Protocol Plain Language Summary

A clinical study of MK-5475 to treat pulmonary arterial hypertension (MK-5475-007)

Protocol Title: A Phase 2/3, Multicenter, Randomized, Double-blind, Placebo-Controlled, Adaptive Design Study to Evaluate the Efficacy and Safety of MK-5475 in Adults with Pulmonary Arterial Hypertension

Why is this study needed?

Researchers are looking for ways to treat **pulmonary arterial hypertension (PAH)**. PAH is a type of high blood pressure in the arteries (blood vessels) that go from the heart to the lungs. It causes extra work for the heart and can make it hard to breathe and be physically active.

MK-5475 is a study medicine breathed into the lungs using an inhaler. Other PAH treatments taken by mouth not only work on the lung arteries but can cause low blood pressure and other unwanted effects in the body. Researchers think that using an inhaler to take this study medicine will lower blood pressure in arteries of the lungs only.

The goals of this study are to learn if at least one dose level of MK-5475 taken for 3 months can:

- Lower blood pressure in arteries of the lungs more than the **placebo** (looks like the study medicine but has no actual study medicine in it)
- Increase how far people can walk in 6 minutes more than the placebo

Who will take part in this study?

About 450 people with PAH will take part in this study. They will be ages 18 to 75 years old and:

- Have been taking medicine to treat PAH for at least 3 months
- Not have or had certain heart or lung diseases, other than PAH

What treatments are being studied?

People will be assigned to take the study medicine **MK-5475** or a **placebo** breathed in through an inhaler as a dry powder once a day. Using a placebo helps researchers better understand the effects of a study treatment. People will continue to take their current PAH medicine.

How is this study designed?

A person may be in the study for up to about 5 years and 4 months. This is a 2-part study, and each part will have a base period and an extension period. People will be assigned to either Part 1 or Part 2.

In the **Part 1 base period**, 164 people will be assigned by chance to take 1 of 3 dose levels of **MK-5475** or the **placebo** for 3 months. People will have a 1 in 4 chance of taking the placebo during the base period. Researchers will look at the Part 1 base period data to decide which dose level of MK-5475 to give in Part 2 (**selected dose**) and to see if the study should continue.

In the **Part 1 optional extension period**, people will take MK-5475 for another 2 years. People who took MK-5475 during the base period, will continue the same dose of MK-5475. People who took the placebo during the base period, will be assigned by chance to take 1 of the 3 dose levels of MK-5475. No one will take the placebo during this extension period.

In the **Part 2 base period**, another 286 people will have an equal chance of taking the selected dose of MK-5475 or the placebo for 3 months. In the **Part 2 extension period,** people will continue to take their assigned treatment from the base period for about another 5 years.

Neither the people in the study nor the researchers will know which treatment a person is taking (**double-blind study**). During the study, people will do 6-minute walking and lung function tests, give blood and urine samples, have physical examinations and imaging tests of their heart and lungs, and answer questions about how they are feeling and their ability to perform daily tasks.

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What are the goals of this study and how will they be measured?

Main goals	How they will be measured
To learn if people who take MK-5475 have lower blood pressure in the arteries of their lungs compared to people who take the placebo	Part 1 base period: researchers will measure people's **pulmonary vascular resistance (PVR)** using a catheter (a flexible tube) after 3 months of treatment. PVR is the amount of pressure against blood flowing from the heart to the lungs.
To learn if people who take MK-5475 can walk further in 6 minutes compared to people who take the placebo	Part 2 base period: the change in how far people can walk after 3 months of treatment using a **6-minute walking test** The 6-minute walking test measures: • How far the person can walk in 6 minutes • If the person has trouble breathing • The person's oxygen levels in the blood, blood pressure, heart rate, and tiredness

Other goals	How they will be measured
To learn if people who take MK-5475 can walk further in 6 minutes compared to people who take the placebo	The change in how far people can walk after: • 3 months of treatment (Part 1 base period only) • 6 months of treatment (Part 2 extension period only)
To learn about the effect of MK-5475 on blood flow compared to the placebo	Part 1 base period: researchers will measure these after 3 months of treatment: • The average blood pressure in the heart's top right chamber (right atrium), which receives blood from the body • The amount of blood that the heart pumps each minute related to a person's size • The amount of blood that the heart pumps per each heartbeat related to a person's size
To learn how MK-5475 affects people's World Health Organization functional class (WHO-FC) assessment of PAH compared to people who take the placebo	Part 2 base period: the percent of people whose PAH symptoms did not get worse and limit their everyday activities after 3 months of treatment
To learn about the safety of MK-5475 and how well people tolerate it	The number of people who: • Had an adverse event (AE). An AE is a health problem that happens or worsens during a study. • Stopped treatment due to an AE

What are the possible benefits and risks?

People may or may not benefit from the treatment received during the study. This study has an external group of experts that will oversee the overall risk and benefit. If this group of experts decides that the study treatment is not safe or does not show benefit, the study can be stopped.

More information about the benefits and risks is in the Investigator Brochure, Protocol, and Informed Consent documents.