Data Summary of the Phase 1/2 NGN-401 Gene Therapy Trial for Rett Syndrome 1E15 vg Dose

NEUROGENE®

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WHAT IS NGN-401? NGN-401 IS...

An investigational gene therapy that is a potential **one-time treatment** for Rett syndrome.

Designed to deliver functional copies of the **full-length human *MECP2* gene,** which create fully functioning MeCP2 protein.

Delivered by a well-established, routinely performed neurosurgical procedure called intracerebroventricular (ICV) administration. ICV has been shown in animals to **deliver gene therapy to the areas of the brain** and nervous system responsible for Rett syndrome more effectively than other methods.

Designed using Neurogene's **EXACT™ technology to prevent the production of too much MeCP2 protein**, which can be harmful.

WHAT IS THIS PHASE 1/2 TRIAL ABOUT?

The goal of this trial is to understand the safety, tolerability, and efficacy of NGN-401. Efficacy is a measure of how well a treatment addresses the disorder.

1. Participants were given a one-time 1E15 vg dose of NGN-401
2. Researchers monitor participants for safety and tolerability
3. Researchers also look for improvements in scales used to evaluate Rett syndrome and functional abilities

This study is the first time people were given NGN-401 for Rett syndrome. NGN-401 is not approved by any regulatory agency for use outside of clinical trials.

**Claims regarding the efficacy and safety of the investigational drug, NGN-401, cannot be made.*

vg = vector genome

***CGI-I = Clinical Global Impression of Improvement*

WHAT DATA ARE INCLUDED IN THIS SUMMARY?

This Phase 1/2 trial data update includes data as of the cutoff date of June 16, 2026.*

EFFICACY AND SAFETY DATA include all 10 participants

Participants are 12-30 months post-dose

Pediatric Group:
8 participants ages 4-10

Adolescent/Adult Group:
2 participants ages 11 and older

WHAT ARE THE PHASE 1/2 EFFICACY DATA?*

- 4.7 developmental milestones gained on average per participant
- 100% gained at least one milestone and improved on a scale measuring improvement (CGI-I)**
- The improvements observed led to new abilities, showing enhanced independence and reduced caregiver burden
- Milestones acquired in a developmentally ordered stepwise sequence—suggesting a restart of the developmental trajectory
- **All acquired milestones have remained durable:** None of the participants have lost any of the skills gained in the trial

WHAT ARE THE LATEST PHASE 1/2 TRIAL SAFETY FINDINGS?*

PARTICIPANTS 1 - 10...

- **The 1E15 vg dose was generally well tolerated.**
  Participants continue to be monitored for safety and side effects, which are also called adverse events.
- **All NGN-401 treatment-related adverse events have been mild or moderate in severity.**
  The majority are known potential risks of adeno-associated virus (AAV) that have resolved or are resolving. AAV is commonly used to deliver gene therapies into the body.
- **No new treatment-related serious adverse events reported since last cut-off date (October 2025).**
  Two previously disclosed serious adverse events in a single participant have resolved.
- **The most common treatment-related adverse event was mild liver enzyme elevations.**
- **No cases of extreme immune response (HLH) in any participant.**
  HLH is a rare, extreme immune response associated with higher doses of AAV gene therapy. There have been no cases of HLH in any participant who has received the 1E15 vg dose.
- **No intracerebroventricular (ICV) procedure-related adverse events.**
- **No signs or symptoms of MeCP2 overexpression.**
- **Seizures have remained well controlled following NGN-401.**

*As of data cutoff date of June 16, 2026.

EXAMPLES OF NEW ABILITIES PARTICIPANTS GAINED*

PARTICIPANTS DID NOT HAVE THESE ABILITIES WHEN THEY ENTERED THE CLINICAL TRIAL

RECONNECTING AND PLAYING WITH FAMILY

- Turns when called
- Says words with meaning
- Waves
- Gives high-fives
- Can follow commands

NAVIGATING INDEPENDENTLY

- Gets in/out of car and shuts door
- Gets in/out of bathtub
- Gets on and off furniture
- Walks up and down stairs

REQUIRING LESS PHYSICAL ASSISTANCE AND CONSTANT SUPERVISION

- Can feed herself with a utensil
- Can hold her drink
- Can pick up her blanket
- Can sit up from lying down

FOLLOWING INSTRUCTIONS AND USING BOTH HANDS

- Carries backpack, walks up step to front door and closes door
- Can play puzzle with family
- Can catch a ball

COMMUNICATING NEEDS MORE CONSISTENTLY, INTENTIONALLY

- Can more consistently communicate wants/needs with AAC device

*Summary list of abilities gained as of data cutoff date of June 16, 2026; not every participant gained all of the abilities listed.

WHAT HAPPENS NEXT?

- Participants in the Phase 1/2 trial will continue to be monitored.
- The Phase 1/2 trial was converted into Embolden™, the Phase 3, registrational, or pivotal, trial of NGN-401.
- Embolden enrolled and dosed 25 females who are 3 years of age or older.
- Embolden participants received the same 1E15 vg dose of NGN-401 used in the Phase 1/2 trial.
- Neurogene plans to use data from Embolden to seek approval from regulatory agencies, such as the U.S. Food and Drug Administration (FDA), to use NGN-401 as a treatment for Rett syndrome.
- Topline results from Embolden are expected in the second half of 2027.

Embolden™
A Clinical Study for Rett Syndrome

WITH DEEP APPRECIATION...

On behalf of the entire Rett syndrome community and Neurogene, thank you to all the families who have participated in clinical trials. Your commitment and bravery are how advances in treatments are able to move forward. Read our message at www.Neurogene.com/patients-and-families/#thankyou.