



Neurogene Presents New Data at ESGCT Congress that Reinforce Key Differentiators of NGN-401 Gene Therapy for Rett Syndrome

October 27, 2026

New data showing rapid and durable full-length MECP2 expression in vivo with single-stranded AAV support improvements observed in NGN-401 Phase 1/2 trial

New in vivo data demonstrate that miRNA-based auto-regulatory technology is not responsive to endogenous MeCP2 levels on a cell-by-cell basis

Preclinical data demonstrate broad CNS biodistribution following ICV administration, a routinely performed neurosurgical procedure, reinforcing NGN-401's route of delivery strategy

NEW YORK--(BUSINESS WIRE)--Oct. 27, 2026-- Neurogene Inc. (Nasdaq: NGNE), a clinical-stage company founded to bring life-changing genetic medicines to patients and families affected by rare neurological diseases, will present data related to its NGN-401 gene therapy program for Rett syndrome at the European Society of Gene and Cell Therapy (ESGCT) 33rd Annual Congress, taking place October 27-30, 2026, in Hamburg, Germany. The new preclinical data are expected to further validate NGN-401's differentiated design, which enables delivery of the fully functional, full-length *MECP2* gene and leverages the EXACT™ transgene regulation technology for controlled expression on a cell-by-cell basis.

"Two widely held assumptions in Rett syndrome gene therapy are that single-stranded AAV leads to slower expression than self-complementary AAV and that miRNA-based transgene auto-regulatory technology can selectively regulate expression based on a cell's MeCP2 levels," said Rachel McMin, Ph.D., Founder and Chief Executive Officer of Neurogene. "Our preclinical studies were designed to directly and rigorously test those assumptions. In these studies, we found that NGN-401's single-stranded design produced rapid and durable expression of the fully functional, full-length *MECP2* gene, which we believe is consistent with the early and sustained clinical improvements observed in our Phase 1/2 trial. Additional evidence generated from the preclinical studies demonstrated that miRNA-based auto-regulatory technology is not responsive to endogenous MeCP2 levels on a cell-by-cell basis but rather dampens transgene expression regardless of MeCP2 levels."

Rapid, durable full-length *MECP2* expression

The poster, "Expression Kinetics and Clinical Onset of Benefit Following Single-Stranded AAV Delivery of NGN-401 in Rett Syndrome," examines whether the reported differences in expression kinetics between single-stranded AAV (ssAAV) vectors and self-complementary AAV (scAAV) vectors translate into a meaningful difference in onset of action in Rett syndrome, a progressive neurodevelopmental disorder rather than one of acute neuronal loss. NGN-401 uses ssAAV9 to accommodate both the fully functional, full-length *MECP2* transgene and the required regulatory elements. A scAAV9 design cannot accommodate both due to its size constraints.

Key findings include:

- In a preclinical study, ssAAV containing the NGN-401 construct achieved rapid expression of full-length MeCP2 in all brain and nervous system tissues evaluated by Day 7, the earliest time point assessed, and remained durable through the three-month study. These data provide additional evidence that scAAV does not provide a meaningful advantage in onset of action in the treatment of Rett syndrome.
- These preclinical results are consistent with early onset and durability of clinical improvements observed in the Phase 1/2 trial of NGN-401 (data cutoff date of June 16, 2026), in which participants demonstrated clinical improvements at a median of two months post-treatment, and improvement continued across follow-up through 30 months.

Data challenging endogenous MeCP2-responsive transgene regulation

The poster, "Myth Versus Measurement: Direct CNS Comparison of Two miRNA-Based Regulated Gene Therapies in a Mosaic Model of Rett Syndrome," analyzes results from an in vivo study evaluating transgene regulation approaches. Rett syndrome is a mosaic disorder in which some cells express functional MeCP2 while others do not, making precise transgene regulation essential to achieve therapeutic MeCP2 levels while also avoiding overexpression toxicity. Building on existing published work, the study was designed to evaluate directly whether miRNA-based technology can selectively regulate transgene expression in cells with endogenous MeCP2 levels and only express in deficient cells. Key findings from the preclinical study include:

- Both technologies, including the miRNA-based auto-regulatory technology, produced comparable transgene expression in MeCP2-null and MeCP2-expressing neurons.
- Both technologies attenuated transgene output, consistent with the mechanism of global transgene dampening.

Therapeutic rationale for ICV delivery method in CNS-targeted gene therapy

Neurogene will also present encore data in the poster, “Gene Therapy Targeting CNS Diseases: ICV Administration as a Growing Standard for Delivery.” Intracerebroventricular (ICV) administration is a standard neurosurgical procedure performed thousands of times per year, and preclinical data demonstrated broader CNS biodistribution to brain regions central to Rett syndrome pathophysiology, as compared with intrathecal lumbar administration. In the Phase 1/2 trial, ICV administration was well-tolerated with no procedure-related adverse events observed among the 10 participants who received the 1E15 vg dose of NGN-401.

The posters will be available in the “Publications” section on the Company’s [website](#).

About Neurogene

Neurogene (Nasdaq: NGNE) is a clinical-stage biotechnology company focused on developing life-changing genetic medicines for people and their families impacted by devastating neurological diseases. The Company is using a biology-first approach paired with optimized delivery to develop purpose-built genetic medicines, including programs powered by its novel and proprietary EXACT™ transgene regulation technology. Neurogene is advancing its lead gene therapy program, NGN-401, as a potential best-in-class, one-time treatment for Rett syndrome. For more information, visit neurogene.com or follow on [LinkedIn](#).

About NGN-401

NGN-401 is an investigational AAV9 gene therapy in late-stage clinical development as a potential best-in-class, one-time treatment for Rett syndrome. It is the only clinical candidate to deliver the full-length human *MECP2* gene and includes Neurogene’s EXACT™ transgene regulation technology, which is designed to deliver consistent, tightly controlled MeCP2 protein expression on a cell-by-cell basis. NGN-401 is delivered through intracerebroventricular administration to achieve the broadest targeting directly to the brain and nervous system based on nonclinical biodistribution data. NGN-401 is being evaluated in the Embolden™ registrational clinical trial. Data from the Phase 1/2 trial (as of June 16, 2026) have shown that participants experienced multidomain, durable gains with continued developmental milestone acquisition observed over time, and NGN-401 at the 1E15 vg dose has been generally well-tolerated. NGN-401 has received Breakthrough Therapy, Regenerative Medicine Advanced Therapy, Fast Track, Orphan Drug and Rare Pediatric Disease designations and selection for the START Pilot Program from the U.S. Food and Drug Administration, Advanced Therapy Medicinal Product, Orphan and Priority Medicines designations from the European Medicines Agency and Innovative Licensing and Application Pathway designation from the United Kingdom Medicines and Healthcare products Regulatory Agency.

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, including its potential to restart development in individuals with Rett syndrome; the safety and tolerability profile of NGN-401, including in connection with ICV administration; the applicability of reported interim results from the NGN-401 Phase 1/2 clinical trial to other participants; the expected durability and deepening of clinical responses observed in the NGN-401 Phase 1/2 clinical trial; the extent to which results of preclinical studies are predictive of or consistent with clinical results; the interpretation of comparative preclinical data; the potential for NGN-401 to be a best-in-class gene therapy for Rett syndrome; the potential for future approval for commercialization of NGN-401 as a treatment for Rett syndrome; the potential for success of the Embolden registrational clinical trial of NGN-401 for Rett syndrome; the clinical benefit of distinctions between NGN-401 and other gene therapy product candidates including the use of a full-length gene, regulatory elements to prevent overexpression toxicity and delivery of NGN-401 via ICV administration; potential market acceptance of the benefit of such distinctions; the anticipated benefits of any regulatory designation for NGN-401, including the FDA’s Breakthrough Therapy designation, Rare Pediatric Disease designation, RMAT designation and participation in the FDA’s START Pilot Program; and the content and timing of, and any conclusions that may be drawn from, the data to be presented at the ESGCT 33rd Annual Congress. 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, those identified under the heading “Risk Factors” included in Neurogene’s Annual Report on Form 10-K for the year ended December 31, 2025, filed with the Securities and Exchange Commission (“SEC”) on March 24, 2026, the Quarterly Report on Form 10-Q for the quarter ended June 30, 2026, filed with the

SEC on August 11, 2026, and other filings that the Company has made and may make with the SEC in the future. Nothing in this press release 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 press release 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.

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