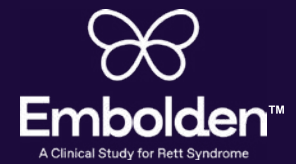


Understanding the Embolden™ Phase 3 Gene Therapy Trial of NGN-401 for Rett Syndrome



What is NGN-401?

NGN-401 is an investigational gene therapy that is a potential treatment for Rett syndrome.

The investigational gene therapy NGN-401 is not approved by any regulatory agency for use outside of the clinical trial.

Why do researchers think NGN-401 is a potential treatment for Rett syndrome?



Rett syndrome is caused by having too little of a protein called MeCP2



NGN-401 is designed to deliver functional copies of the **full-length human MECP2 gene** to create fully functioning MeCP2 protein



NGN-401 uses **Neurogene's EXACT™ technology, designed to prevent the production of too much MeCP2 protein**, which can be harmful

How is NGN-401 given?



NGN-401 is 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 methods¹



30,000 ICV infusions take place each year in the U.S. and 10,000 of those are in children²

¹Burstein, S. R., et al (2025). 32nd ESGCT Annual Congress. Seville.

²Analysis conducted by 81qd (<https://81qd.com>) using CHRONOS™ © 2024 Forian Inc. and its licensors (<https://forian.com>). All rights reserved.

What is Embolden?

Embolden is the Phase 3, or registrational, clinical trial of NGN-401.



3 year long study + 12 years follow-up



100% enrolled, females with Rett syndrome (ages 3 and up)



Every participant receives a one-time 1E15 vg dose of NGN-401



No placebo given

What will Embolden measure?

In addition to safety, the Embolden study is evaluating the following as the primary endpoint:

Rett syndrome scale: CGI-I of ≤ 3

- Clinical Global Impression-Improvement (CGI-I) scale is used by clinicians to rate improvement over time. On the scale, 1 is very much improved and 7 is very much worse

Gain of any one developmental milestone

- Neurogene worked with caregivers to understand what improvements would be meaningful to them
- Captured through video recordings that are rated by independent, blinded central raters

What happens after Embolden?

At 12 months, if both of the above objectives are achieved, the primary endpoint will be met. Since this is a registrational, or pivotal trial, Neurogene will use the Embolden trial data to pursue regulatory approval to make NGN-401 available as a treatment for Rett syndrome.

LEARN MORE ABOUT CLINICAL TRIALS AND GENETICS:

International Rett Syndrome Foundation

rettsyndrome.org/rett-forward

Rett Forward: A Clinical Trial Master Class—a free educational platform to better understand gene therapy and clinical trials

Rett Syndrome Research Trust

reverserett.org/genetics-primer

Genetics 101—a free online tutorial that explains genetics

LEARN MORE ABOUT EMBOLDEN



Talk to your physician



Visit clinicaltrials.gov and search for NCT05898620



For more information visit Neurogene.com/patients-and-families