INSPIRE

A clinical trial of investigational AT-007 in people 16 and older living with Sorbitol Dehydrogenase (SORD) Deficiency

APPLIED THERAPEUTICS

What You Need to Know About the INSPIRE Clinical Trial of AT-007 in People Living With SORD Deficiency

The INSPIRE clinical trial is currently enrolling eligible participants to study investigational AT-007 for the treatment of SORD Deficiency. If you think you may have SORD Deficiency, consider asking about enrolling in the INSPIRE clinical trial.

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What is SORD Deficiency?

Sorbitol Dehydrogenase (SORD) Deficiency is a recently discovered rare, progressive genetic disease.[1]

SORD Deficiency affects approximately 1 in every 100,000 people.[2] In the United States, it is estimated that there are approximately 3,300 individuals living with this disease.[3]

People with SORD Deficiency are missing a key enzyme needed to process a substance known as sorbitol.[2,4] Sorbitol is a form of sugar found in many foods, drinks, and even certain medications.[5]

In healthy individuals, the body converts sorbitol into fructose for energy.[4] Without the necessary enzyme, when sorbitol is not able to be converted by the body, it builds up and damages cells and tissues.[2,4] This results in significant muscle weakness, numbness, pain, and disability.[2]

Before the recent discovery of the SORD gene and based on their symptoms, people living with SORD Deficiency were diagnosed based on their symptoms as having Charcot-Marie-Tooth disease type 2 (CMT2) or distal hereditary motor neuropathy (dHMN).[2]

Currently, there are no approved treatments for people living with SORD Deficiency. However, a SORD genetic test is now available, and a clinical trial of an investigational new treatment is currently enrolling.

The U.S. Food and Drug Administration (FDA) has authorized AT-007 for investigational use only. AT-007 has not been approved to treat SORD Deficiency or any other disease.

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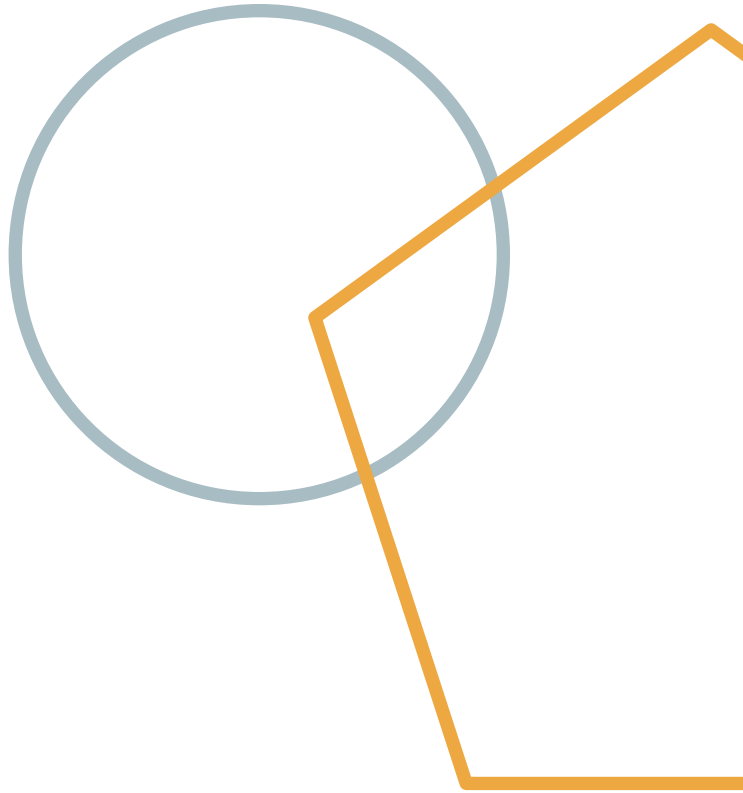
What do I need to know about AT-007?

AT-007 is an investigational drug being studied in those living with SORD Deficiency, specifically designed to inhibit (or “turn off”) the enzyme Aldose Reductase. Aldose Reductase converts glucose, a type of sugar you get from foods you eat, into sorbitol in the body. In people living with SORD Deficiency, sorbitol builds up and becomes toxic to the body.

In an earlier, smaller clinical trial in people with SORD Deficiency, AT-007 demonstrated a favorable safety profile and reduced levels of sorbitol in the body.

AT-007 is taken once a day and is an oral suspension.



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What do I need to know about the clinical trial of AT-007 in SORD Deficiency?

This trial is designed to investigate the ability of AT-007 versus placebo to reduce toxic sorbitol levels, and to evaluate the effect of AT-007 on improving symptoms of the disease over a longer period of time.

Data will be collected, handled, and processed in compliance with applicable regulatory guidelines. Participant data will not be shared with anyone other than in circumstances that will be explained on the consent form.

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How can I or my loved one participate in the trial? Who do I contact?

This trial is enrolling up to 72 participants between the ages of 16 and 55 with SORD Deficiency.

Participants will need to have a genetic confirmation of SORD Deficiency and elevated sorbitol levels. Genetic testing for SORD Deficiency will be provided at no charge to those potentially eligible for the trial. Participants must be between 16 to 55 years of age and have no significant health problems (other than SORD Deficiency) that could prevent their participation in the trial. Female participants must not be pregnant or lactating. Female and male participants must agree to use a form of birth control until 30 days after the end of the study.

The trial team will ask potential participants about their medical history and will also gather information from their medical records to see if they qualify for this trial. This process may take a few days, and the trial team will explain what to expect in terms of timeline and next steps.

For more information about additional trial eligibility requirements or to inquire about participating in the trial of AT-007 in SORD Deficiency, please email SORD@appliedtherapeutics.com.

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Where is the nearest participating doctor or center?

The trial of AT-007 will be conducted through home health visits and at sites in the United States or Europe.

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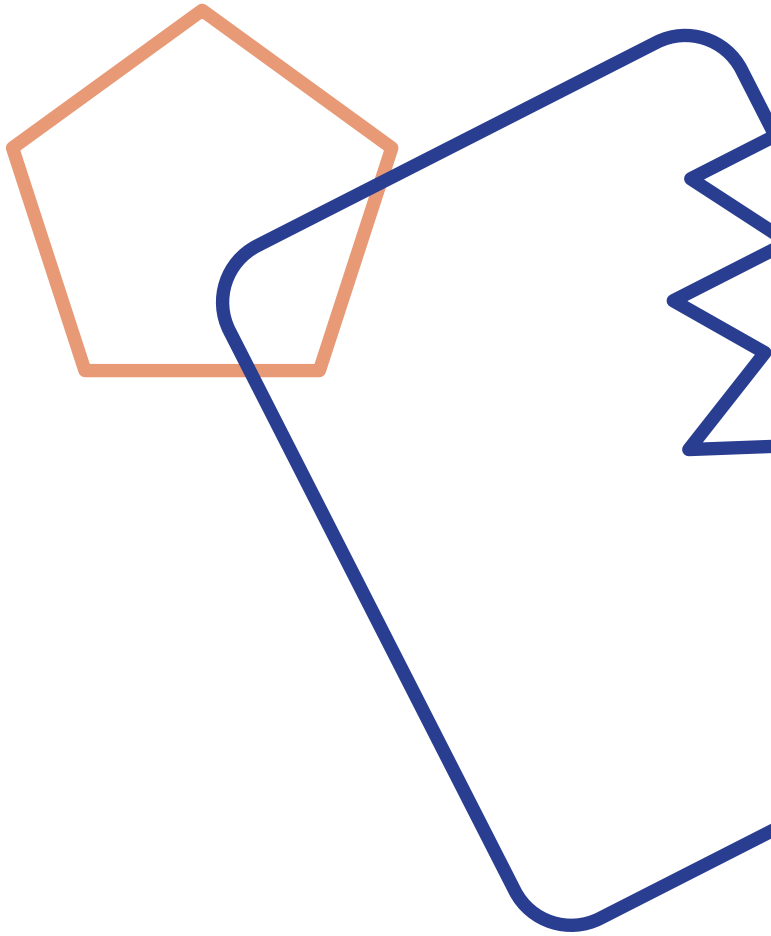

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What do I need to know before taking AT-007?

Participants will first be provided additional details about the trial, including the potential risks and benefits. Participants are encouraged to ask questions and make sure they understand the trial requirements before agreeing to participate.

To help determine eligibility, participants will be seen by a healthcare team that will review medical history, perform blood and urine tests, conduct a physical exam, and verify a diagnosis of SORD Deficiency.

While participating in the clinical trial, participants will still see their regular doctors. The trial healthcare team will monitor each participant's progress throughout the trial. Participants are free to leave the trial at any point, which will not impact their care.

Participants will also continue on their current medications as AT-007 is being evaluated as a treatment for SORD Deficiency in addition to currently used medications.

For any additional questions about the trial of AT-007 in SORD Deficiency, please email **SORD@appliedtherapeutics.com**.

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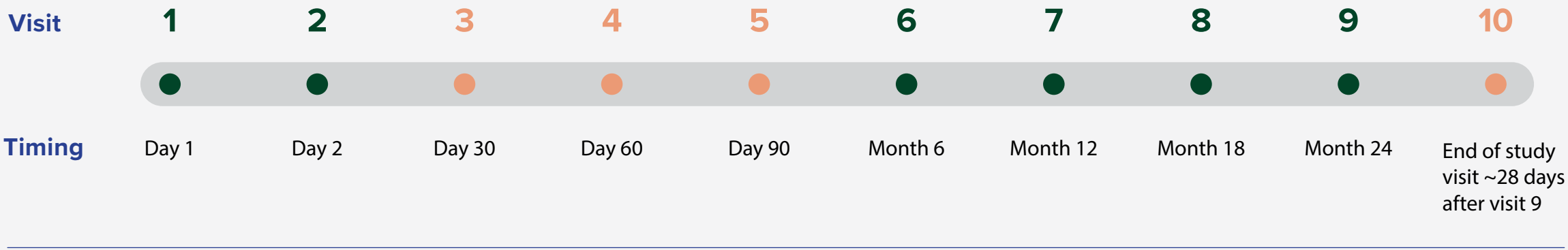
What types of tests will I or my loved one have to take, and how often?

Trial staff will work with each participant to coordinate these visits within their schedule and may be able to aid with transportation to the trial site.

The healthcare team will routinely ask participants about their experience during the trial. They will also conduct regular health assessments that will include medical evaluations, physical examinations, and samples of blood and urine.

10 VISITS OVER 24 MONTHS



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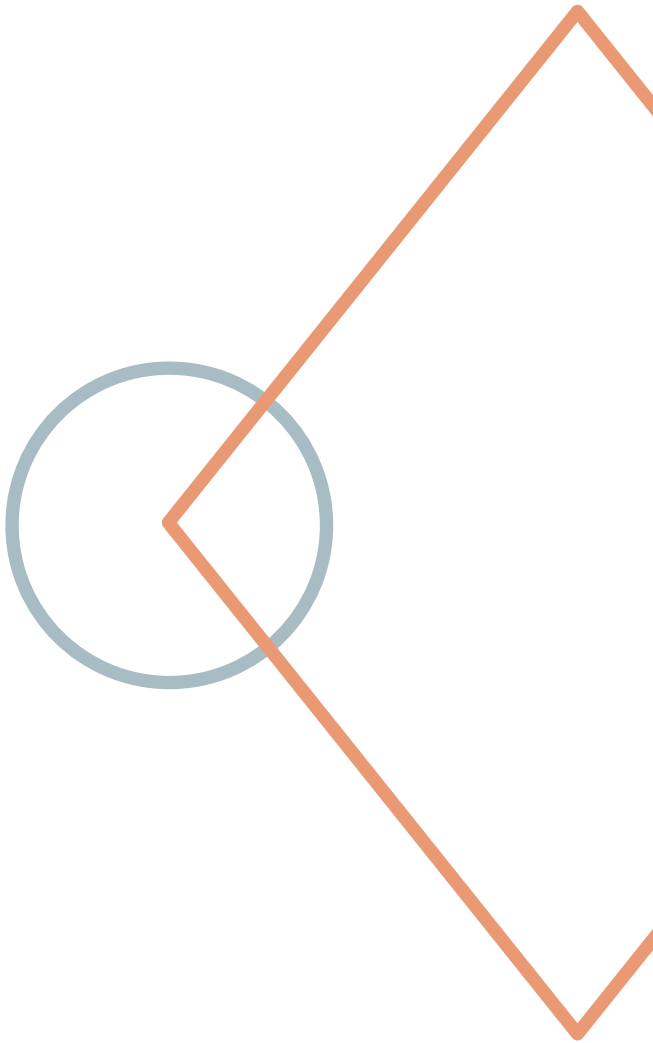
Could I receive a placebo (no active drug in the medicine) in this trial?

Yes, this is a placebo-controlled trial as required by the FDA. A placebo-controlled trial helps doctors determine how the trial drug performs compared to placebo. For every 2 participants who get the active drug, 1 participant will get placebo. The doctor and trial healthcare team will review the trial information with each participant, including what to expect and how participant progress will be monitored.

Participants who receive placebo treatment in the main study, will have the opportunity to transition to the open-label extension part of the study and receive AT-007 for 24 months.



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What are the goals of the INSPIRE clinical trial?

The objectives of this clinical trial include understanding the ability of AT-007 to reduce sorbitol levels and determining the impact AT-007 has on SORD Deficiency clinical symptoms and outcomes.

This clinical trial is supported by doctors, nurses, and other healthcare professionals. The commitment of each participant and the entire study team is important to help meet the objectives of the clinical trial. This trial follows strict ethical and governmental guidelines to ensure that participants' rights are protected while the information is being collected.

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How can I learn more about participating in the INSPIRE clinical trial of AT-007 in SORD Deficiency?

Email: SORD@appliedtherapeutics.com

References:

1. Applied Therapeutics. What is SORD deficiency? Accessed March 2, 2022. https://www.appliedtherapeutics.com/patients-caregivers/sord-deficiency/
2. Cortese A, Zhu Y, Rebelo AP, et al. Biallelic mutations in SORD cause a common and potentially treatable hereditary neuropathy with implications for diabetes. *Nat Genet* 52(5):473-481. https://doi.org/10.1038/s41588-020-0615-4
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4. Morava, E. Elevated sorbitol underlies a heritable neuropathy. *Nat Genet* 2020;52(5):469-470. https://www.nature.com/articles/s41588-020-0619-0
5. National Center for Biotechnology Information. PubChem compound summary for CID 5780, sorbitol. Accessed March 2, 2022. https://pubchem.ncbi.nlm.nih.gov/compound/Sorbitol

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