Protocol Plain Language Summary

A study to learn about the effects and safety of MK-5475 in people with pulmonary hypertension (MK-5475-013)

Protocol Title: A Phase 2a Randomized, Placebo-Controlled Clinical Study to Evaluate the Efficacy and Safety of MK-5475 in Adults With Pulmonary Hypertension Associated With Chronic Obstructive Pulmonary Disease (INSIGNIA-PHCOPD)

Why is this study needed?

Researchers are looking for ways to treat **pulmonary hypertension (PH)** caused by **chronic obstructive pulmonary disease (COPD)**. PH due to COPD is a type of high blood pressure in the arteries that go from the heart to the lungs. It causes extra work for the heart and makes it hard to breathe and be physically active. When people with PH due to COPD take certain blood pressure medicines by mouth as pills, it may cause low blood pressure and low oxygen levels in the body. **MK-5475** is a study medication breathed into the lungs using an inhaler. Researchers think that using an inhaler to take this study medication will lower blood pressure in arteries of the lungs only without causing low blood pressure and low oxygen levels in the rest of the body.

The goal of this study is to learn if PH symptoms change in people who take **MK-5475** using an inhaler, based on how far they can walk in a **6-minute walking test**. This walking test also measures:

- Oxygen levels in the blood
- Blood pressure
- Heart rate
- Trouble breathing
- Tiredness

Who will take part in this study?

About 120 people between 40 and 85 years old with PH due to COPD will take part in this study. They must have:

- COPD, based on certain lung tests
- PH, based on a test that measures the blood pressure in the heart and lungs. This test must be done less than 1 year before a person starts the study
- Symptoms of PH that limit their physical activity
- Lung images that show their loss of lung tissue (emphysema) is not severe

What treatments are being studied?

People will be assigned by chance to take one of the following:

- **MK-5475** breathed in through the mouth as a dry powder through an inhaler once a day
- **Placebo** breathed in through the mouth through an inhaler once a day. A **placebo** looks like the study medicine but has no actual study medicine. Using a placebo helps researchers better understand the effects of a study treatment.

All people will continue to take their COPD treatments. People assigned to take the placebo may switch to **MK-5475** after the first 6 months.

How is this study designed?

This is a 2-part study. People who complete Part 1 may choose to continue into Part 2.

- In **Part 1**, people will be assigned by chance to take **MK-5475** or a **placebo** for 6 months. Neither the people in the study nor the study staff will know which treatment a person takes (double-

blind). People will have a 1 in 3 chance of taking the placebo. Researchers will look at the data after about 50 people have completed or stopped Part 1, to see if the study should continue.

- In **Part 2**, people will take **MK-5475** for up to 18 months. The people assigned to placebo in Part 1 will switch to take **MK-5475**. The people assigned to **MK-5475** in Part 1 will continue to take **MK-5475** for an additional 18 months. The people in the study and the study staff will know that everyone will take **MK-5475.**

Each person will be in the study for up to 24 months. During the study, people will do 6-minute walking tests, give blood samples, have imaging tests of their heart and lungs, and answer questions about their symptoms and quality of life.

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

Main goal	How it will be measured
To learn if people who take MK-5475 can walk further in 6 minutes at Week 24 compared to people who take the placebo	The change in how far people can walk from before treatment to Week 24

Other goals	How they will be measured
To learn if people who take MK-5475 can walk further in 6 minutes at Week 12 compared to people who take placebo	The change in how far people can walk from before treatment to Week 12
To learn if MK-5475 changes the blood level of NT-proBNP at Weeks 12 and 24. The heart makes NT-proBNP (a hormone) during heart failure.	The change in the blood levels of NT-proBNP from before treatment to Week 12 and to Week 24
To learn how MK-5475 affects people's World Health Organization (WHO) Functional Class assessment at Weeks 12 and 24 compared to people who take placebo	The percent of people whose PH symptoms did not get worse based on the WHO Functional Class assessment at Week 12 and at Week 24
To learn about the safety and tolerability of MK-5475. Safety is an assessment of the likelihood of causing an undesired effect. Tolerability is how well the person tolerates (manages) the study treatment.	The number of people who: • Had an adverse event during or after they stopped taking study treatment. An adverse event is a medical problem that happens or worsens during a study and may or may not be caused by the treatment. • Stopped taking the study treatment due to an adverse event

What are the possible benefits and risks?

People may or may not benefit from treatment they get in this study.

More detail about the benefits and risks for people in this study is in the MK-5475-013 Protocol and Informed Consent form and the Investigator Brochure.