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): January 5, 2024

NEUROGENE INC.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-36327**	**98-0542593**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

535 W 24th Street, 5th Floor **New York, NY**	**10011**
(Address of Principal Executive Offices)	**(Zip Code)**

(877) 237-5020
(Registrant's Telephone Number, Including Area Code)

Not Applicable
(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:

☐ 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, par value $0.000001 per share	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 7.01. Regulation FD Disclosure.

On January 5, 2024, Neurogene Inc. (the "Company") issued a press release announcing business updates and its outlook for 2024. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K. Also on January 5, 2024, 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 Item 7.01 of this Current Report on Form 8-K, including the information in the press release attached as Exhibit 99.1 and the presentation attached as Exhibit 99.2, is furnished pursuant to Item 7.01 of Form 8-K and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section. Furthermore, the information in Item 7.01 of this Current Report on Form 8-K, including the information in the press release attached as Exhibit 99.1 and the presentation attached as Exhibit 99.2, shall not be deemed to be incorporated by reference in the filings of the Company under the Securities Act of 1933, as amended.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Press Release, dated January 5, 2024.
99.2	Corporate Presentation (January 2024).
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

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

NEUROGENE INC.

Date: January 5, 2024

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

Neurogene Announces Business Update and 2024 Outlook

DSMB clears third pediatric patient for dosing in ongoing NGN-401 Phase 1/2 clinical trial for Rett syndrome; On track to dose third pediatric patient in early 1Q:24

CTA clearance obtained from UK MHRA for NGN-401

Ended 2023 in a strong financial position with approximately $200 million in cash and runway into 2H:26

NEW YORK — (BUSINESS WIRE) — January 5, 2024— Neurogene Inc. (NASDAQ: NGNE) ("Neurogene" or "the Company"), a clinical-stage company founded to bring life-changing genetic medicines to patients and families affected by rare neurological diseases, announced today a business update and provided its outlook for 2024. Key milestones for the Company's clinical-stage gene therapy product candidates remain on track for 2024, while the Company continues to advance its discovery-stage transgene regulation portfolio.

Anticipated 2024 Key Milestones

- Rett Syndrome – NGN-401
  - Expand ongoing Phase 1/2 clinical trial for NGN-401 for Rett syndrome in 1H:24 to enroll a larger cohort of patients
  - Report interim Phase 1/2 clinical data for NGN-401 for Rett syndrome in 4Q:24
- CLN5 Batten Disease – NGN-101
  - Report interim Phase 1/2 clinical data for NGN-101 in 2H:24
  - Engage in discussions with U.S. Food and Drug Administration (FDA) regarding a streamlined registrational pathway for NGN-101 in 2H:24

"2023 was a transformational year for Neurogene, with the clearance by the FDA of our Investigational New Drug application for NGN-401 in female pediatric patients with Rett syndrome, completing the manufacturing of clinical-grade NGN-401 in-house at our GMP viral vector manufacturing facility, dosing the first two patients in our Phase 1/2 clinical trial for Rett syndrome with no treatment-emergent or procedure-related serious adverse events, or signs of overexpression-related toxicity, and completing a reverse merger and private financing to capitalize Neurogene into the second half of 2026," said Founder and Chief Executive Officer, Rachel McMinn, Ph.D. "We remain on track to deliver interim results for our potentially best-in-class Rett syndrome gene therapy program in the fourth quarter of 2024."

Rett Syndrome Program Update

Neurogene announced that the Data Safety Monitoring Board ("DSMB") for the ongoing Phase 1/2 clinical trial of NGN-401 in female pediatric patients with Rett syndrome has recommended that the trial continue, which enables dosing of the third patient. This recommendation was based on safety data collected to date, following dosing of the first patient in the third quarter of 2023 and the second patient in the fourth quarter of 2023.

Neurogene also announced that the United Kingdom (UK) Medicines and Healthcare products Regulatory Agency (MHRA) has approved the Company's clinical trial application (CTA) for NGN-401, marking the second regulatory clearance for NGN-401 in pediatric patients with Rett syndrome. This clearance enables Neurogene to expand enrollment in the Phase 1/2 trial beyond the United States to include patients with Rett syndrome in the UK, and is part of Neurogene's global development and trial expansion strategy.

The ongoing NGN-401 Phase 1/2 clinical trial specifies a cohort of five patients, each receiving a total dose of 1×10^{15} total vector genomes delivered via intracerebral ventricular administration, which Neurogene believes may show promising efficacy results based on the nonclinical data package generated for NGN-401. In the first half of 2024, Neurogene plans to expand the trial to include (1) more patients in Cohort 1 of the trial for the low dose, and (2) a higher dose cohort to maximize the efficacy potential while still maintaining a favorable safety profile, pending regulatory clearances. Importantly, based on a comprehensive nonclinical dataset, the EXACT transgene regulation technology embedded in NGN-401 mechanistically constrains *MECP2* transgene expression levels, allowing for the potential to dose escalate and enhance biodistribution to the brain, without the commensurate increase in *MECP2* transgene expression observed with conventional gene therapy.

Neurogene expects to report interim clinical data from Cohort 1 in the fourth quarter of 2024, which is expected to include extensive follow up data on the first number of patients dosed.

CLN5 Program Update

Neurogene has completed enrollment of Cohorts 1 and 2 in the ongoing Phase 1/2 clinical trial for CLN5 Batten disease, and interim clinical data are expected in the second half of 2024. Neurogene is currently enrolling a final higher dose cohort. In the fourth quarter of 2023, Neurogene completed a positive meeting with the FDA regarding the future potency assay. The FDA accepted Neurogene's proposed potency assay strategy and provided alignment with the testing approach, which will allow release of all future NGN-101 batches.

To enable a go/no-go decision to advance the program into a registration study, Neurogene is collecting and analyzing natural history data for CLN5 Batten disease and planning to request a clinical/regulatory strategy meeting with the FDA in the second half of 2024. The focus of this meeting will be to align with the FDA on the expected clinical requirements to support a streamlined registration pathway, which will be necessary to move this program forward into a pivotal clinical trial.

Discovery Portfolio Update

Neurogene announced that it has extended its research collaboration with the University of Edinburgh by an additional three years. This extension allows Neurogene to continue advancing multiple products for commercially attractive indications in its discovery-stage, transgene regulation gene therapy portfolio.

Neurogene plans to advance one product from its discovery-stage pipeline into the clinic in 2025.

About EXACT

Neurogene's novel and proprietary EXACT gene regulation platform technology is a self-contained transgene regulation platform that can be tuned to deliver a desired level of transgene expression within a narrow and therapeutically relevant range, with the goal of avoiding transgene-related toxicities associated with conventional gene therapy. EXACT is compatible with viral and non-viral delivery platforms.

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 technology. The EXACT technology utilized in NGN-401 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. The robust nonclinical data package for NGN-401 provides evidence of a potentially compelling efficacy and safety profile in Rett syndrome.

About NGN-101

NGN-101 is being developed as a one-time treatment for both ocular and neurological manifestations of CLN5 Batten disease using AAV9 to deliver the gene encoding CLN5, which is deficient in children with the disease.

About Neurogene

Neurogene's mission 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 by 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. GMP production of NGN-401 was conducted in this facility and will support pivotal clinical development activities. For more information, visit www.neurogene.com.

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Cautionary Note Regarding Forward-Looking Statements

This communication contains forward-looking statements (including within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended). 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. 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. Statements that are not

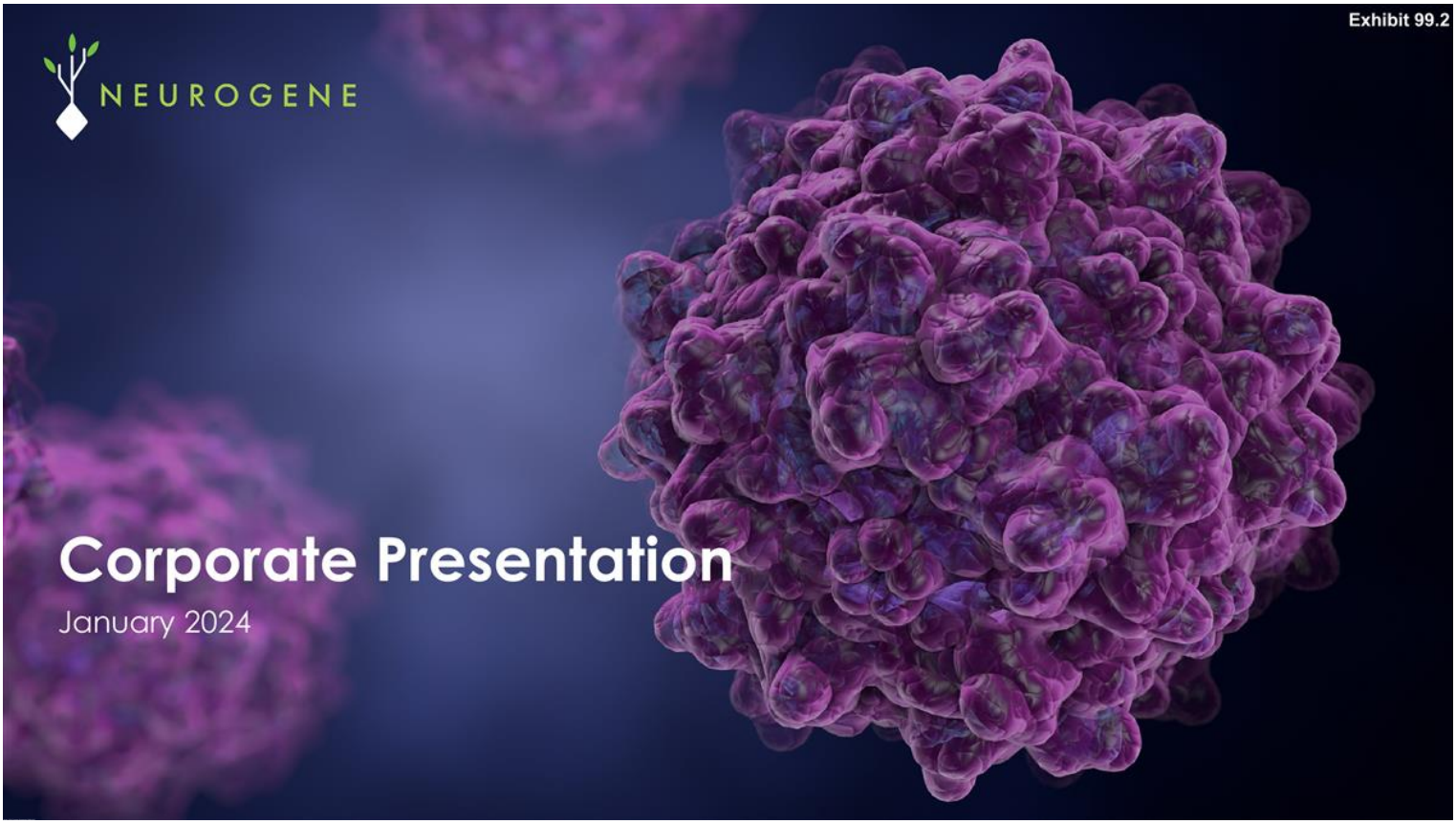
historical facts are forward-looking statements. Forward-looking statements in this communication include, but are not limited to, statements regarding the expected enrollment of and timing of data from Neurogene's Phase 1/2 clinical trials; statements regarding the potential of, and expectations regarding, Neurogene's programs, including NGN-101, NGN-401 and its research stage opportunities; the expected dosing of additional patients in Neurogene's Phase 1/2 clinical trials; statements regarding the potential expansion of Neurogene's Phase 1/2 clinical trial in Rett syndrome into the United Kingdom and/or the expansion of Cohort 1 to include additional patients; the timing of any regulatory interactions regarding Neurogene's programs, including NGN-101 and NGN-401; statements regarding Neurogene's projected cash runway; and statements by Neurogene's Founder and Chief Executive Officer. 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 to advance product candidates through non-clinical and clinical development; the ability to obtain regulatory approval for, and ultimately commercialize, Neurogene's product candidates; the outcome of non-clinical testing and early clinical trials for Neurogene's product candidates, including the ability of those trials to satisfy relevant governmental or regulatory requirements; Neurogene's limited experience in designing clinical trials and lack of experience in 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; the substantial competition Neurogene faces in discovering, developing, or commercializing products; 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; the ability of Neurogene to protect its intellectual property and proprietary technologies; reliance on third parties, contract manufacturers, and contract research organizations; risks related to Neurogene's ability to correctly estimate its respective operating expenses, including its projected cash runway, and any unexpected costs, charges or expenses resulting from the merger with Neoleukin Therapeutics, Inc. ("Neoleukin"); the outcome of any legal proceedings that may be instituted against Neoleukin, Neurogene or any of their respective directors or officers related to the merger; and legislative, regulatory, political and economic developments and general market conditions. These and other risks and uncertainties are identified under the heading "Risk Factors" included in Exhibit 99.1 to the Company's Current Report on Form 8-K filed with the SEC on December 19, 2023, 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.

Exhibit 99.2

NEUROGENE



Corporate Presentation

January 2024

Disclaimer

Forward Looking Statements

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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. 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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 to advance product candidates through non-clinical and clinical development; the ability to obtain regulatory approval for, and ultimately commercialize, Neurogene's product candidates; the outcome of non-clinical testing and early clinical trials for Neurogene's product candidates, including the ability of those trials to satisfy relevant governmental or regulatory requirements; Neurogene's limited experience in designing clinical trials and lack of experience in 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; the substantial competition Neurogene faces in discovering, developing, or commercializing products; 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; the ability of Neurogene to protect its intellectual property and proprietary technologies; reliance on third parties, contract manufacturers, and contract research organizations; the ability to attract, hire, and retain skilled executive officers and employees; 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 any unexpected costs, charges or expenses resulting from the merger with Neoleukin Therapeutics, Inc. ("Neoleukin"); 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, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K filed with the Securities and Exchange Commission (SEC), the registration statement on Form S-4 filed with the SEC, 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 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:26 cash runway enables operations beyond clinical inflection points

NEUROGENE

Funding for Key Near Term Milestones Obtained in Reverse Merger and Concurrent Private Financing Completed in 2023

Merger and concurrent financing secures funding to position Neurogene to deliver on anticipated near term milestones:

Rett syndrome (NGN-401)

- Expand ongoing Phase 1/2 clinical trial in 1H:24 to enroll a larger cohort of patients
- Interim Phase 1/2 clinical data 4Q:24
- Additional Phase 1/2 clinical data from expansion and higher dose cohorts in 2H:25

CLN5 Batten disease (NGN-101)

- Interim Phase 1/2 clinical data in 2H:24
- Engage in FDA discussions regarding a streamlined registrational pathway in 2H:24

Early-stage discovery

- Advance one early-stage program into the clinic (2025)

Transaction Highlights

- **Merger closed on December 18, 2023**
- Post-merger company trades on Nasdaq as Neurogene Inc. with ticker **"NGNE"**
- Simultaneously closed on **~$95M concurrent private placement**
- 16,887,060 shares of common stock outstanding at closing*
- Cash balance of approximately **$200M at closing**
- Expected cash runway to fund operations into 2H:26

*After the closing of merger, private placement, and 1-for-4 reverse stock split. This number includes 4,063,364 Neurogene Pre-Funded Warrants.

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				Interim Data 4Q:24, Additional Data 2H:25
NGN-101	CLN5 Batten Disease				Interim Data 2H:24

*IND = investigational new drug.

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

NEUROGENE

EXACT Developed to Solve the Limitations of Conventional Gene Therapy in Complex Neurological Disorders

Today's Gene Therapy is Limited By:	Neurogene's Solutions:
Variable Gene Expression	**Novel, modular EXACT gene regulation technology and other regulatory elements** designed to optimize transgene expression to maximize the therapeutic window
Safety Limitations	**Novel and proprietary EXACT gene regulation technology** designed to avoid transgene related toxicity associated with conventional gene therapy
Inefficient Gene Delivery	Select **ICV delivery approach** to maximize **AAV9** distribution to target CNS tissues Design products to **maximize potency and purity** for potentially optimized efficacy/safety profile

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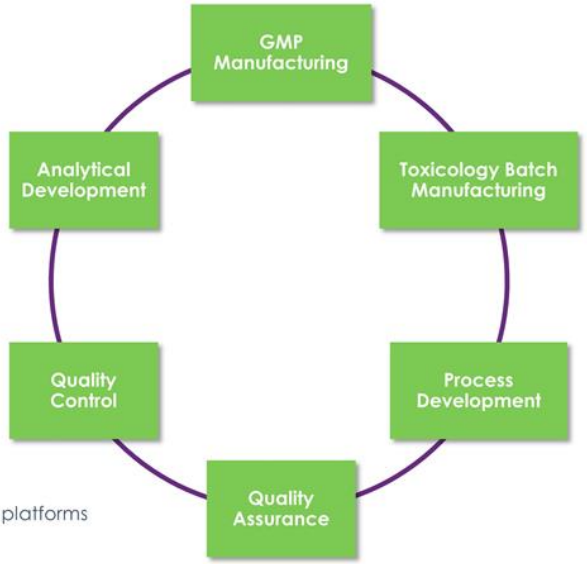
ICV = intracerebroventricular
AAV = Adeno-associated virus
CNS = central nervous system

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

NEUROGENE

Experienced Leadership Team Backed by Top Tier Investors

Leadership and Senior Management Team

Rachel McMinn, Ph.D.
Founder and CEO

Christine Mikail, J.D.
President and CFO

Stuart Cobb, Ph.D.
CSO

Ricardo Jimenez
SVP, Technical Operations

Albena Patroneva, M.D.
SVP, Clinical Development

Effie Albanis, M.D.
SVP, Early Clinical and Translationall Research

Andrew Mulberg, M.D.
SVP, Regulatory Affairs

Arvind Sreedharan
SVP, Business Operations

Backed by a Syndicate of Thought-Leading Investors

Healthcare Investment Fund

NEUROGENE

NGN-401 for Rett Syndrome

Leveraging EXACT gene 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)
- One of the most common genetic causes of developmental and intellectual impairment in females
- 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 - 1:10,000-1:15,000 live female births

High Unmet Need

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

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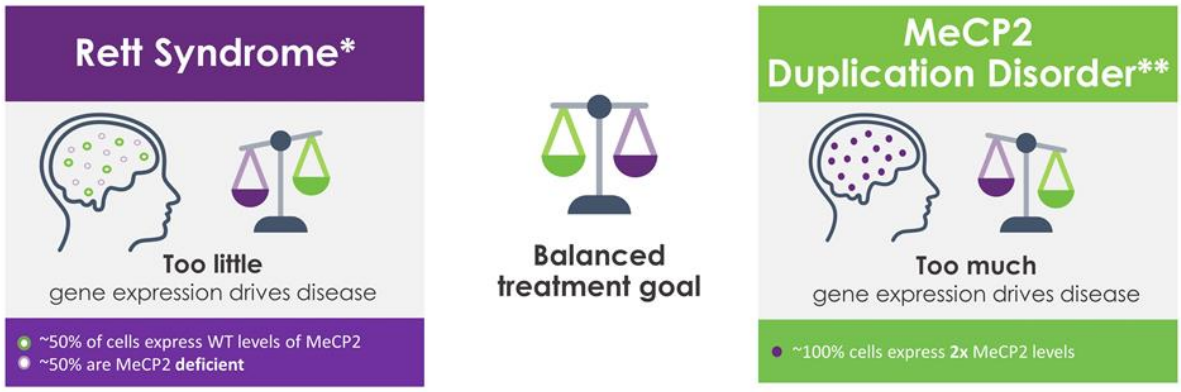
U.S. prevalence estimate based on published incidence rates: Laurvick CL, et al. J Pediatr 2006;148(3):347–35.
WW incidence estimate based on published incidence rates: Pini G, et al. Orphanet Journal of Rare Diseases (2016) 11:132.

Rett Syndrome Treatment Requires Tight Gene Regulation



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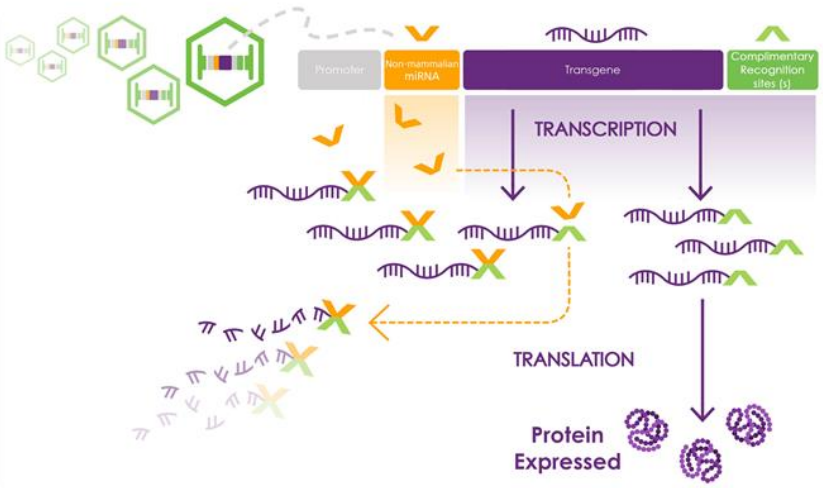
*Represents female Rett syndrome; **Represents male duplication disorder; WT = wildtype
Pini G, et al. Orphanet Journal of Rare Diseases (2016) 11:132.

EXACT Acts As a Genetic Thermostat, Limiting Transgene Expression

EXACT miRNA controls transgene levels to targeted range

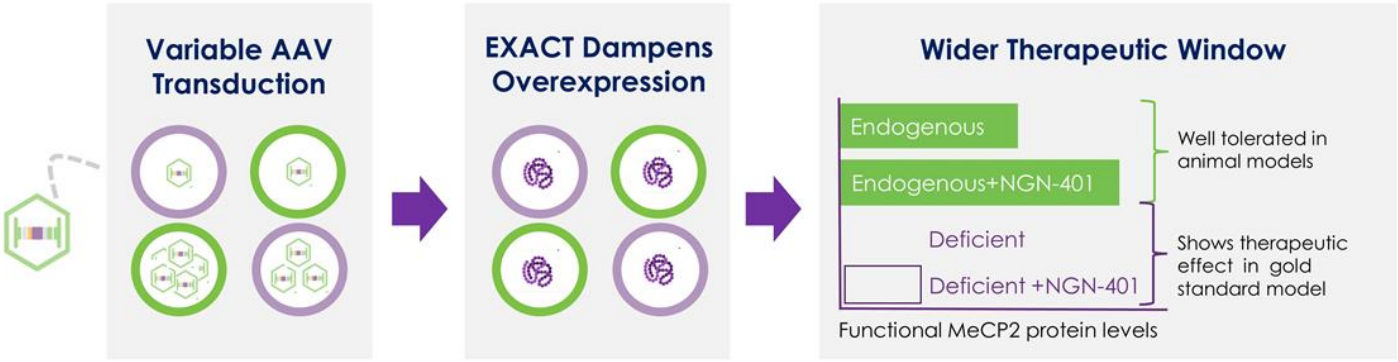
Regulatory elements designed to avoid off-target effects

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



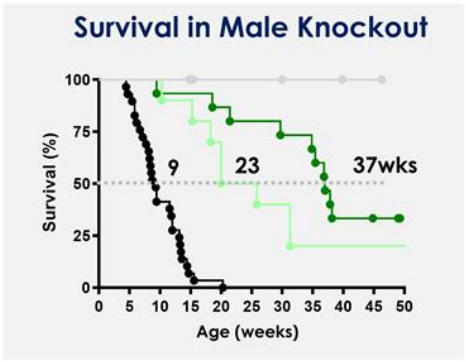
NEUROGENE

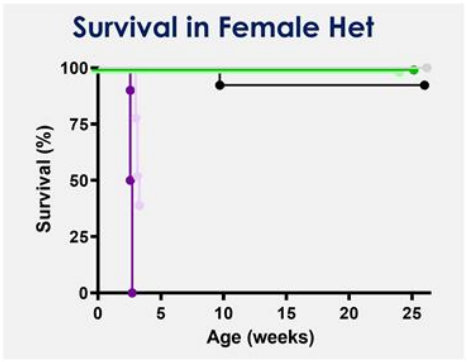
EXACT Designed to Widen Therapeutic Window and Enable Gene Therapy for Rett Syndrome

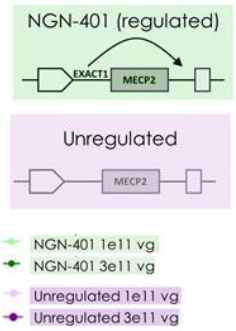


- ~50% of cells express WT levels of MeCP2
- ~50% are MeCP2 **deficient**

NGN-401 Demonstrates Efficacy and Safety in Mecp2 Mouse Models







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

NGN-401 Preclinical Data Enabled Pediatric Clinical Approach

Promising efficacy, favorable safety profile

DEMONSTRATED CONTROLLED MeCP2 LEVELS

Delivery of full-length MeCP2

MAXIMIZES THERAPEUTIC POTENTIAL

Robust MeCP2 levels to key brain areas

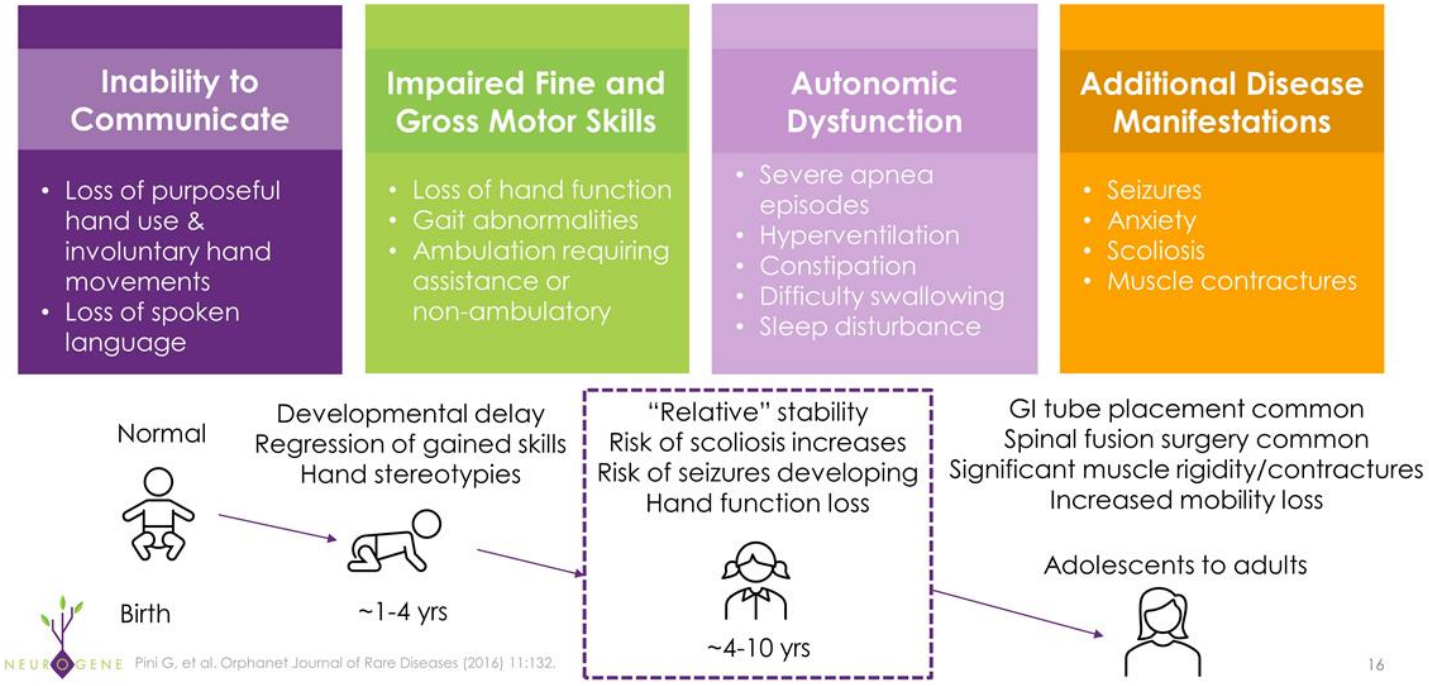
PROVIDES TRANSLATIONAL FOUNDATION FOR HUMANS

No evidence of off-target or MeCP2 tox

GENERATED COMPREHENSIVE SAFETY PACKAGE

U.S. FDA and UK MHRA cleared dosing directly into pediatric patients

Cardinal Clinical Features of Rett Syndrome



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

Clinical Study For NGN-401 Designed to Evaluate Pediatric Population

- **Starting dose of 1E15 vg (total) bracketed by two efficacious mouse doses, with > 4x safety margin from GLP tox study**
- **Preparing for dose escalation and cohort expansion to generate additional clinical data**
- **Key assessments at 3, 6, and 12 months, which include caregiver and clinician assessments – RSBQ, CGI-I and CGI-S**

Key Eligibility Criteria

- Female, age ≥4 to ≤10 years with Classic Rett syndrome
- Clinical diagnosis & genetic confirmation of pathogenic MeCP2 mutation
- Clinical Global Impression-Severity (CGI-S) score of 4-6

Efficacy Assessments of Interest

Autonomic Function	Objective device to monitor breathing
Hand Function	Physician assessment of improvement
Communication	Physician assessment of improvement
Gross Motor Function	Physician assessment of improvement

NEUROGENE GLP = Good Laboratory Practice

NGN-401 Study Inclusion Criteria is Driven by Severity of Rett Syndrome Domains Under CGI-S

Limited impairment | **Modest impairment** | **Eligible for Phase 1/2 clinical trial**

Clinical domains	CGI-S=1	CGI-S=2	CGI-S=3	CGI-S=4	CGI-S=5	CGI-S=6	CGI-S=7
Language/ Communication	Normal	May have unusual features (eg echolalia, reading disability)	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	No words No vocalizations Screams No choices
Ambulation	No impairment	Normal, may have slight evidence of dystonia/ ataxia/ dyspraxia	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	Cannot sit Doesn't stand or walk
Hand use	Normal, no impairment	Normal, may have slight fine motor issue	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	None
Social (eye contact)	Normal	Occasional eye gaze avoidance	Appropriate eye contact, >30s	Eye contact <20s	Eye contact <10s	Eye contact, inconsistent 5s	None
Autonomic	None	Minimal	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	Breathing dysrhythmia constantly with cynanosis Cold UE and LE, Mottled/blue
Seizures	None	None or controlled	None, with or without meds	Monthly-weekly	Weekly	Weekly-daily	Daily
Attentiveness	Normal	Occasional inattention	Attentive to conversation, follows commands	50-100%	50%	<50%	0%

NGN-401 Phase 1/2 Clinical Trial Status Update and Anticipated Near Term Milestones

Phase 1/2 Clinical Trial Status

- First patient dosed 3Q:23, second patient dosed 4Q:23
- DSMB meeting completed in January 2024 to enable third patient dosing in early 1Q:24
- No treatment-emergent, procedure-related or overexpression toxicity observed to date

2024 Anticipated Key Milestones

- Expand ongoing Phase 1/2 clinical trial in 1H:24 to enroll a larger cohort of patients
- Interim Phase 1/2 clinical data 4Q:24
- Additional Phase 1/2 clinical data from expansion and higher dose cohorts in 2H:25

NEUROGENE DSMB = Data safety monitoring board

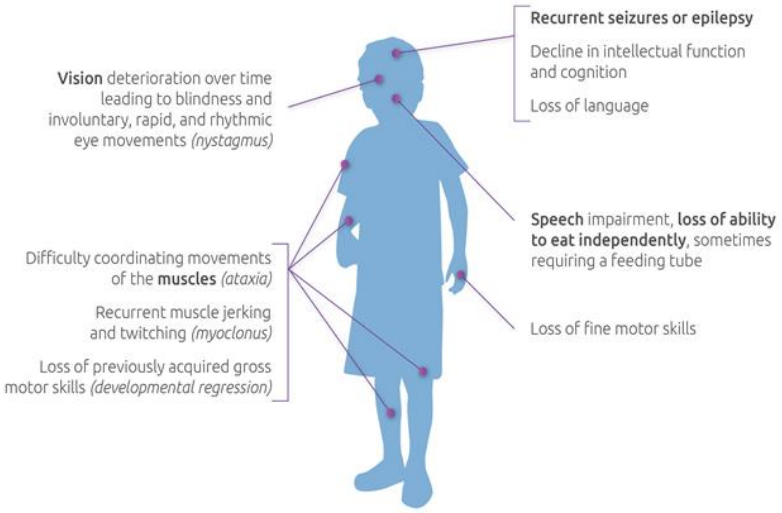
NGN-101 for CLN5 Batten Disease

Treating both CNS and vision through dual route of administration

CLN5 Batten Disease - Fatal, Neurodegenerative Disease With No Disease-Specific Treatment Options

CLN5 Batten disease has no available treatment options

Brineura, approved globally for a similar indication, CLN2, has transformed clinical outcomes in Batten disease

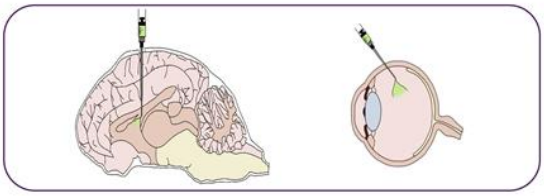


NEUROGENE Simonati A et al. Phenotype and natural history of variant late infantile ceroid-lipofuscinosis 5. Dev Med Child Neurol. 2017 Aug;59(8):815-821.

NGN-101 Dual Delivery Supported by Compelling Preclinical Data

Dual route of administration

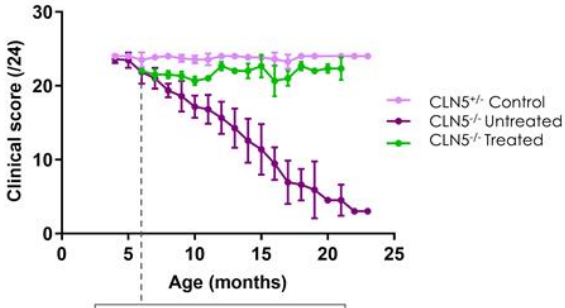
First clinical gene therapy study targeting both neurodegeneration and vision loss



NGN-101 product design

NGN-101 dosing (ICV+IVT) in CLN5 knockout sheep

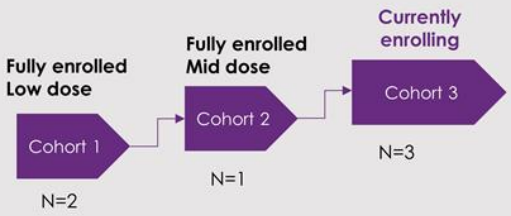
Combination dosing leads to halting of disease progression



NGN-101 dosing

NEUROGENE IVT = Intravitreal

Clinical Study Design For NGN-101 Addresses Vision and CNS



- **Dose selection based on sheep studies showing significant treatment effects**
- **Key assessments every 6 and 12 months**

Key Eligibility Criteria

- Age ≥3 to ≤9 years
- Genetic diagnosis of CLN5
- Onset of disease ≤5 years of age
- Score of ≥1 on the Hamburg motor domain at minimum, the equivalent of 20/200 visual acuity or better at the time of screening

Efficacy Endpoints/Markers of Interest

Optical Coherence Tomography (OCT)	Preservation of key retinal layers is a leading indicator of vision stability
Visual Acuity	Stability in treated eye vs. worsening in untreated eye could provide evidence of clinical benefit
Hamburg Motor Scale	Scale has been used previously to support BMRN's ERT Brineura® for CLN2 disease

NEUROGENE ERT = Enzyme replacement therapy

NGN-101 — Defining a Registration Path

FDA meeting focused on finalizing CMC plans completed 4Q:23

Potency Assay

FDA accepted proposed potency assay strategy, a first milestone in determining continuation of the program

Improved Manufacturing Process

FDA alignment on proposed comparability strategy for using Neurogene-made material with substantially improved profile to Phase 1/2 drug product

Plan to request FDA meeting in 2H:24 to align on clinical requirements for streamlined registration

- **Complete enrollment of high dose cohort in 2024**
- **Continue collection of clinical trial data on vision and motor for analysis**
- **Ongoing natural history data collection and analysis**

Alignment with FDA on Streamlined Registration Pathway Required to Move Program Forward

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Key Milestone Events

Key Upcoming Anticipated Milestones and Pipeline Developments

Rett syndrome (NGN-401)

- Expand ongoing Phase 1/2 clinical trial in 1H:24 to enroll a larger cohort of patients
- Interim Phase 1/2 clinical data 4Q:24
- Additional Phase 1/2 clinical data from expansion and higher dose cohorts in 2H:25

CLN5 Batten disease (NGN-101)

- Interim Phase 1/2 clinical data in 2H:24
- Engage in FDA discussions regarding a streamlined registrational pathway in 2H:24

Early-stage discovery

- Advance one program into the clinic (2025)

Approximately $200 million cash on hand as of Dec 2023 expected to fund operations into 2H:26

Why Neurogene?

- **Unlocking multi-billion dollar neurological disease markets**
- **Proprietary capabilities and technology enable addressing complex diseases**
- **Strategy focused on efficiency and maximizing probability of success**
- **Leadership team with deep operational, technological and clinical experience**
- **Leading life sciences investor syndicate**
- **Strong balance sheet and fiscally disciplined approach**

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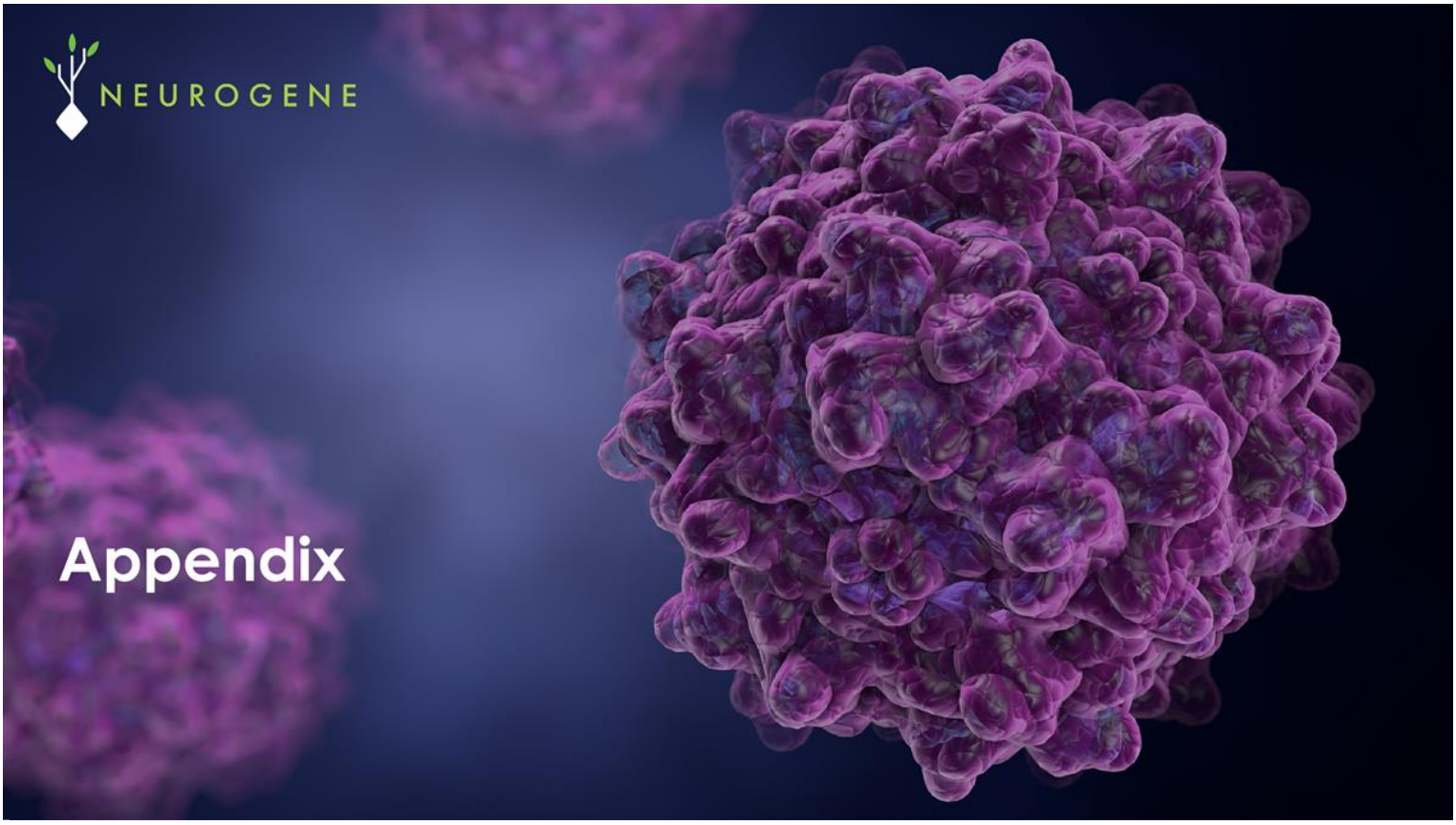
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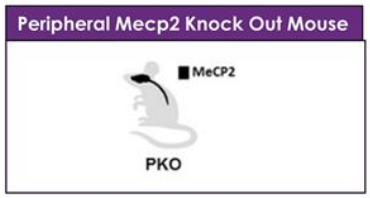
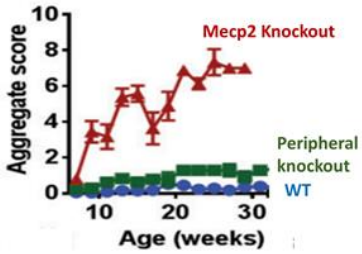
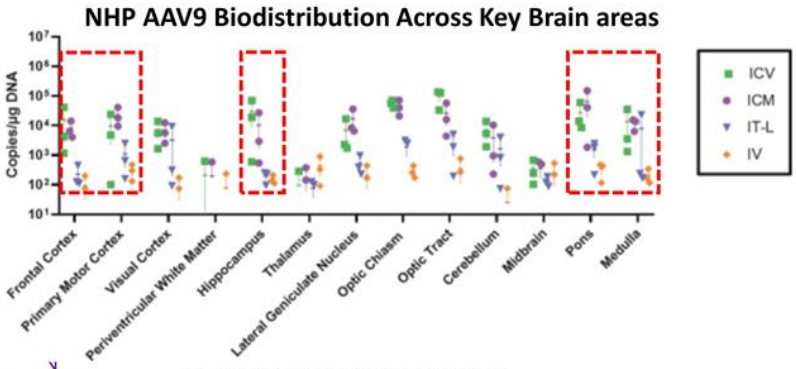
Appendix

Rett Syndrome Primarily Results from Loss of MECP2 Function in the Brain, Making the Brain the Key Target Area for Gene Therapy







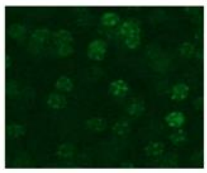
- Limiting expression of MeCP2 to only the brain/spinal cord results in a near normal mouse
- NHP biodistribution study shows 10-100x greater distribution for ICV/ICM compared to IT-L
- Delivery of NGN-401 via ICV chosen to maximize *MECP2* expression in the brain

Ross et al., 2016 Hum. Mol. Genetics. PMID: 28173151

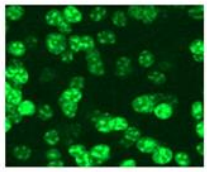
NHP data from ASGCT 2021 Annual meeting May 11-14

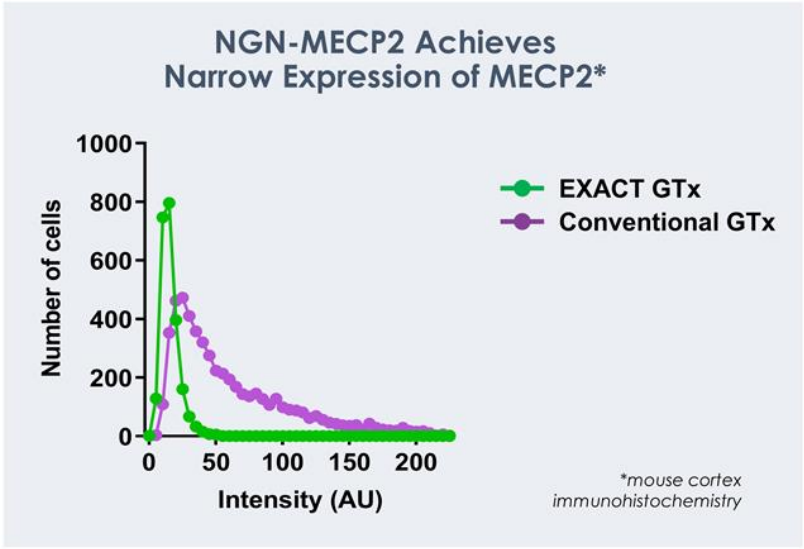
EXACT Delivers Consistent Levels of MECP2 Expression on Cell-by-Cell Basis

EXACT



Conventional

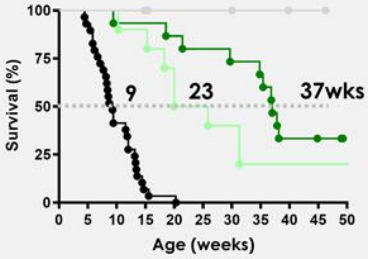




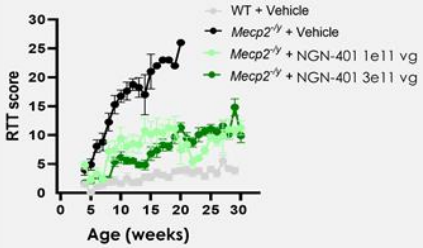
NGN-401 Demonstrates Tight MECP2 Regulation That Translates to Compelling Outcomes in a Knockout Mouse Model

ICV Delivery of NGN-401 Delivers Targeted MECP2 Levels

Survival



Clinical Score*



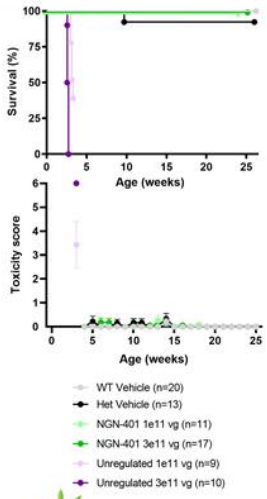
Key domains improved:

- Motor
- Gait
- Breathing

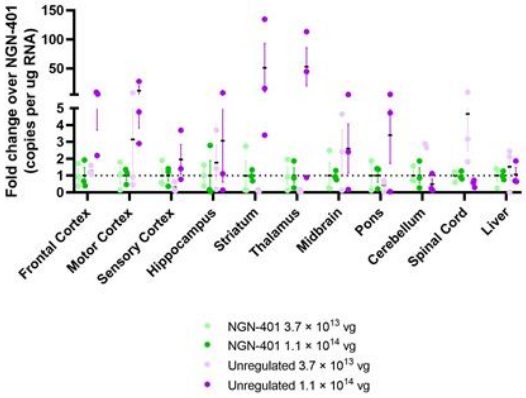
NEUROGENE *RTT scored 0-5 for six domains: mobility, gait, clasping, breathing, tremor, body condition

NGN-401 Via ICV Delivery Well Tolerated in Multiple Studies While Conventional Unregulated Gene Therapy is Toxic

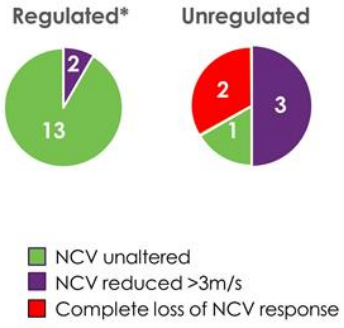
NGN-401 Well Tolerated in Female Mouse Model, Unregulated MeCP2 Highly Toxic



Tight mRNA Levels in NHPs for NGN-401, While Unregulated Has Substantially Greater Variance



NGN-401 Well Tolerated in NHP studies, While Unregulated MeCP2 Demonstrates Early Toxicity

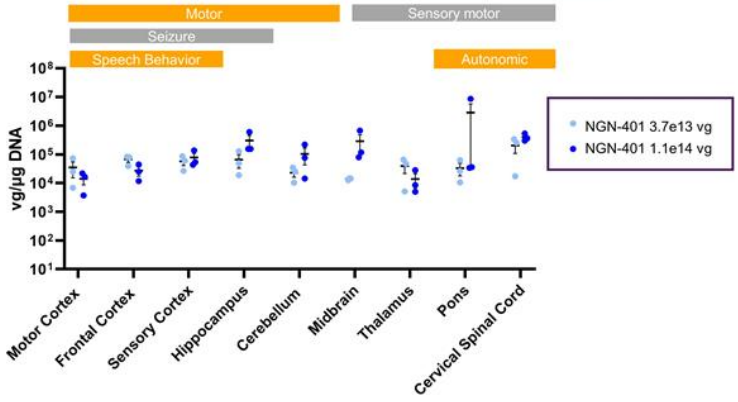


NOTE: toxicity scoring developed to capture phenotypes associated with MeCP2 overexpression including general condition, tremor, loss of limb use.
*Regulated includes NGN-401 and another EXACT vector; data at 30 days
NCV=nerve conduction velocity; NHP = non-human primates

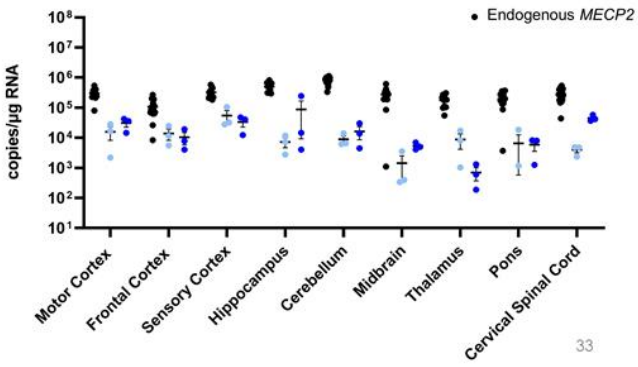
NGN-401 Distribution and Expression Levels in NHPs Support Encouraging Profile for Human Testing

- NGN-401 distributes to key regions underlying RTT pathophysiology in WT non-human primates
- Degree of mRNA expression tracks vector genome biodistribution of AAV9 across key brain regions
- Aggregate transgene expression below levels of endogenous MECP2 mRNA (100% of cells), avoiding overexpression concerns

Vector Biodistribution with ICV Administration Addresses Key Areas of the Brain Affected in Rett Syndrome



NGN-401 mRNA Expression Levels Below Endogenous



GLP Toxicology in NHPs Support Favorable Safety Profile

- NGN-401 evaluated in GLP NHP toxicology study with 90-day and 180-day cohorts
- No signs or symptoms of MeCP2 overexpression observed
- >4x safety margin relative to NGN-401 clinical starting dose in Phase 1/2
- Overall toxicology profile consistent with typical profile of intra-CSF administered AAV9 product
  - Slight to minimal non-adverse pathology detected in the dorsal root ganglion (DRG) nerves
  - Early and transient liver enzyme elevations observed, which resolved quickly without intervention

Explanation of CGI-I and RSBQ

CGI-I
(Clinician Global Impression of Improvement)

RSBQ
(Rett Syndrome Behavior Questionnaire)

Score	Definition
0	not true
1	somewhat or sometimes true
2	very true

Domain	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
Other	18