Unleashing the power of gene therapy to **correct the code**

A Potential Treatment for Transforming Alpha-1 Antitrypsin Deficiency (AATD, or Alpha-1)

For people who have Alpha-1-associated lung and/or liver disease

YOUR GUIDE TO THE BTX-302-001 (BEAM-302) CLINICAL STUDY

Thank You for Your Interest in the BEAM-302 Clinical Study

With the help of potential study participants like you, new and improved treatments for Alpha-1 may be discovered and help to improve patients' lives.

Who We Are

We are Beam Therapeutics Inc, founded in 2017 to develop advanced precision genetic medicines. Our vision is to provide lifelong cures for people suffering from serious diseases. To achieve that, we have built a strong, values-driven company focused on people, advancing cutting-edge science, and developing a new class of of genetic medicines.

Alpha-1 is a genetic condition that can lead to lung and/or liver disease, and there is an unmet need for new treatments. In addition, because people who have Alpha-1 may experience both lung disease and liver disease, there is an especially high need for treatments that can address both diseases.

Beam THERAPEUTICS

With the BEAM-302 Clinical Study, a potential treatment may be possible for people who have Alpha-1.

Facts About Alpha-1

What is the AAT protein?

- Alpha-1 antitrypsin (AAT) is a protein made mostly in the liver. The AAT protein is a protease inhibitor, which is referred to as *Pi*. This protein normally circulates through the bloodstream to the lungs
- A key role of the AAT protein is to balance the activity of other proteins, called proteases, in the lungs
- Proteases are enzymes that help our immune cells fight infections, but if there is too much protease activity, it can damage the lungs

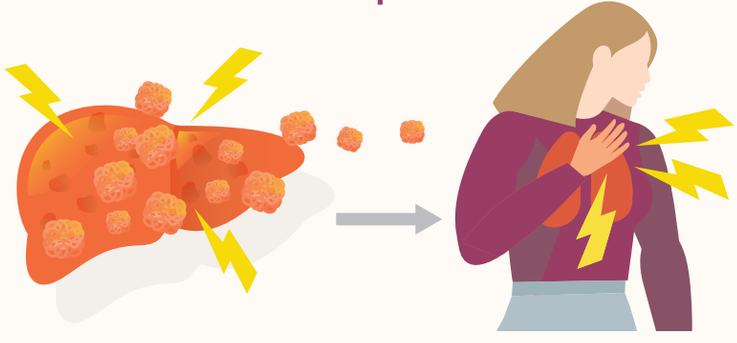
What is Alpha-1?

Alpha-1 antitrypsin deficiency

- is an inherited rare genetic condition
- affects the shape of AAT proteins so that they clump together, build up in the liver, and are not secreted properly. These problems lead to a decreased level of AAT protein in the bloodstream
- can lead to lung and/or liver disease

The main function of AAT protein is to block proteases and protect the lungs from uncontrolled inflammation and breakdown of the lung tissue, which can potentially lead to emphysema.

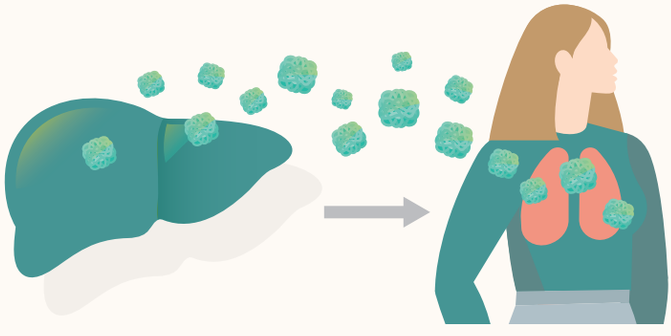
With Alpha-1



Abnormal PiZ AAT aggregates in the liver, causing damage

Lack of AAT secretion leads to lung damage

Without Alpha-1



AAT protein is secreted from liver, protecting lungs

Facts About Alpha-1 *(cont'd)*

How is Alpha-1 inherited?

The *SERPINA1* gene provides the instructions for producing AAT protein

- Mutations or changes in the *SERPINA1* gene reduce the amount of functional AAT protein

Our genes are passed from one generation to the next, and each parent provides one copy of the *SERPINA1* gene.

The *SERPINA1* gene can have several different variants. The normal variant is called PiM. Other variants include PiS and PiZ, both of which inhibit the production of functional AAT protein.

- PiZ, which is the most common variant, produces an abnormal protein that gets stuck in the liver and is poorly secreted, leading to very little functional AAT protein in the bloodstream
- Therefore, individuals with two PiZ variants (PiZZ), one from each parent, typically have the most severe presentation of Alpha-1

How is testing for Alpha-1 performed?

Alpha-1 can be diagnosed by a simple blood test that measures the AAT protein level. If the level is lower than normal, genetic testing of the *SERPINA1* gene can determine the causative variants.

Liver and lung imaging and lung function tests may also be performed to assess disease severity and organ function.

The **BEAM-302** Clinical Study

Clinical trials offer opportunities for study participants to partner with researchers to help develop potentially new treatments for diseases.

Purpose

The BEAM-302 Clinical Study is a phase 1/2 study to evaluate the safety and optimal dose of a potential new therapy for the treatment of alpha-1 (PiZZ)-associated lung disease (part A) and liver disease (part B). The investigation therapy is called BEAM-302.

Goals

The goals of the BEAM-302 Clinical Study are to learn

- more about the safety and potential side effects of BEAM-302
- how BEAM-302 is processed and eliminated by the body
- if BEAM-302 can increase the amount of corrected functional AAT protein and decrease the amount of abnormal AAT protein in the bloodstream
- more about the optimal dose of BEAM-302 for future studies

About Base Editing and **BEAM-302**

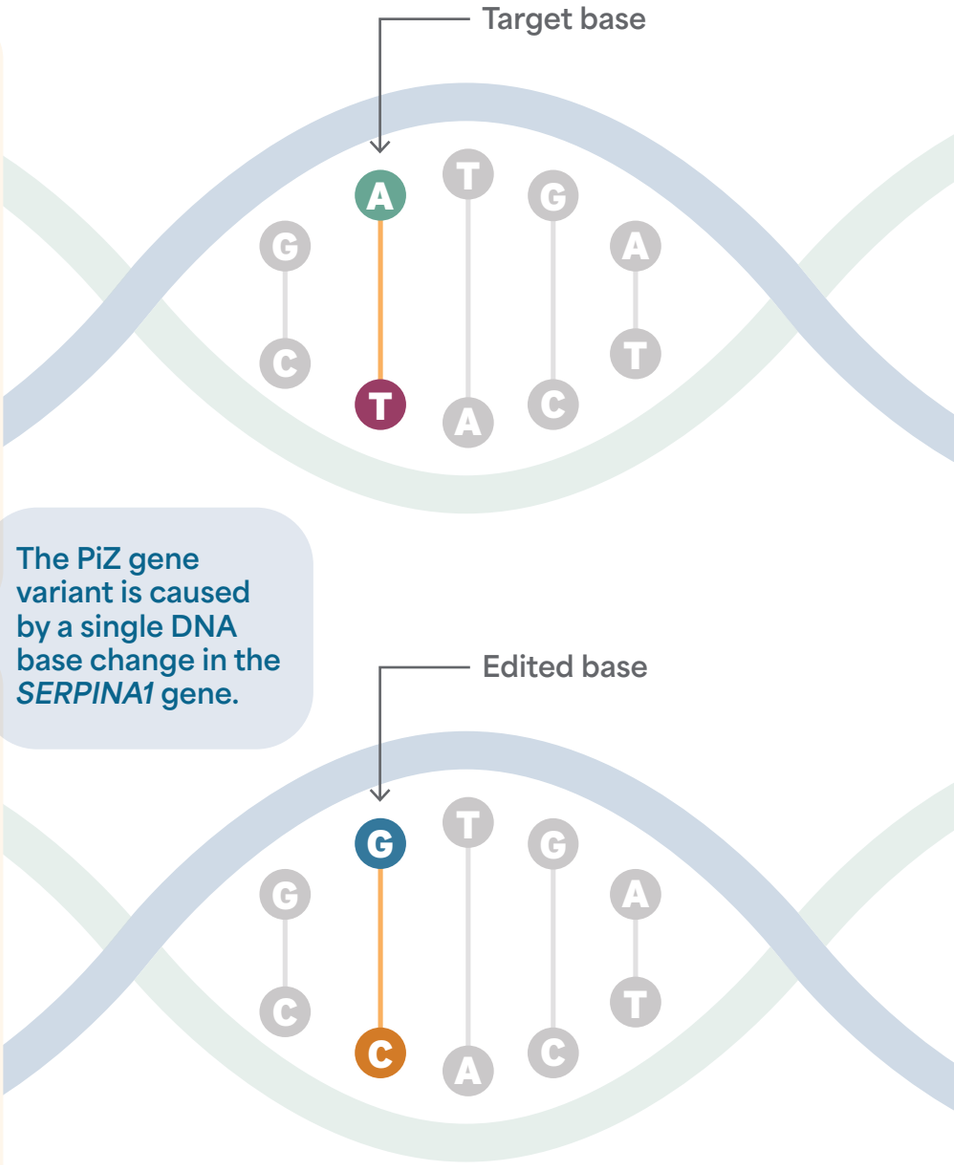
What is a DNA base?

The foundational unit of your genetic information is a single DNA base. These bases pair up in a specific way and form sequences that spell out the genetic information carried in your DNA, much like letters of the alphabet are sequenced to form the words in a language. A change to a single base can mean the difference between health and disease.

Base-editing technology

Base-editing therapies are an emerging new class of **precision genetic** medicines designed to overcome the limitations of existing therapies.

Base editors can change and rewrite a single base in your DNA. That very basic change can potentially treat a wide range of conditions.



The PiZ gene variant is caused by a single DNA base change in the *SERPINA1* gene.

How does BEAM-302* work?

Through base editing, BEAM-302 is designed to correct the PiZ variant in the *SERPINA1* gene associated with Alpha-1.

- BEAM-302 is administered through an intravenous infusion and travels to the liver
- If the gene is corrected, the liver will no longer produce or accumulate abnormal AAT protein
- From that point on, normal AAT protein can be produced and circulate from the liver to the lungs, where it can protect the lungs from any imbalances of protease enzymes

*BEAM-302 is an investigational drug because it is not approved by the US Food and Drug administration, European Medicines Agency, or any other regulatory authority.

Taking part in the **BEAM-302** Clinical Study

How is the BEAM-302 Clinical Study being conducted?

BEAM-302 therapy will be studied

- in up to 106 participants aged 18 to 70 years who have lung disease (part A) or lung and liver disease (part B) caused by PiZZ
- at approximately 15 study sites around the world
- in 16 visits over approximately 2 years with 1 hospital stay lasting 2 to 5 days
- in a separate additional 13-year study, with minimal requirements, to provide insights into any possible long-term side effects of BEAM-302

Do I qualify to participate?

Individuals between the ages of 18 and 70 years who have a confirmed genetic (PiZZ) diagnosis of Alpha-1 may be eligible to participate. Participation is voluntary and can be stopped at any time. To learn more about the BEAM-302 Clinical Study, including the exclusion and inclusion criteria, contact clinicalinfo@beamtx.com.

What should I expect?

During study visits, you will undergo certain procedures and tests both before and after you receive the BEAM-302 intravenous infusion. Some of these tests and procedures include the following:


A physical exam


Blood and urine collection for laboratory testing


An electrocardiogram, or ECG, to measure the electrical activity of your heart


Lung functioning and imaging tests


Liver imaging tests


Questionnaires to assess any symptoms of Alpha-1 and your quality of life

Do I have to go to the study site for all visits?

You may have the option of participating in some of the study visits at home. A visiting nurse may come to your home to take blood and urine samples and check your overall health.

Are there any costs related to the clinical study covered?

Your approved travel expenses, and those of your caregiver, to and from the study site may be covered. You will not be charged for the study drug or for any of the tests that you undergo in association with this study. The study sponsor will not pay for routine care or doctor visits that are not part of this study.

What are the potential risks and benefits if I participate in this study?

- BEAM-302 may help treat your Alpha-1, halting its progression. It is also possible that your health may worsen or stay the same
- Your participation in this study will help doctors learn more about BEAM-302 and Alpha-1. This knowledge may benefit people in the future who have the condition
- Every clinical trial studying investigational treatments may have risks associated with it. It is important to understand these risks before consenting to participate in a clinical trial

Your health and safety will be closely monitored throughout the study. The safety of study participants is our top priority.

Quiz

The following **true-or-false** questions were created to help you assess your understanding of the information contained in this brochure. They may also spark questions that you may have for your healthcare team.

1	Genetic diseases are always caused by large deletions in DNA.	☐ TRUE	☐ FALSE
2	The Beam-302 Clinical Study is for individuals who have Alpha-1 caused by PiZZ.	☐ TRUE	☐ FALSE
3	The Beam-302 Clinical Study is designed only for people who have Alpha-1-associated lung disease.	☐ TRUE	☐ FALSE
4	The initial study takes 5 years to complete.	☐ TRUE	☐ FALSE
5	Some of the study visits may be able to occur in the home.	☐ TRUE	☐ FALSE
6	You can ask questions only during the consent process.	☐ TRUE	☐ FALSE

Please see the answer key on the back cover

Thank you for considering joining us!

Together, we can learn more about the potential for new and improved therapies for people living with Alpha-1.

For more information, send an email to: clinicalinfo@beamtx.com.

Search NCT06389877 on www.clinicaltrials.gov

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Answer Key

1. **False.** A change to a single base can mean the difference between health and disease.
2. **True.** Although other gene versions may be associated with an increased risk of liver or lung disease, the BEAM-302 Clinical Study is focused on PiZZ, the most severe genotype.
3. **False.** The BEAM-302 Clinical Study is investigating BEAM-302 in individuals who have either lung and/or liver disease.
4. **False.** The BEAM-302 Clinical Study will take approximately 2 years to complete.
5. **True.** A visiting nurse may come to your home to take blood and urine samples and check your overall health.
6. **False.** You are allowed to ask questions at any time throughout the entire clinical trial period. Do not hesitate to ask questions.