About **NGN-401**

The experimental gene therapy study treatment, NGN-401, uses a virus called an adeno-associated virus (AAV) to deliver a normal copy of the *MECP2* gene to your child's body.

The virus (AAV) is designed so that it will not cause disease. AAV has been used in many clinical trials, including FDA approved gene therapies. The *MECP2* gene in NGN-401 is designed to make a complete MeCP2 protein. Having too much or too little MeCP2 protein can cause disease. Having too little MeCP2 protein results in Rett syndrome. Having too much MeCP2 protein causes *MECP2* duplication syndrome. NGN-401 used in this research study has been designed with a built-in mechanism aimed to prevent producing too much MeCP2 protein.

NGN-401 has not been given to people before this research study (first-in-human study). As with any experimental treatment, there is a chance for unexpected side effects or it may not work.

NGN-401

Have questions about this **research study?**

Write them down here and ask the study team at your local site. Their contact information can be found below.

Boston Children's Hospital

Where the world comes for answers

Phone:

617-355-5173

Email:

RettResearch@childrens.harvard.edu

Consider Enrolling Your Child in an Experimental Gene Therapy Research Study for Patients with

Rett Syndrome

About This **Rett Syndrome Study**

This study will test an experimental gene therapy study treatment on pediatric females with Rett syndrome. An experimental treatment is a treatment that has not been approved by the Food and Drug Administration (FDA) but has been cleared to test in humans. Experimental treatments are also called study treatments. The purpose of this first-in-human research study is to test if NGN-401 is safe, tolerable and effective in female children who are 4 to 10 years old with a diagnosis of Rett syndrome. Patients must have a documented disease-causing mutation in the methyl-CpG-binding protein 2 (MECP2) gene.

This study will take place over a period of 5 years. This study includes a screening period of up to 70 days, a baseline visit and a 5 day stay in the hospital, followed by approximately 40 to 42 in-person visits and 4 telephone visits over the 5 years. Each in person visit can last over multiple days, with a majority of visits occurring in the first 6 months.

Your child may or may not benefit from this research as there is no guarantee that being in this research study will help her. Previous animal research studies have shown benefits to animals who have received the experimental treatment, NGN-401. There are potential risks, as well as risks that are not known yet.

NEUROGENE®

Information about **Clinical Research Studies**

A clinical research study is a carefully controlled study that helps determine whether an experimental product is safe and effective in the condition/disorder in which it is being studied. The physician who enrolls your child in the clinical trial is called the "principal investigator", "clinical trial physician/doctor", or "study doctor"

An experimental gene therapy, such as NGN-401, goes through several phases of clinical research to evaluate its safety and effectiveness. Depending on the results of the research the experimental gene therapy study treatment could later be available to the public as a marketed product if approved by a regulatory agency. There are several stages of a clinical research study. This study is a combined Phase 1 and 2 study, (where Phase 1 evaluates safety and Phase 2 evaluates tolerability and effectiveness) out of the 3 possible phases required by the Food and Drug Administration (FDA) and other regulatory agencies in order to approve an experimental gene therapy study treatment for public use.

An external review board, often known as an Institutional Review Board (IRB) or Ethics Committee (EC) made up of doctors, ethicists, members of the public, and administrators help ensure that a clinical trial does not present an unreasonable risk to individuals who are participating. Before enrolling your child in this clinical study, consult with your child's doctors about her participation. The study doctor and study staff are available to answer any questions you may have. Whenever you agree to enter your child into a clinical trial, you are given the name and telephone number of a contact in your study doctor's office who will answer any questions you may have.

Before your child is enrolled in the clinical trial, a parent/legal guardian must provide consent.

Study **Criteria**

To participate in this study, patients:

- **Must be biologically female**
- **Must be ≥4 years to ≤10 years of age at the time of screening**
- **Must be diagnosed with typical Rett syndrome**
- **Must have a Rett syndrome-causing mutation in the MECP2 gene**
- **If currently taking an anti-epileptic drug for seizures, the patient must be on a stable dosing regimen for at least 12 weeks prior to screening**
- **Must NOT have normal or near normal hand function (e.g., child must not be able to grip a pen/pencil effectively and/or draw a shape)**
- **Must have never taken DAYBUE™ (trofinetide) or discontinued DAYBUE™ prior to study start.**

***DAYBUE™ is a trademark of Acadia Pharmaceuticals Inc.**

Your child and her parent(s)/legal guardian(s) should remain a 2-hour driving distance from the study site for approximately 3 months after the experimental treatment.

Trial-related costs and expenses are paid or reimbursed by the clinical trial sponsor, Neurogene. There is a comprehensive travel and expense policy in place for costs and expenses related to the clinical trial. More details of the specific policy can be provided by the clinical trial site. There may be additional costs associated with your temporary re-location to live within a 2-hour driving distance of the study site. You should discuss your relocation costs with your study team to determine what expenses will be covered.

Providing consent is a process which begins with an explanation of the clinical study and review of an Informed Consent Form (ICF). The ICF contains important information about the study, such as study procedures, potential risks, and details about study participation. A parent/legal guardian must review and agree to the terms of the ICF.

When participating in a clinical trial, it is critical that all communication about your child's healthcare be shared with the study doctor.

For many people, taking part in a clinical trial is important because their participation may help make new treatments possible for a rare condition.