

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



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 common 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.



Participants were given a one-time 1E15 vg dose of NGN-401



Researchers monitor participants for safety and tolerability



Researchers also look for improvements in Rett syndrome scales 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 genomes

What is interim data?

Data that are shared while a study is ongoing are called interim data. This Phase 1/2 trial interim data update includes data as of the cutoff date of October 30, 2025.*

EFFICACY DATA from female participants 1-8 in the ages 4-10 pediatric cohort, or group



- Five are 12-24 months post-dose
- Three are 6 months post-dose

SAFETY DATA includes participants 1-8 in the pediatric cohort and two female participants in the ages 11 and up adolescent/adult cohort



What are the interim Phase 1/2 efficacy data?*

Gained 35 skills with no plateau: Participants continued to gain developmental milestones/skills over time across multiple domains, including hand function, gross motor function, and communication. Improvements in autonomic function have also been observed.

All acquired skills have remained durable: None of the participants have lost any of the skills previously gained in the study.



What are the latest interim Phase 1/2 trial safety findings?*

PARTICIPANTS 1-10...

The 1E15 vg dose remains 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 (TEAEs) 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 evidence of extreme immune response in any participant.

HLH is a rare, extreme immune response associated with higher doses of AAV gene therapy. There has been no evidence of HLH in any participant who has received the 1E15 vg dose.

Examples of Key Skills and Functional Improvements Gained*

Fine Motor/Hand Function	Gross Motor/Ambulation	Communication	Autonomic
 Uses hands to self-feed, drink, play with toys, self-soothe	 Sits without support	 Says words with meaning	 Improvements in constipation
 Decreased to no stereotypies	 Walks up and down stairs unassisted	 Follows daily routine, e.g., getting ready for school	 Drinks clear liquids, eats solids for first time
 Uses utensils to self-feed	 Bends at waist and stands back up	 Communicates needs and wants; can ID colors	 Absent aspiration pneumonia events
	 Bears more weight for ease of transfer	 Engages with friends and family; shows affection	 Can sleep through the night
	 Can get on/off furniture, out of bathtub, into car unassisted	 Starting/improved communication with use of assisted device	

*As of data cutoff date of October 30, 2025

What happens next?

- Researchers continue to monitor Phase 1/2 trial participants.
- Data from two more participants who are in the ages 11 and up adolescent/adult cohort are expected to be shared in 2026.
- Embolden™ is the Phase 3, registrational, or pivotal, trial of NGN-401 (the Phase 1/2 trial is no longer enrolling).
 - Enrollment for Embolden has begun.
 - Embolden will enroll 20 females who are 3 years of age or older.
 - Embolden participants will be given the same 1E15 vg dose of NGN-401 used in the Phase 1/2 trial.
 - Data from Embolden will be used 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.

