DO YOU HAVE A PATIENT WITH AATD-ASSOCIATED LIVER DISEASE?

The [redacted] Study is recruiting participants for a [redacted] phase 3 study to evaluate the safety and efficacy of [redacted] in adults 18 to 75 years of age with **Alpha-1 Antitrypsin Deficiency–Associated Liver Disease**, and METAVIR stage F2 to F4 fibrosis.

We invite you to refer any patients who may be eligible for this study.

About The [redacted] Study

Study Design
[redacted]

ClinicalTrials.Gov Identifier
NCT[redacted]

Recruitment Status
Active, recruiting

Estimated Enrollment
160 participants

Primary Objective

To evaluate the safety of [redacted] and if [redacted] reduces liver fibrosis compared to placebo in individuals with AATD-Associated Liver Disease.

Primary Outcome Measure

Reduction from baseline of at least 1 stage of histologic fibrosis (METAVIR staging) in centrally read liver biopsy at Week 106 in AATD-Associated Liver Disease with METAVIR stage F2 and F3 fibrosis.

Selected Secondary Outcome Measures

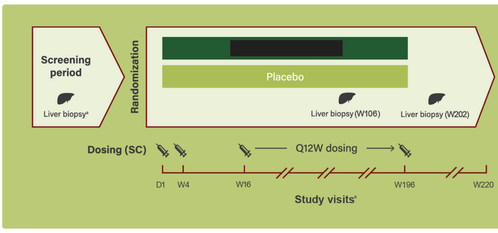
Change from baseline in:

- Intrahepatic Z-AAT protein (percent change) in Week 106 (F2–F3) and Week 202 (F2–F4)
- Serum Z-AAT protein at Week 202
- Intrahepatic Z-AAT protein polymer burden assessed by periodic acid-Schiff diastase (PAS+D) staining at Week 202
- Vibration-controlled transient elastography (VCTE)-derived liver stiffness at Week 202
- Intrahepatic portal inflammation at Week 202

Number of participants with:

- Reduction from baseline of at least 1 stage of histologic fibrosis (METAVIR staging) in centrally read liver biopsy at Week 202 (F2–F4)
- Liver-related clinical events up to Week 202
- Treatment-emergent adverse events (TEAEs) and serious TEAEs up to Week 220
- Clinically significant declines in lung function parameters up to Week 220
- Clinically significant changes in clinical laboratory assessments up to Week 220

Study Design



*Fibrosis evaluated by centrally read liver biopsy during the screening period or by central reading of previous biopsy within 6 months before estimated enrollment date.
Q12W = every 12 weeks; SC = subcutaneous

About the Investigational Study Drug

[redacted] is a GalNAc-based RNA interference (RNAi) investigational compound. [redacted] has not been approved for use by the U.S. Food and Drug Administration, the European Medicines Agency, or any other regulatory authorities. This information is intended for healthcare professionals.

Select Inclusion Criteria

- Have a diagnosis of the Pi*ZZ genotype AATD. Pi*ZZ diagnosis from source verifiable medical records is permitted. Otherwise, participants must undergo Pi*ZZ confirmatory testing (genotyping for Pi*S and Pi*Z alleles) at screening. Pi*MZ or Pi*SZ genotypes are not permitted.
- Be of any gender and aged 18 to 75 years, inclusive.
- Have evidence of METAVIR stage F2, F3, or F4 liver fibrosis, evaluated by a centrally read baseline liver biopsy during the screening period; or confirmed as meeting all the entry criteria by central reading of a previous biopsy conducted within 6 months before the estimated enrollment date using an adequate liver biopsy and slides as defined in the study laboratory manual.
- Be a nonsmoker for at least 6 months before screening with pulmonary status meeting the protocol's requirements.

Select Exclusion Criteria

- Have a history of liver decompensating events (overt hepatic encephalopathy [West Haven Grade ≥ 2] documented by a physician or healthcare professional, clinically significant ascites, spontaneous bacterial peritonitis, gastrointestinal bleeding from varices, hepatopulmonary syndrome, hepatorenal syndrome, portal pulmonary hypertension, or bleeding portal hypertensive gastropathy).
- Have evidence of chronic liver disease attributable to other diseases, including viral hepatitis B or C, primary biliary cholangitis, primary sclerosing cholangitis, Wilson disease, alcoholic hepatitis, hemochromatosis, liver cancer, history of biliary diversion, or autoimmune hepatitis.
- Have ALT or AST levels > 250 U/L.
- Have platelet count < 60,000 per mm^3 (< 60 x 10^9/L).
- Have albumin ≤ 2.8 g/dL.
- Have INR ≥ 1.7.
- Have had previous treatment with [redacted] or any other RNAi for AATD-Associated Liver Disease.

Additional eligibility criteria, according to approved protocol, apply.

Abbreviations:
AATD = AATD = Alpha-1 antitrypsin deficiency; ALT = alanine aminotransferase; AST = aspartate aminotransferase; INR = international normalized ratio; RNAi = RNA interference

References:
1. [redacted]
2. [redacted]

[redacted]