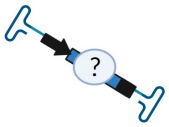
Gene Therapy Clinical Trial for GM1 Gangliosidosis

At Sio, we operate with a sense of urgency and compassion to develop gene therapies that transform the treatment of serious neurodegenerative diseases. We combine cutting-edge science with rigorous testing to fill unmet medical needs for patients with therapies that are intended to deliver lifelong benefits.

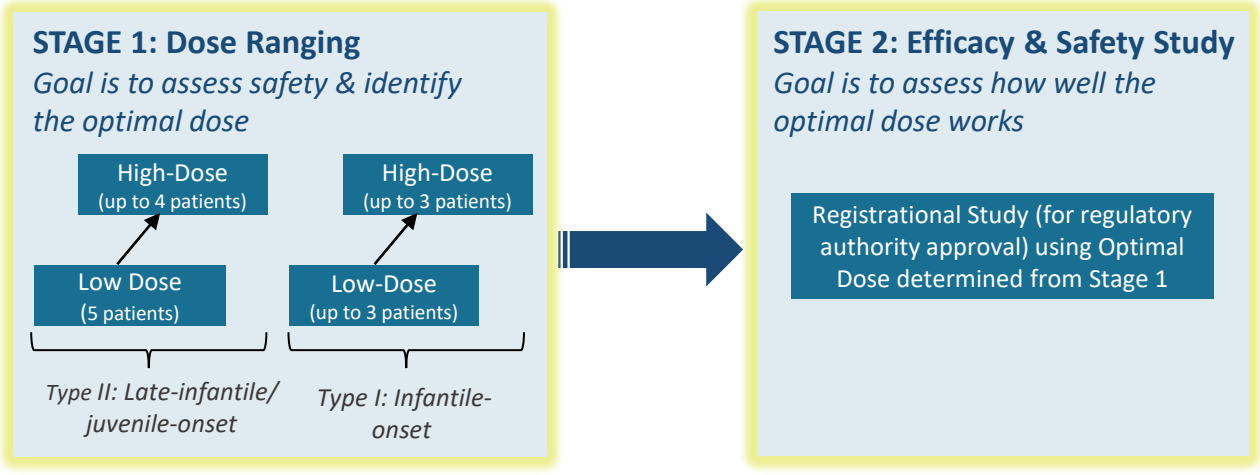
GM1 Gangliosidosis



GM1 is a fatal disease caused by a mutation in the *GLB1* gene which results in low levels of the ß-gal enzyme and accumulation of toxic storage materials in the brain and peripheral organs. No disease modifying treatments are currently available.

AXO-AAV-GM1 Gene Therapy Clinical Study for GM1 Gangliosidosis

A Phase 1/2 clinical trial is being conducted to learn if an experimental gene therapy called AXO-AAV-GM1 (also called AAV9-GLB1) can help treat children with infantile and juvenile-onset GM1 gangliosidosis. AXO-AAV-GM1 delivers a working copy of the *GLB1* gene. This trial consists of two stages as shown below. Detailed information about the trial and eligibility requirements are listed at www.clinicaltrials.gov (Identifier: NCT03952637).

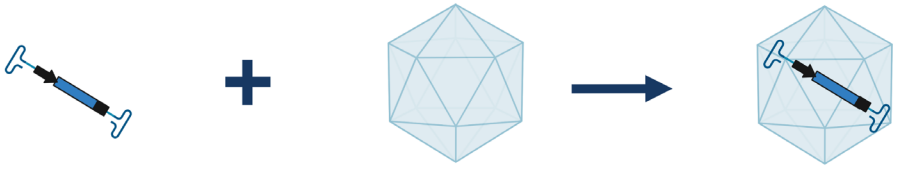


In Stage 1, for each infantile-onset patient, a thorough safety evaluation is required before the next patient can be treated. This staggered dosing is included to protect patient safety during this initial stage.

Gene Therapy for GM1 Gangliosidosis

What is AXO-AAV-GM1 gene therapy?

AXO-AAV-GM1 is a liquid that contains working copies of the *GLB1* gene delivered by vectors to cells in the brain and peripheral organs. AXO-AAV-GM1 has the potential to slow or stop disease progression.



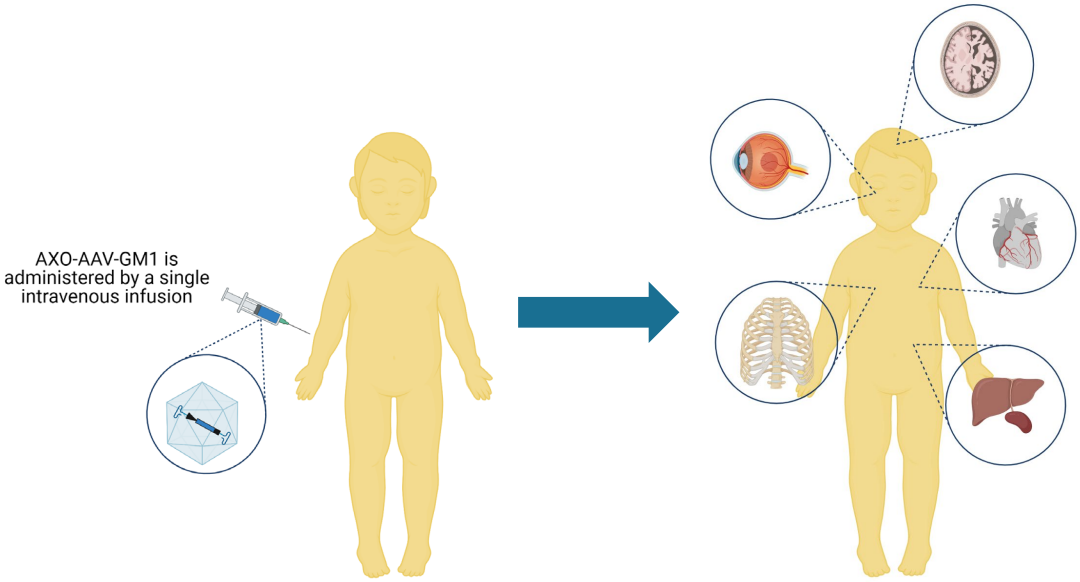
New, working copy of GLB1 gene which is mutated in patients with GM1 gangliosidosis

AAV9 vector can cross into the brain and provide widespread delivery of a gene throughout the body. AAV9 is used for a currently marketed gene therapy

AXO-AAV-GM1 is made up of a working GLB1 gene placed in AAV9 vector

What does the gene therapy procedure involve?

AXO-AAV-GM1 is administered intravenously to allow broad distribution of therapy to the brain and other organs and potentially reduce accumulation of toxic storage materials throughout the body.



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How long is the study and how often are study assessments conducted?

On site Screening
~4-6 weeks prior to treatment

Administration AXO-AAV-GM1

Frequency of site visits

Month 1	Month 2-6	Month 7-Year 2	Year 3-5
weekly	at 3 & 6 months	every 6 months	yearly

Type I: 1-year assessment; 4-year long term follow-up
Type II: 3-year assessment; 2-year long term follow-up

Frequently asked questions

Is my child eligible to participate?

- To assess eligibility for the trial, the study investigators will evaluate many factors. A few of the key eligibility criteria are listed below:
  - ✓ Confirmed genetic and biochemical diagnosis of GM1 gangliosidosis
  - ✓ 6-12 months of age for Type I (infantile-onset) patients and 1-12 years of age for Type II (late-Infantile and juvenile-onset) patients.
  - ✓ Study investigators will also do a series of assessments and discuss other factors with you such as disease severity and other medical conditions to ensure the trial is appropriate for your child.

What is the status on trial enrollment?

- For Stage 1 of the trial, we are continuing to actively screen and enroll Type I (infantile-onset) patients for both the low dose and high dose cohorts. We completed enrollment of Type II (late infantile and juvenile-onset) patients in the low dose cohort in April 2020 and have identified the last Type II candidate to be enrolled in the high dose cohort in Stage 1. As of July 2021, we are not screening any additional Type II patients for enrollment in Stage 1. We will continue to collect contact information of Type II patients for potential enrollment in Stage 2 of the trial.

How soon will I need to arrive at the study site to determine study eligibility?

- The study Investigator and their staff will usually do an initial virtual evaluation at least 2 months prior to treatment to determine if your child could be a good candidate for the study. If they determine your child may be suitable for the trial, a coordinator will work with you to arrange travel to the site. The on-site screening to determine study eligibility will begin approximately 4-6 weeks prior to treatment.
- Enrollment between all Type I patients is spaced to allow sufficient time to assess safety of the gene therapy prior to dosing another patient. Therefore, even though your child may be determined to be a good candidate, they may not immediately undergo on-site screening.

What assessments are made during the study?

- After AXO-AAV-GM1 gene therapy, your child will have regular follow-up visits at the clinical trial site to assess their health, symptoms, and ability to perform various physical and mental tasks. A variety of assessments will be performed including physical exams, MRIs, x-rays, scans, lumbar punctures, and blood draws.
- The main outcome of the trial will be assessed 1 year after treatment for Type I (infantile-onset) patients and 3 years after treatment for Type II (late infantile/juvenile-onset) patients. Children will then continue to have regular follow-up visits for 2-4 additional years to further evaluate the safety and efficacy (how well it works) of the therapy.

Does vaccination impact eligibility for the study?

- Patients should not receive vaccines while receiving immune suppressive therapy prior to gene transfer and within the first year after gene therapy.

Frequently asked questions (continued)

What are the risks and benefits of participating in the trial?

- Participation may help lead to a future treatment. Study participants may or may not benefit from AXO-AAV-GM1 as the treatment benefits have only been demonstrated in animal models at this time.
- There are potential and unknown risks with AXO-AAV-GM1. Children are also required to take immune suppressive medicines to allow gene therapy to work in the body. The study investigator can explain the potential risks associated with this study.

Who is conducting the study?

- The study is being conducted in partnership with the National Institutes of Health (NIH) and the National Human Genome Research Institute (NHGRI) under the leadership of the Principal Investigator Cynthia J. Tifft MD, PhD.

Where will the study take place? What types of travel/accommodation support are provided to families whose child is enrolled in the study?

- Clinical trial visits will be conducted in person at the NIH Clinical Center in Maryland in the US. Following AXO-AAV-GM1 administration, patients will need to remain near the study site at least 1 month following treatment and will return to the site periodically for five years to undergo various tests and medical exams to continue to monitor safety and efficacy (how well the product works).
- If you are not local to the study site, a company will coordinate your travel and accommodations. Eligible and appropriate expenses incurred while at the study site for clinical trial visits such as flights, accommodations, driving/mileage, tolls/parking, rental cars, public transportation/taxi, meals/food will be covered. Details related to the amount covered will be discussed with you prior to the initial screening visit.

Are patients from outside the US eligible?

- Yes, patients from outside the US are eligible. Several patients enrolled in the trial are from outside the US.

Who should I contact if I'm interested in having my child participate in the trial?

- Please discuss the eligibility criteria with your child's physician and for more information, contact the Clinical Research Coordinator at the study site, Jean Johnston RN, MS *johnstonjm@mail.nih.gov*
- To learn more about AXO-AAV-GM1 or gene therapy, please contact Sio Gene Therapies at *patients@siogtx.com*

Where can I find more information on GM1 gangliosidosis?

- Global patient organizations such as the ones below have many helpful disease related resources.

NTSAD
National Tay-Sachs & Allied Diseases Association, Inc.

CURE GM1 FOUNDATION