as valuable information by the Rett syndrome and gene therapy communities

- There has been no evidence of HLH/hyperinflammatory syndrome in any NGN-401 trial participant at the 1E15 vg dose level, as of the date of this press release

Upcoming Events

- Stifel Biotech Summer Summit: Management will participate in a fireside chat at 12:00 p.m. ET on August 12 (not webcast)
- H.C. Wainwright Annual Global Investment Conference: Management will participate in a fireside chat at 2:30 p.m. ET on September 8 and participate in 1x1 meetings

Second Quarter 2025 Financial Results

- **Cash, Cash Equivalents and Short-Term Investments**: Cash, cash equivalents and short-term investments as of June 30, 2025 were $274.5 million. We currently expect cash, cash equivalents and short-term investments to fund planned operations into early 2028.
- **Research & Development (R&D) Expenses**: R&D expenses were $19.4 million for the three months June 30, 2025 compared to $15.7 million for the three months ended June 30, 2024. The increase in R&D expenses for the three months ended June 30, 2025 was primarily driven by an increase in Rett syndrome clinical trial costs and employee-related expenses due to an increase in R&D headcount.
- **General & Administrative (G&A) Expenses**: G&A expenses were $6.7 million for the three months ended June 30, 2025 compared to $5.3 million for the three months ended June 30, 2024. The increase in G&A expenses for the three months ended June 30, 2025 was primarily driven by an increase in employee-related expenses due to an increase in stock-based compensation, headcount and other corporate expenses.
- **Net Loss**: Net loss was $22.0 million for the three months ended June 30, 2025 compared to $18.5 million for the three months ended June 30, 2024.

About Neurogene

The mission of Neurogene is to treat devastating neurological diseases to improve the lives of patients and families impacted by these rare diseases. Neurogene is developing novel approaches and treatments to address the limitations of conventional gene therapy in central nervous system disorders. This includes selecting a delivery approach to maximize distribution to target tissues and designing products to maximize potency and purity for an optimized efficacy and safety profile. The Company's novel and proprietary EXACT™ transgene regulation platform technology allows for the delivery of therapeutic levels while limiting transgene toxicity associated with conventional gene therapy. Neurogene has constructed a state-of-the-art gene therapy manufacturing facility in Houston, Texas. CGMP production of NGN-401 was conducted in this facility and will support pivotal clinical development activities. For more information, visit www.neurogene.com.

About NGN-401

NGN-401 is an investigational AAV9 gene therapy being developed as a one-time treatment for Rett syndrome. It is the first clinical candidate to deliver the full-length human *MECP2* gene under the control of Neurogene's EXACT™ transgene regulation technology. EXACT technology is an important advancement in gene therapy for Rett syndrome, specifically because the disorder requires a treatment

approach that enables targeted levels of *MECP2* transgene expression without causing overexpression-related toxic effects associated with conventional gene therapy.

NGN-401 was selected by the U.S. Food and Drug Administration (FDA) for its START Pilot Program and has also received Regenerative Medicine Advance Therapy (RMAT) designation, orphan drug designation, Fast Track designation and rare pediatric designation from the FDA. Neurogene was previously granted an INTERACT meeting with the FDA regarding the EXACT technology. NGN-401 also received Priority Medicines (PRIME) designation, orphan designation and advanced therapy medicinal product designation from the European Medicines Agency (EMA) and the Innovative Licensing and Application Pathway (ILAP) designation from the United Kingdom (UK) Medicines and Healthcare products Regulatory Agency (MHRA).

Cautionary Note Regarding Forward-Looking Statements

Statements in this press release are made as of the date of this press release. Neurogene does not undertake any obligation to make any updates to these statements to reflect events that occur or circumstances that arise after the date of this press release, except as may be required under applicable U.S. securities law.

Statements in this press release which are not historical in nature are intended to be, and hereby are identified as, 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 NGN-401; trial designs, clinical development plans and timing for NGN-401, including elements of the registrational clinical study trial design subject to final approval of the FDA, such as the proposed number of participants in the Embolden trial, and the timing of the conversion of the NGN-401 Phase 1/2 clinical trial to a registrational clinical trial, anticipated timing of additional updates for the Embolden registrational trial of NGN-401 for Rett syndrome; expected timing for additional interim data from the Company's NGN-401 Phase 1/2 trial for Rett Syndrome, expected future interactions with or positions of the FDA; and the time period over which existing cash resources may be sufficient to fund the Company's operations. 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," "on track," 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. Forward-looking statements are based on current beliefs and assumptions that are subject to risks, uncertainties and assumptions that are difficult to predict with regard to timing, extent, likelihood, and degree of occurrence, which could cause actual results to differ materially from anticipated results and many of which are outside of Neurogene's control. Such risks, uncertainties and assumptions include, among other things: the expected timing of additional results from the NGN-401 clinical trial; the potential for negative impacts to participants in the Phase 1/2 clinical trial of NGN-401 for the treatment of Rett syndrome; the risk that the Company may not be able to report data on the predicted timeline; risks related to the Company's ability to obtain regulatory approval for, and ultimately commercialize, its product candidates, including NGN-401; risks related to timing of initiating the Embolden trial of NGN-401 for Rett syndrome; and other risks and uncertainties identified under the heading "Risk Factors" included in

Neurogene's Quarterly Report on Form 10-Q for the quarter ended June 30, 2025, filed with the Securities and Exchange Commission ("SEC") on August 11, 2025, and other filings that the Company has made and may make with the SEC in the future. Nothing in this communication should be regarded as a representation by any person that the forward-looking statements set forth herein will be achieved or that the contemplated results of any such forward-looking statements will be achieved. Forward-looking statements in this communication speak only as of the day they are made and are qualified in their entirety by reference to the cautionary statements herein. Except as required by applicable law, Neurogene undertakes no obligation to revise or update any forward-looking statement, or to make any other forward-looking statements, whether as a result of new information, future events or otherwise.

This communication contains hyperlinks to information that is not deemed to be incorporated by reference into this communication.

- Financial Tables Follow -

Neurogene Inc.
Condensed Consolidated Balance Sheet Data
(In thousands of U.S. dollars)

	June 30, 2025	December 31, 2024
Assets		
Cash and cash equivalents	$ 58,813	$ 136,586
Short-term investments	215,706	175,819
Other current assets	4,467	3,518
Non-current assets	18,330	19,807
Total assets	$ 297,316	$ 335,730
Liabilities		
Current liabilities	15,440	15,157
Non-current liabilities	8,621	10,198
Total liabilities	24,061	25,355
Stockholders' equity	273,255	310,375
Total liabilities and stockholders' equity	$ 297,316	$ 335,730

Neurogene Inc.
Condensed Consolidated Statements of Operations
(In thousands of U.S. dollars, except share information)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2025	2024	2025	2024
Revenue under licensing agreements	—	925	—	925
Operating expenses:				
Research and development expenses	19,366	15,744	37,131	29,285
General and administrative expenses	6,715	5,315	14,869	10,553
Total operating expenses	26,081	21,059	52,000	39,838
Loss from operations	(26,081)	(20,134)	(52,000)	(38,913)
Other income, net	4,065	1,642	7,337	3,500
Net loss	$ (22,016)	$ (18,492)	$ (44,663)	$ (35,413)
Per share information:				
Net loss per share, basic and diluted	$ (1.05)	$ (1.09)	$ (2.12)	$ (2.09)
Weighted-average shares of common stock outstanding, basic and diluted	21,055,378	16,941,524	21,025,996	16,922,630

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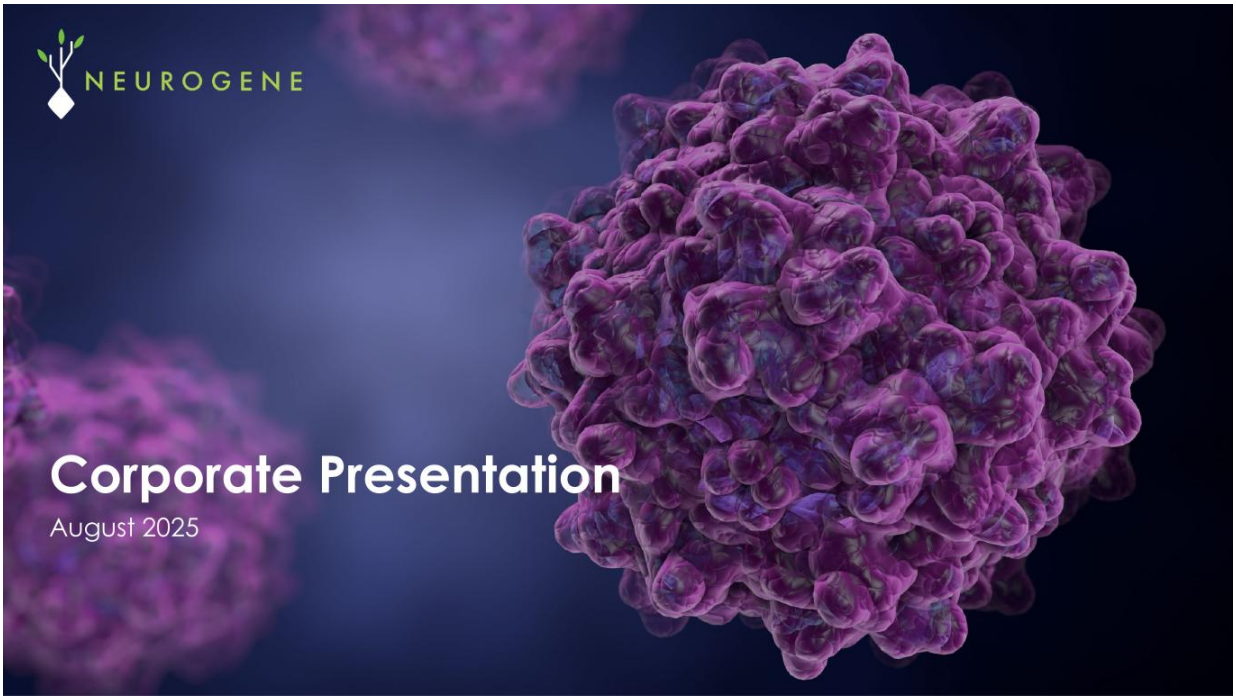

NEUROGENE
Corporate Presentation
August 2025

Disclaimer

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 elements of the registrational clinical trial study design subject to final approval of the FDA, such as the proposed number of participants in the Embolden trial, and timing and conversion of the NGN-401 Phase 1/2 clinical trial to a registrational clinical trial; enrollment and dosing in Neurogene's NGN-401 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; expected future interactions with or positions of the FDA; 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, including the time period over which existing cash resources may be sufficient to fund the Company's operations. 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: uncertainties regarding interactions with and feedback received from the FDA staff responsible for approving the design of Neurogene's registrational trial; 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 use 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 operating expenses, including its projected cash runway; and legislative, regulatory, political and economic developments and general market conditions.

The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including the risk factors included in the Company's most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q filed with the Securities and Exchange Commission, as well as risk factors associated with companies, such as Neurogene, that operate in the biopharma industry. These forward-looking statements involve a number of risks, uncertainties (some of which are beyond Neurogene's control) or other assumptions that may cause actual results or performance to be materially different from those expressed or implied by these forward-looking statements. Nothing in this communication should be regarded as a representation by any person that the forward-looking statements set forth herein will be achieved or that the contemplated results of any such forward-looking statements will be achieved. Forward-looking statements in this communication speak only as of the day they are made and are qualified in their entirety by reference to the cautionary statements herein. Except as required by applicable law, Neurogene undertakes no obligation to revise or update any forward-looking statement, or to make any other forward-looking statements, whether as a result of new information, future events or otherwise.

Industry and Market Data

Certain information contained in this Presentation relates to or is based on studies, publications, surveys and Neurogene's own internal estimates and research. In this Presentation, Neurogene relies on, and refers to, publicly available information and statistics regarding market participants in the sector in which Neurogene competes and other industry data. Any comparison of Neurogene to any other entity assumes the reliability of the information available to Neurogene. Neurogene obtained this information and statistics from third-party sources, including reports by market research firms and company filings. In addition, all of the market data included in this Presentation involve a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while Neurogene believes its internal research is reliable, such research has not been verified by any independent source and Neurogene has not independently verified the information.

Trademarks

This Presentation may contain trademarks, service marks, trade names and copyrights of other companies, which are the property of their respective owners. Solely for convenience, some of the trademarks, service marks, trade names and copyrights referred to in this Presentation may be listed without the TM, SM © or ® symbols, but Neurogene will assert, to the fullest extent under applicable law, the rights of the applicable owners, if any, to these trademarks, service marks, trade names and copyrights.

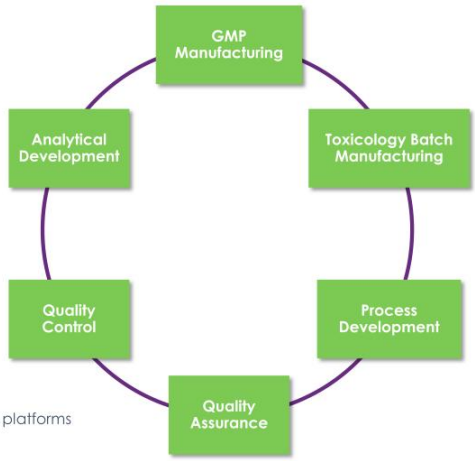
Neurogene: Developing Life-Changing Genetic Medicines For Rare Neurological Diseases

- Lead program NGN-401 for Rett syndrome demonstrated promising interim clinical data
- Registrational trial start up activities for NGN-401 underway
- Rett syndrome represents an attractive commercial opportunity with substantial unmet need
- NGN-401 uses EXACT™, a proprietary transgene regulation technology to overcome a key limitation in gene therapy
- Internal manufacturing capabilities provide strategic flexibility
- Cash runway extended to fund operations into early 2028

Neurogene Clinical Stage Pipeline

*IND = investigational new drug

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 is a Debilitating, Progressive Neurological Disorder, with No Approved Treatments Addressing Root Cause

Loss of Function Over Time

Early Onset: ~6–18 mos.	Developmental Regression: ~1–3 yrs.	"Relative Stability:" ~3–10 yrs.	Disease Progression: Adolescence to Adulthood

Cardinal Clinical Features

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

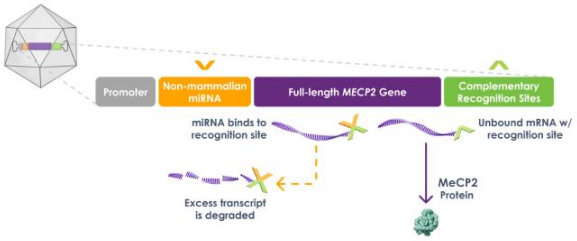
- Seizures
- Anxiety
- Scoliosis
- Muscle contractures

NEUROGENE

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

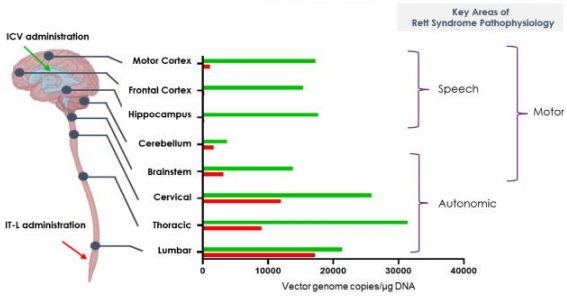
EXACT™ transgene regulation technology designed to deliver consistent and tightly controlled MeCP2 protein expression on a cell-by-cell basis.

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



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.



ICV = Intracerebroventricular

NGN-401 Embolden™ Registrational Trial

Obtained Written Agreement from FDA on Key Elements of Embolden™ Registrational Trial Design

Design	Open-label, single arm, baseline control (i.e., patient acting as own control)		
Patient Population	Females ages ≥ 3 years with Rett syndrome, consistent with our natural history study analysis that shows patients rarely learn new skills/reach developmental milestones or relearn skills once lost post-regression (~age ≥ 3)*		
Dose	1E15 vg		
Primary Endpoint	Responder-based composite endpoint at 12 months of:		
	CGI-I of ≤ 3	and	Gain of any one developmental milestone/ skill captured through video recordings

*U.S. Natural History Study of Rett Syndrome (RNHS), sponsored by NIH, Clinicaltrials.gov identifier: NCT02738281. Accessed from International Rett Syndrome Foundation (IRSF); based on analysis of >400 subjects.

FDA Accepts Conversion of Phase 1/2 to Registrational Trial

Phase 1/2 Portion

- 10 participants received NGN-401 (1E15 vg)
  - 8 females in age 4–10 cohort
  - 2 females in ages ≥ 11 cohort
- Initial clinical data reported on 4 participants Nov 2024
- Updated data expected to be reported 2H 2025

Embolden™ Registrational Clinical Trial

Open-label, baseline-controlled trial evaluating single dose of NGN-401 (1E15 vg)

Ages ≥ 3 years

N = 20*

Key Eligibility Criteria

- Females with Classic Rett syndrome in post regression stage of illness
- Clinical diagnosis and genetic confirmation of pathogenic *MECP2* mutation
- Clinical Global Impression-Severity (CGI-S) score of 4–6

Written agreement obtained on open-label arm study design;
*N=20 is proposed, subject to feedback from the FDA

Three pediatric participants previously received 3E15 vg dose in Phase 1/2 portion

28 Developmental Skills/Milestones from the Natural History Study to Be 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 ≥ 3 Years*

*U.S. Natural History Study of Rett Syndrome (RNHS), sponsored by NIH, Clinicaltrials.gov identifier: NCT02738281. Accessed from International Rett Syndrome Foundation (IRSF); based on analysis of >400 subjects.

Rett Syndrome Caregiver Research Demonstrated Clinical Meaningfulness of Developmental Milestone/Skill Acquisition

- Rett syndrome caregivers provided perspective on meaningfulness of gains of developmental milestones/skills in the core domains of Rett syndrome: fine motor, gross motor and communication
- All skills queried, across all categories, were considered meaningful by majority of respondents
- Caregivers indicated that Rett syndrome burden is immense, with 24-hour care needed to support their daughter's needs
- Skill gains or symptom improvement would provide respite not just to the patients, but to their caregiver(s), siblings, and extended family
- Any skill gain or symptom improvement that would provide some level of independence/reduce dependence for their daughter would be highly meaningful

Quantitative research conducted in November and December 2024 with 30 Rett syndrome caregivers to daughters aged 3-22 years old; follow-up qualitative research conducted in December 2024 and January 2025 with 27 Rett syndrome caregivers (sub-set of quantitative respondents) to daughters aged 3-22 years old

Feedback on Meaningfulness of Developmental Milestones/Skills Showed Real-Life Examples of Potential Impact

Caregiver Feedback

Fine Motor Gains:

- Increase communication abilities
- Provide level of independence in eating
- Social improvements/ participating in mealtimes

> I have to feed her every spoonful, every bite that she eats. But if we could scatter some food in front of her and she could feed herself, that would be a huge help. It is probably one of the bigger things for her to do to be independent.

Gross Motor Gains:

- Foster greater physical autonomy
- Reduce caregiver physical strain
- Enhance safety by lowering fall risks
- Enhance feeding safety by holding body upright
- Provide dignity and independence

> Even a small improvement would definitely be meaningful because even if she could stand with support or bear her own weight, even for 30 seconds or less, that would allow us to be able to pivot her into her wheelchair versus having to lift her.

Communication Gains:

- Decrease suffering if daughter could indicate injuries/pain
- Better ensure daughter's needs and wants are appropriately met without guessing
- Eliminate safety concerns around interactions with others/strangers

> You immediately go to the usual, 'Is your tummy hurting? Is this? Is that?' …It's hard to tell if she's just uncomfortable or something is happening to her…The frustration on her part is, as you can imagine, it's just trying to tell someone and nobody's understanding what she is trying to tell.

NEUROGENE

Quantitative research conducted in November and December 2024 with 30 Rett syndrome caregivers to daughters aged 3-22 years old; follow-up qualitative research conducted in December 2024 and January 2025 with 27 Rett syndrome caregivers (sub-set of quantitative respondents) to daughters aged 3-22 years old

Phase 1/2 Data Support Registrational Trial Design

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**

1E15 vg NGN-401 dose believed to be **generally well-tolerated**

- No evidence of HLH

As of data cut-off date of 17 October 2024
HLH monitoring and treatment protocol added to Phase 1/2 protocol in January 2025
HLH = Hemophagocytic lymphohistiocytosis

Baseline Characteristics of Dosed Participants Range from Moderate to Severe Disease

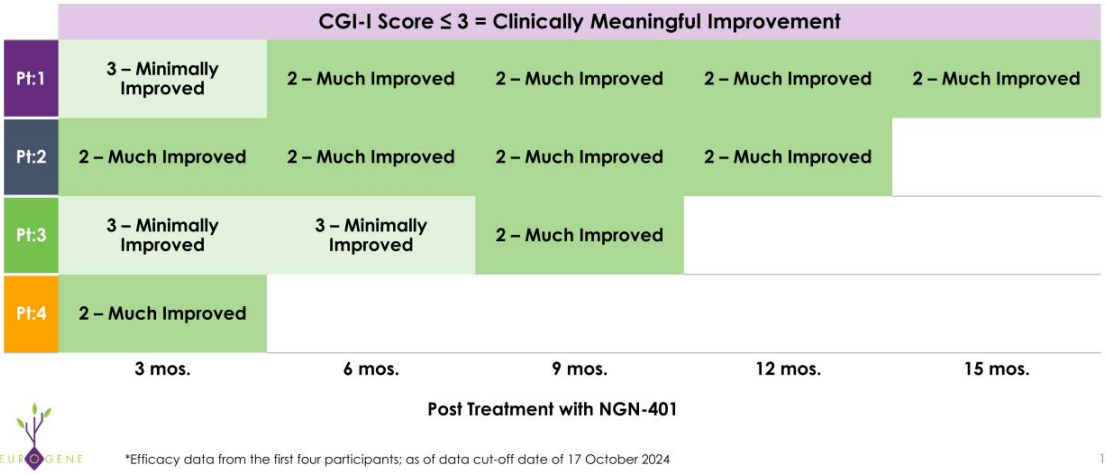
	1E15 vg				
	Participant 1 (Pt:1)	Participant 2 (Pt:2)	Participant 3 (Pt:3)	Participant 4 (Pt:4)	Participant 5 (Pt:5)
Age at Dosing in Years	7	4	6	7	6
***MECP2* Mutation Severity**	Mild	Severe	Severe	Severe	Severe
Baseline Disease Severity as Indicated by CGI-S Score	4 (moderately ill)	5 (markedly ill)	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

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

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

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



*Efficacy data from the first four participants; as of data cut-off date of 17 October 2024

Improvements in Clinician and Caregiver Assessments with Aggregate 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

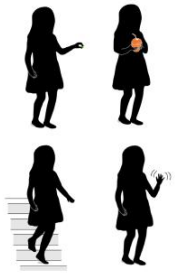
NEUROGENE

Efficacy data from the first four participants; 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

	Select Pt:1 Developmental Skills Post-NGN-401	Months Post-NGN-401				
		3	6	9	12	15
Raking, no ability to hold objects — Fine Motor	Uses a pincer grasp		✓	✓	✓	✓
	Holds bottle or cup unpropped		✓	✓	✓	✓
	Uses spoon/fork to self-feed					✓
	Transfers objects between hands					✓
Walking, ataxic gait, no ability to climb stairs — Gross Motor	Heel-to-toe walking			✓	✓	✓
	Climbs up stairs without help		✓	✓	✓	✓
	Climbs down stairs without help				✓	✓
Severe impairment, unable to follow commands — Communication	Follows a command without gesture		✓	✓	✓	✓
	Waves hello*				✓	✓
	Taps for wants				✓	✓



Post Treatment with NGN-401

*Skill learned is "Wave hello;" however, RNHS tracked "Waves Bye Bye"
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:2 Multi-Domain Improvements from Severe Impairments at Baseline Deepened Over Time, and Not Expected Based on Rett Syndrome Natural History

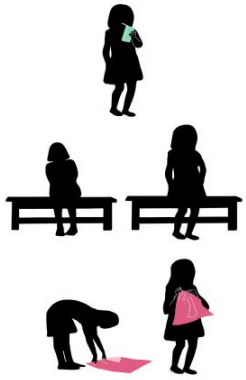
Baseline: 4 Yrs Old

Severe impairment, unable to use hands

Impaired, ataxic, help to stand

Severe impairment, unable to follow commands, non-verbal

	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	✓	✓	✓	✓



Post Treatment with NGN-401

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

Severe Dysphagia

Baseline: 6 Yrs Old

Raking grasp

Cannot sit, stand or walk

	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	✓	✓	✓

Post Treatment with NGN-401

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

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

Post Treatment with NGN-401

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

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

Pt:1 and Pt:2	Pt:1, Pt:2 and Pt:4	Pt:3
Had **sleep** deficits at Baseline, and experienced improvements in sleep parameters, as measured by a wearable device • LD:1 sleep efficiency increased from 83% to 90% at 6 months • LD:2 sleep efficiency increased from 90% to >95% at 6 months, considered ideal	Had **constipation** at Baseline, and experienced improvements over time as measured by the caregiver-reported modified Bristol Stool Form Scale	Had **dysphagia**, or difficulty swallowing, at Baseline, requiring a pureed diet and had to be spoon-fed by caregiver due to aspiration; at 9 months after dosing, she gained the ability to swallow liquids from a cup and chew and swallow food items

*Efficacy data from the first four participants; as of data cut-off date of 17 October 2024
Detailed data provided in Appendix

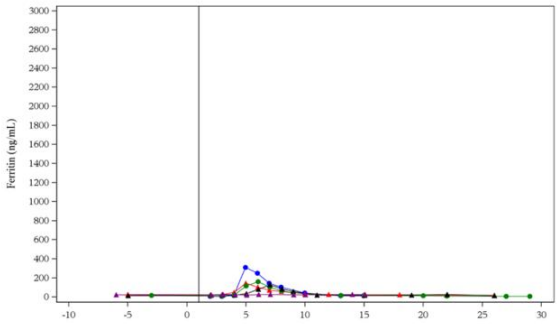
Phase 1/2 Trial

- In 2025, dosed 3 participants in the 4–10 years cohort **and 2 participants** in the ≥ 11 years cohort
  - No evidence of HLH
- HLH risk mitigation included in Phase 1/2 and registrational trial design
  - Dose level **at/above** 1E14 vg/kg not allowed
  - In the first week post dosing: employ daily **monitoring of HLH, focused on** "the three Fs" – ferritin, fever, and falling blood counts (cytopenia)
  - Exclude subjects with any illness within 30 days of dosing and COVID within 6 weeks of screening
  - Prior to dosing, require sites to have anakinra available and encourage availability of a local HLH expert
  - Included HLH treatment algorithm: 1st line – high-dose corticosteroids, 2nd line – anakinra

No Evidence of HLH/Hyperinflammatory Syndrome at the 1E15 vg Dose Level

- 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 clinical symptoms of HLH/ hyperinflammatory syndrome have been observed

Ferritin Levels of Most Recently Dosed Participants – 1E15vg



Galletta et al. publication reported case of HLH following high-dose systemic AAV treatment (1.1E14 vg/kg); the patient presented with the "three Fs" - fever, falling blood counts (cytopenia) and ferritin of 2,959 ng/ml 36 hours post-dose. The patient was treated with high-dose steroids and recovered[1].

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

Key Anticipated Milestone Events

Key Upcoming Anticipated Milestones and Pipeline Developments

Rett Syndrome (NGN-401)

- ✓ Provide regulatory update in 1H:25 regarding registrational trial
- ✓ Initiate registrational trial activities
- ○ Announce additional Phase 1/2 clinical data in 2H:25

CLN5 Batten Disease (NGN-101)

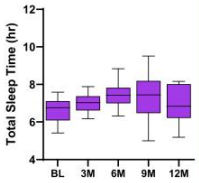
- ○ Evaluate opportunities for the program

Cash Runway Expected to Fund Operations Into Early 2028

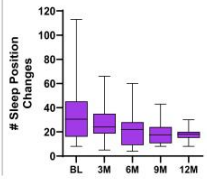
Appendix

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

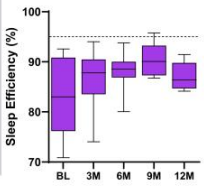
Improvements in All Sleep Parameters, as Assessed by Wearable Device



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



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



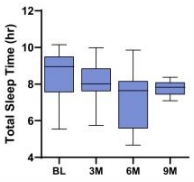
Sleep efficiency* **increased from 83% to ~90%** (95% is ideal)

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

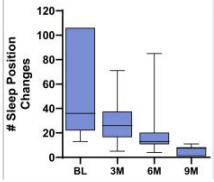
*Sleep efficiency defined as time spent asleep vs. total time spent in bed
**As measured by Caregiver on modified Bristol Stool Form Scale
As of data cut-off date of 17 October 2024

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

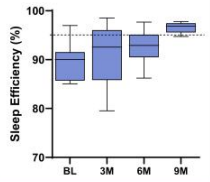
Transition to More Restful Sleep, as Assessed by Wearable Device



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

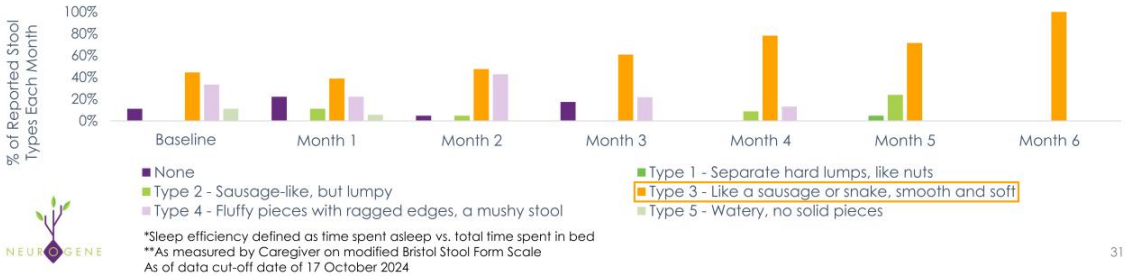


Number of position changes **decreased from 37 to 8** per night



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

Pt:4 Autonomic Function: Objective Improvement Observed in Constipation

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

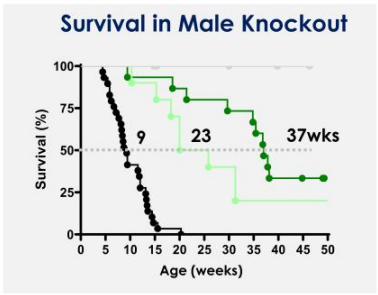
- None
- Type 1 - Separate hard lumps, like nuts
- Type 2 - Sausage-like, but lumpy
- Type 3 - Like a sausage or snake, smooth and soft
- Type 4 - Fluffy pieces with ragged edges, a mushy stool
- Type 5 - Watery, no solid pieces

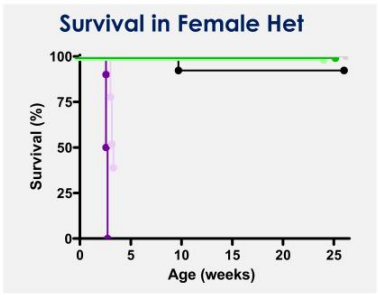
Pt:4 did not have Baseline deficits in autonomic category of sleep

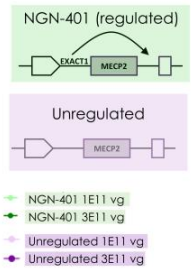
Sleep quality maintained post-treatment

*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





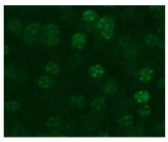


WT + Vehicle
Male or female + Vehicle

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