Protocol Number: INS1202-101 V2.0, 17 Oct 2025 **US Study Number:** NCT07290062
Full Study Title: A Phase 1, Multicenter, Open-label, Dose-Finding Study to Investigate the Safety and Pharmacodynamics of a Single Intrathecal Injection of INS1202 in Patients With Amyotrophic Lateral Sclerosis

Why is the study being done?

Researchers are looking for different ways to treat people with **amyotrophic lateral sclerosis (ALS)**.

ALS is a condition that affects certain nerve cells called **motor neurons** in the brain and spinal cord. Motor neurons are important cells that send signals to control muscle movement throughout the body. In people with ALS, motor neurons gradually die over time, causing muscles to become weak and eventually stop working properly. This muscle weakness leads to difficulty walking, speaking, eating, and breathing. It is a progressive disease, which means that it gets worse with time.

Genes are small pieces of DNA that provide instructions to the cells of the body.

ALS in some people is caused by a defect in a **gene** called **superoxide dismutase 1 (SOD1)**. The SOD1 gene contains information to make SOD1 protein which helps protect cell components from damage. However, a defect in the SOD1 gene leads to an abnormal form of SOD1 protein. This abnormal protein may lead to the death of motor neurons and causes the condition. Sporadic ALS occurs in people who do not have gene changes that cause the disease. The SOD1 protein may also fold abnormally and build up in these people who do not have changes in the SOD1 gene for reasons that are not yet fully understood.

The treatments currently approved to treat ALS may not work for everyone. That is why researchers are testing a new experimental medicine called **INS1202**.

INS1202 is a type of **gene therapy** designed to help treat ALS. It works by delivering genetic material to the nerve and glial (support) cells by using a viral vector. This may reduce the abnormal SOD1 proteins that damage motor neurons in ALS and may help slow the worsening of ALS. INS1202 is given as a single injection into the spinal fluid, also known as an intrathecal (IT) injection.

Gene therapy changes how genes work inside cells. This can include modifying faulty genes, replacing missing genes, or adding new genes to help treat or prevent diseases. A viral vector is given as part of a treatment to deliver the gene to the target cells in the body.

What are the objectives and endpoints of the study?

MAIN

Objective: To learn about the safety of INS1202 in participants with ALS when given as an IT injection.
Endpoints:
- How often do participants have side effects and how severe are they?
- How often do participants have **side effects that are of special interest**?
- How often do participants have **serious side effects**?

SECONDARY

Objective: To find out the best dose to use in the next phases of studies with INS1202.
Endpoint: What is the **recommended** dose of INS1202 that could be used for next phases of the study?

Objective: To check the **viral vector shedding** after participants receive an IT injection.
Endpoint: How much of the vector can be found in the blood, urine, stool, and saliva at Weeks 1, 2, 4, 16, and 32 after treatment?

GLOSSARY

- **Side effects of special interest** are those that the researchers think may be common in people with ALS or have been commonly observed in gene therapies.
- **Serious side effects** are the ones that may cause death, threaten life, cause ongoing health problems, or need a hospital stay or a longer stay in hospital disability, or birth defects.
- **Recommended** dose is the amount of medicine that researchers observe to work well while remaining safe and well tolerated, based on safety information from the study.
- **Viral vector shedding** is a process in which small amounts of a viral vector may leave the body after treatment. This can happen through fluids like blood, urine, saliva, or stool. Researchers carefully monitor viral shedding in clinical studies to understand how long the viral particles stay in the body and to ensure the treatment is safe.

How is the study designed?

There are many types of clinical studies. This study will be:

Phase 1

In a Phase 1 study, a new treatment is tested in a small number of participants. Researchers check its safety and how the treatment works in the body.

Open label

Both the researchers and participants will know the drug and dose that the participants will receive.

Who can enroll in the study?

About **23 people**, with up to a maximum of 32 people with ALS who are between 18 to 79 years of age can enroll in the study. Participants must have had ALS for 42 months or less. Some participants must have an abnormal SOD1 gene and some participants cannot have any known ALS causing abnormal gene.

For a full list of requirements, please contact the study doctor.

How will the study be done?

The study will have 4 periods as noted in the table below.

SCREENING	STUDY TREATMENT	AFTER TREATMENT	LONG-TERM EXTENSION
About 3 clinic visits	Single dose of INS1202 by IT injection 1 clinic visit and in-hospital stay	13 clinic visits	8 clinic visits
Up to 45 days	2 days	48 weeks	4 years

About 5 years and up to 25 clinic visits

Initially, participants will be screened to make sure they are a good fit for the study. The study will include 3 groups of participants. Researchers will test different doses of INS1202 in each group of participants with ALS including those who have SOD1 defective gene and participants that have no known ALS related genetic defects.

On Day 1, participants in the first group will receive a **single dose of INS1202 by IT injection**. Based on the data review from the first group, a team of medical experts will decide whether to continue the study with the next group of participants. A similar process will be used for the next group of participants. Researchers will carefully observe the safety information in the first group for 30 days before moving on to the next group of participants. During the study, participants will have blood tests, urine tests, physical exams, and tests to check how their muscles and nerves are working. Participants will be followed up to check their safety, and how well the medicine works for 48 weeks. After completing the visit at Week 48, participants will be required to enroll in a long-term follow-up study to learn more about the safety of INS1202 for an additional 4 years.

Testing and Monitoring

In addition to a physical exam, participants will have the following tests and procedures:

- Blood and urine tests
- Stool tests
- Saliva tests
- Imaging tests
- Heart tests
- Spinal fluid sample test
- Questions about health and quality of life

What are the potential benefits and risks of enrolling in this clinical study?

The possible benefit of INS1202 for each participant is that it may help slow down ALS. Participants and their caregivers may also benefit by knowing that they are helping researchers learn more about possible treatments for ALS.

However, there are possible risks to being in any clinical study. One risk is that the study drug may not help treat ALS, or it may make the condition worse. Another risk is that there may be side effects from receiving INS1202. Possible side effects include:


Allergic reaction


Liver injury


Small clots in blood vessels


Problems with nerves near the spine


Immune system reaction against vector (Immune system is the body's germ fighting system)


Decrease in platelet count (Platelets are components that help the blood to clot)

Participants may experience other side effects or may not have any side effects.

Insmed Incorporated
New Jersey, USA