By joining a clinical study, your child may benefit from a new treatment before it is available to the public. You and your child may also help in the development of new ways to improve the health of others.

Being in a clinical study is voluntary and you and your child can leave the study at any time for any reason.

For more information on the Lysogene gene therapy clinical study for GM1 gangliosidosis:
Contact patientadvocacy@lysogene.com
Visit www.lysogene.com
Visit clinicaltrials.gov (NCT04273269)

What is the LYS-GM101 Study?
This study is testing an investigational gene therapy called LYS-GM101, to see how safe it is and how well it works in children with GM1 gangliosidosis. LYS-GM101 contains the GLB1 gene, which is the gene that doesn’t work in children with this disease.

Who can take part in the study?*
✓ Children with early infantile GM1 gangliosidosis at least 4 months and less than 12 months old and are able to swallow
✓ Children with late infantile GM1 gangliosidosis who are less than 3 years old and can sit up by themselves or with props

*This is not a full list of criteria. The study doctor will let you know if your child is eligible to join.
What happens during the study?
Your child will have a total of 18 clinic visits during the study.

How does LYS-GM101 work?
1. A working GLB1 gene is delivered directly into the fluid that surrounds the brain and spinal cord (cerebrospinal fluid), allowing it to reach many nerve cells. The gene is packaged inside a special virus to help get it into the cells. This virus is not active and cannot cause any diseases.

2. This working GLB1 gene may then help the nerve cells make the enzyme that they are missing. This enzyme is important to stopping or slowing the brain and spinal cord damage seen in GM1 gangliosidosis.

After the initial 2 years follow-up, your child's health will be monitored for a further 3 years.

Screening:
Up to 4 weeks

Treatment:
Up to 1 week

Follow-up:
2 years

Long-term follow-up:
3 year

How is the gene therapy given?
All children in the study will receive the gene therapy as a single, one-time injection into a fluid-filled space in the back of the head called the cisterna magna. Injecting into this area helps to get as much therapy as possible to the brain and spinal cord. The doctors will take pictures of your child's brain to guide the injection. The actual injection takes 2 to 9 minutes and your child will be asleep the whole time.

Your child will also receive other medicine orally to make sure his/her immune system doesn't react to the gene therapy. Your child will take this medicine about 7 days prior to receiving the gene therapy and for about 6 months after the treatment.

Cell has faulty GLB1 gene

Working GLB1 gene is inserted

Gene packaged inside virus

New GLB1 gene makes working enzyme

How long is the study?
Your child will be in the study for 5 years. There are 4 parts to the study.

Visit 1 (Screening):
You will answer questions and your child will have some tests to see if he or she is eligible to join the study.

Visits 2 to 3 (Treatment):
Your child will receive the gene therapy. Your child will then stay in the hospital for at least 3 days so that the doctors can keep a close eye on him/her. You will need to stay near the hospital for about 2 weeks before going back home.

Visits 4 to 12 (Follow-up):
Your child will visit the clinic 9 times: at 1, 3, 6, 9, 12, 15, 18, 21, and 24 months after treatment. At these visits, the study team will perform tests to check your child's health.

Visits 13 to 18 (Long-term follow-up):
Your child will then visit the clinic 6 times at 30, 36, 42, 48, 54, and 60 months after treatment. At these visits, the study team will perform tests to check your child's health.

You will be given the option to join a video portion of this study. If you agree, you will record your child at home doing certain activities and anything new that he/she is able to do.
Below is a summary of what to expect at your child’s scheduled visits, including some of the tests that will take place. Your child will not have all of these tests at each visit. Check the glossary and speak with the study doctor to learn more about the tests.

### Visit Schedule summary

**SCREENING**

- Visit 1 (month 1)
  - Physical exam
  - Eye exam
  - Electroencephalogram (EEG, brain activity)
  - Brain imaging (MRI) with spinal tap
  - Blood test
  - Urine test
  - Survey
  - Home video

- Visit 2 (month 2)
  - Physical exam
  - Eye exam
  - Electroencephalogram (EEG, heart check)
  - Blood test
  - Urine test

**TREATMENT**

- Visit 3 (month 3)
  - Physical exam
  - Eye exam
  - Electroencephalogram (EEG, brain activity)
  - Blood test
  - Urine test

- Visit 4 (month 4)
  - Physical exam
  - Eye exam
  - Electroencephalogram (EEG, brain activity)
  - Blood test
  - Urine test

- Visit 5 (month 5)
  - Physical exam
  - Eye exam
  - Electroencephalogram (EEG, brain activity)
  - Blood test
  - Urine test

- Visit 6 (month 6)
  - Physical exam
  - Eye exam
  - Electroencephalogram (EEG, brain activity)
  - Blood test
  - Urine test

**FOLLOW UP**

- Visit 7 (month 6)
  - Physical exam
  - Eye exam
  - Electroencephalogram (EEG, brain activity)
  - Blood test
  - Urine test

- Visit 8 (month 12)
  - Physical exam
  - Eye exam
  - Electroencephalogram (EEG, brain activity)
  - Blood test
  - Urine test

**LONG-TERM FOLLOW-UP**

- Visit 9 (month 18)
  - Physical exam
  - Eye exam
  - Electroencephalogram (EEG, brain activity)
  - Blood test
  - Urine test

- Visit 10 (month 24)
  - Physical exam
  - Eye exam
  - Electroencephalogram (EEG, brain activity)
  - Blood test
  - Urine test

- Visit 11 (month 30)
  - Physical exam
  - Eye exam
  - Electroencephalogram (EEG, brain activity)
  - Blood test
  - Urine test

- Visit 12 (month 36)
  - Physical exam
  - Eye exam
  - Electroencephalogram (EEG, brain activity)
  - Blood test
  - Urine test

- Visit 13 (month 42)
  - Physical exam
  - Eye exam
  - Electroencephalogram (EEG, brain activity)
  - Blood test
  - Urine test

- Visit 14 (month 48)
  - Physical exam
  - Eye exam
  - Electroencephalogram (EEG, brain activity)
  - Blood test
  - Urine test

- Visit 15 (month 54)
  - Physical exam
  - Eye exam
  - Electroencephalogram (EEG, brain activity)
  - Blood test
  - Urine test

- Visit 16 (month 60)
  - Physical exam
  - Eye exam
  - Electroencephalogram (EEG, brain activity)
  - Blood test
  - Urine test

### Glossary

- **Behavior skills**: The doctor will assess and score your child’s behavior, including how he/she communicates and interacts with others.

- **Blood test**: Small samples of your child’s blood will be taken to look at different parts of the blood and your child’s overall health.

- **Brain function**: The study doctor will watch your child play to see how his/her brain is working. Depending on your child’s age, the doctor will look at skills such as language, memory, and attention.

- **Brain imaging (MRI) with spinal tap**: Your child will have a scan called an MRI scan that uses magnets to take pictures of the brain. The study team will also take a small sample of fluid from your child’s spine (spinal tap) during this time. Your child will not be able to eat or drink for 4 hours prior to the test and will be asleep throughout the test.

- **Electroencephalogram (EEG)**: A painless test that measures your child’s brain activity. Small, metal discs called electrodes will be placed on your child’s head and connected to a computer to look at the health of your child’s heart.

- **Electrocardiogram (ECG)**: A painless test that measures your child’s heart activity. Small, metal discs (electrodes) will be placed on your child’s chest and connected to a computer to look at the health of your child’s heart and belly.

- **Eye exam**: You will have a small sample of fluid from your child’s spine taken in a sterile environment. This will be stored in special tubes for research. The study doctor will also check your child’s overall health, including height, weight, breathing, temperature, blood pressure, heart rate, and symptoms of GM1 gangliosidosis.

- **Gene therapy**: Your child will receive medicine by mouth 7 days before and 6 months after therapy to make sure his/her immune system doesn’t react to the gene therapy. Your child will receive medicine by mouth 7 days before and 6 months after therapy to make sure his/her immune system doesn’t react to the gene therapy. Your child will receive medicine by mouth 7 days before and 6 months after therapy to make sure his/her immune system doesn’t react to the gene therapy.

- **Immunology (ultrasound)**: This painless test uses sound waves to take pictures of your child’s heart and belly.

- **Immunostaining block**: Your child will receive medicine by mouth 7 days before and 6 months after therapy to make sure his/her immune system doesn’t react to the gene therapy. Your child will receive medicine by mouth 7 days before and 6 months after therapy to make sure his/her immune system doesn’t react to the gene therapy. Your child will receive medicine by mouth 7 days before and 6 months after therapy to make sure his/her immune system doesn’t react to the gene therapy.

- **Informed consent**: After the study doctor explains the study, you will sign forms to give your permission for your child to join. You must sign the informed consent form before your child can have any tests.

- **Medical history**: The study doctor will review your child’s past and current health, including any prior surgeries or procedures. The doctor will also ask if your child has any feeding difficulties, seizures, or breathing problems.

- **Medicine review**: The study doctor will review any medicine your child has taken in the past or is currently taking.

- **Motor skills**: The study doctor will see how well your child can perform certain movements, such as sitting, crawling, standing, and walking.

- **Movement and speech scoring**: The study doctor will look at your child’s movements and language abilities to see how he or she compares to other children of the same age.

- **Neurological exam**: The study doctor will check your child’s nerve and muscle function, including movement, reflexes, and muscle strength.

- **Physical exam**: The study doctor will check your child’s overall health, including height, weight, breathing, temperature, blood pressure, heart rate, and symptoms of GM1 gangliosidosis.

- **Survey**: You will answer some questions about your child’s illness and how it affects your family’s and your child’s overall well-being and quality of life.

- **Urine test**: These tests can measure the amount of sugar, protein, blood, and other markers in your child’s urine.