If you have a diagnosis of Alpha-1 Antitrypsin Deficiency–Associated Liver Disease or have a family history of the condition, The Redwood Study may be an option. To learn more, talk to your doctor and visit **TheRedwoodLiverStudy.com** today.

WHAT YOU SHOULD KNOW ABOUT CLINICAL RESEARCH STUDIES

Clinical research studies aim to answer specific questions about how medicines work in the volunteers who take them. You should feel fully informed about what to expect from participation in a clinical research study.

Researchers use clinical research studies to:

- Answer specific health questions
- Learn about the effects and safety of investigational drugs
- Help find new ways of using approved medications

Regulations and policies have been developed to help protect the rights, safety, and well-being of people who take part in clinical research studies and to help ensure that these studies are conducted according to strict scientific and ethical principles. Before a clinical research study can begin, an institutional review board (IRB) or ethics committee (EC) must review and approve the study.

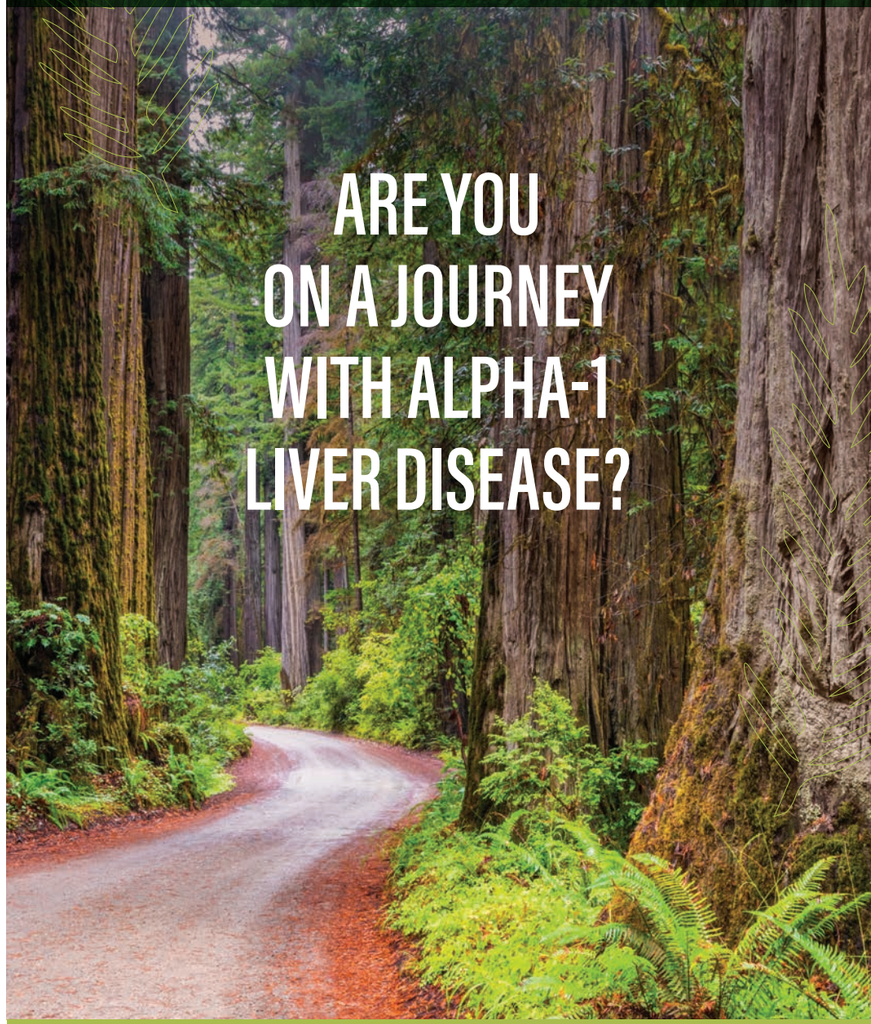
Participation in any clinical research study is completely voluntary, and you may withdraw from the study at any time for any reason. Before volunteering for a clinical research study, it is important to weigh the potential risks and benefits of participation, which the study team will inform you of, as well as possible side effects. To make an informed decision, gather as much information as possible and talk to your healthcare providers about any questions you may have.

Visit **TheRedwoodLiverStudy.com** for more information.

Thank you for considering The Redwood Study.

TAK-999-3001_RecruitmentBrochure_V2.0_10OCT2024

A CLINICAL RESEARCH STUDY FOR ALPHA-1 ANTITRYPSIN DEFICIENCY-ASSOCIATED LIVER DISEASE



ARE YOU ON A JOURNEY WITH ALPHA-1 LIVER DISEASE?

TheRedwoodLiverStudy.com

The Redwood Study

EXPLORE A NEW PATH FOR ALPHA-1 LIVER DISEASE

Alpha-1 Antitrypsin Deficiency (AATD) is an inherited condition that can cause damage to the liver and/or the lungs.[1] Liver disease associated with AATD is caused by abnormal AAT protein building up in the liver.[2] This causes the liver to become damaged because it cannot break down the protein, which can lead to scarring (also called fibrosis), and that may progress to cirrhosis, a late stage of scarring of the liver, potentially necessitating a liver transplant.[2,3,4,5]

If you're living with Alpha-1 Liver Disease, or if it runs in your family, then you may know that currently there is no approved treatment option for this condition.[6] While the disease is passed down from parents to their children, environmental exposures or other factors can affect if, and to what degree, it progresses. Right now, research is underway to help find a potential treatment for Alpha-1 Liver Disease. No matter where you are in your journey with this condition, you may be able to take part.

If you are interested, a participating research site can confirm a diagnosis of Alpha-1 Liver Disease, as well as other study criteria, to determine your eligibility.

1. Brantly M, et al. Orphanet J Rare Dis 2020;15:96
2. Piccolo P, et al. In: Strnad P, et al (eds). α1-Antitrypsin Deficiency (ERS) Monograph, 93–104. Sheffield: ERS, 2019.
3. Patel D, et al., Clin Liver Dis 2018;22(4):643–655
4. Liedtke C, et al. Front Med (Lausanne) 2022;8:814496.
5. nejm.org/doi/full/10.1056/NEJMoa2205416
6. alpha1.org/newly-diagnosed/learning-about-alpha-1/liver-disease

WHO MAY QUALIFY?

If you are between 18 and 75 years of age, and you or any of your family members have a confirmed or suspected diagnosis of Alpha-1 Liver Disease (AATD-LD with the PiZZ mutation), you may be eligible for this study.

ABOUT THE REDWOOD STUDY

- The purpose of the study is to evaluate the safety and effectiveness of an investigational study drug, called TAK-999 (fazirsiran), in adults 18 to 75 years of age with Alpha-1 Liver Disease.
- The investigational study drug will be compared to a placebo, which may look just like the investigational study drug but contains no active medication.
- Participants will be randomly assigned to receive either the investigational study drug or the placebo. The assigned study treatment will be administered as injections.

Participation in The Redwood Study will last up to approximately four and a half years and consists of three periods:

- **Screening period:** Lasts up to 10 weeks and consists of one or more study visits. During this period, the study team will perform tests and procedures to determine your eligibility for the study. The study team can confirm a diagnosis of Alpha-1 Liver Disease during this period.
- **Treatment period:** Lasts up to four years and consists of up to 20 visits to the study site. During the first year of the study, there will be monthly phone calls between visits. Participants will be randomized to receive the investigational study drug or the placebo. Both the investigational study drug and the placebo are administered as injections.
- **Safety follow-up period:** Participants will be followed for up to six months with two study site visits after their last dose of their study treatment for continued monitoring of their health.
- At certain visits during the study, the study team will perform tests and procedures such as physical examinations, blood and urine sample collections, liver biopsies, and pulmonary function tests. Participants will also answer questions about their health and any medications they are taking.

ABOUT THE INVESTIGATIONAL STUDY DRUG

There is currently no approved treatment available for Alpha-1 Liver Disease. The investigational study drug being tested in this clinical research study aims to reduce the production of the abnormal Z-AAT protein and its buildup in the liver. The reduction in levels of the protein may result in a decrease in liver scarring.

SEE IF YOU MAY QUALIFY

To learn more and see if you qualify, talk to your doctor, contact the participating research site listed below, or visit **TheRedwoodLiverStudy.com**.