WHISTLE-PF
PULMONARY FIBROSIS

Your Guide to Participating in a New Clinical Trial for Patients With Idiopathic Pulmonary Fibrosis

WHISTLE-PF

The WHISTLE-PF Clinical Trial

The WHISTLE-PF clinical trial stands for Wound-Remodelling Hedgehog-Inhibitor ILD Study Testing Lung Function Endpoints. It is a Phase 2b clinical trial testing an investigational treatment, called ENV-101, for idiopathic pulmonary fibrosis (IPF). The trial will further evaluate the therapeutic potential of ENV-101 in individuals with IPF.

Idiopathic Pulmonary Fibrosis

IPF is a lung disease that causes progressive scarring in the lungs, leading to shortness of breath and persistent cough. This disease can worsen over time, which may make it harder for lungs to get oxygen, to breathe and to take deep breaths. This may affect a person's overall quality of life.

Current treatments may help slow the progress of IPF in some people, but they do not stop or reverse it. Individuals living with IPF could benefit from new treatment options that go beyond slowing disease progression to reverse lung fibrosis and improve lung function.

ENV-101

ENV-101 is an oral trial medication being investigated by a company called Endeavor BioMedicines, Inc. to treat fibrotic lung diseases, starting with IPF. ENV-101 blocks a protein in the body that is thought to be involved in lung scarring. By blocking this process, ENV-101 may slow or reverse the disease, which may improve the symptoms of IPF. Researchers previously evaluated ENV-101 in 21 individuals with IPF. Participants in this Phase 2a trial took a 200 mg oral dose of ENV-101 once a day for up to 12 weeks. More information about this trial and the results is available at endeavorbiomedicines.com.

WHISTLE-PF **TRIAL DESIGN**

Medications, drugs and devices have to be approved for use by regulatory agencies in many countries. ENV-101 is an experimental treatment, which means that it has not been approved by regulatory agencies as a treatment for IPF.

A detailed description of the WHISTLE-PF trial has been reviewed by an independent group of doctors, scientists and non-medical experts called an Institutional Review Board (IRB) or Ethics Committee (EC). This is to ensure the rights of trial participants are protected.

The WHISTLE-PF trial is a randomized double-blind trial. This means that neither you nor your trial doctor will know whether you are receiving active trial medication (or which dose) or placebo. Participants taking part in the trial will have a three out of four chance of receiving the active trial medication and a one out of four chance of receiving a placebo. A placebo is a medication with no active ingredients. It looks like the ENV-101 tablets but does not contain the active medication. If you receive the active trial medication, you will be randomly assigned to one of three dose levels: low, medium or high dose.

SCHEDULE OF **EVENTS**

This trial has three main periods: the screening period, the trial treatment period and the follow-up period.

Screening period (28 days)

During the WHISTLE-PF trial screening period, your doctor will explain the trial and any potential risks. The screening period will last up to 28 days. During the screening period, researchers will conduct assessments to determine if the trial is suitable for you. In addition to a thorough review of your medical history and performing various safety assessments (physical exam, vital signs, electrocardiograms (ECG), laboratory testing, etc.), the following assessments will also be performed:

- **Spirometry** — a measurement of how well your lungs are working, the size of your lungs, the volume of air in your lungs and the amount of air you breathe in and out. These tests involve taking a full breath in and then blowing out as hard and fast as possible while measurements are taken.

- **DLCO (diffusing capacity of carbon monoxide)** — a measurement of how well oxygen is transferred from your lungs to your bloodstream. Similar to spirometry, these tests involve taking a full breath in and then blowing out as hard and fast as possible while measurements are taken.

- **High resolution computerized tomography (HRCT) scan** — researchers use these scans to capture images of the lungs.

Treatment period (24 weeks)

If the WHISTLE-PF trial is suitable for you and you decide to participate, you will enter the treatment period. This period will last for approximately 24 weeks and you will receive the trial medication or placebo during this time. The trial staff will administer the active trial medication or placebo to you on Day 1 and you will be sent home with sufficient supply to last until your next monthly trial visit.

You will take two tablets once daily for approximately 24 weeks. The trial staff will explain how you should take them, and you should try to take them at the same time each day. You will also be given a dosing diary, where you will record the doses you have taken.

During the treatment period, you will have a total of seven trial visits at the clinic and one visit via telephone. Various safety assessments are performed at these trial visits, similar to the screening period. At each visit, the trial staff will review your dosing diary to see if you have been taking your trial medication as previously discussed and ask you about how you are feeling and any medications that you may be taking.

Follow-up period (2 weeks)

The follow-up period will last for two weeks and during this period you will no longer receive any trial medication. You will come back to the clinic two weeks after the last dose of trial medication so the trial staff can assess your health.

QUESTIONS ABOUT THE WHISTLE-PF TRIAL

How long will I be in this trial?

Your participation in the trial could be up to 30 weeks, which includes screening, treatment and follow-up periods.

Can I continue to take my other prescribed medicines?

It's important to tell your trial doctor about all of the medications that you have been taking for at least 30 days before you take part in the WHISTLE-PF trial. This includes vitamins, minerals and medications that do not require a doctor's prescription. Some medications are not allowed. Your trial doctor will discuss these with you in detail. If you are currently taking an approved medicine for the treatment of IPF (nintedanib or pirfenidone) you may continue to do so throughout the trial.

How often will I need to undergo tests?

You will come back to the clinic once per month throughout the trial period for tests. At these visits, you will receive a physical exam and other safety assessments including a blood test. You will also complete a questionnaire to assess how IPF is impacting your daily activities. You will complete a spirometry test to evaluate your lung function.

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Will I be reimbursed for my expenses?

There are no additional costs associated with participating in this trial, nor will you be paid for participating. All trial medications, tests and medical care required as part of this research will be provided at no cost to you. You may be reimbursed for any reasonable travel, parking, meals and other expenses associated with the trial center visits.

PARTICIPATING IN **CLINICAL TRIALS**

The Importance of Participating in Clinical Trials

Clinical trials are at the heart of medical advances, helping researchers find new ways to diagnose, treat and prevent diseases. People who participate in clinical trials contribute to a better understanding of their disease and are an essential part of identifying new treatments. Before a new drug can become available to patients to manage their disease, it must go through a lengthy and thorough testing process. After this process is complete, there is a review by regulatory agencies. The process leading up to approval follows strict guidelines and takes years of research, through clinical trials and data analysis, to determine how well people will respond to the medication.

Clinical Trial Three-Phase Research Approach

Clinical trials typically follow a three-phase research approach to prove a drug's effectiveness.

PHASE 1	PHASE 2	PHASE 3
Typically small in size and designed to understand how long a drug stays in the body at different doses, as well as identify potential side effects. A phase 1 study may include healthy volunteers or individuals with active disease.	Typically a larger clinical study and longer in duration, Phase 2 is designed to better understand possible treatment side effects, treatment effectiveness and, in many cases, the ideal strength and frequency of dosing for the drug.	Typically utilized to confirm clinical benefit in a larger set of patients over a longer period of time. A phase 3 study is often utilized for FDA submission for drug approval.