Protocol Plain Language Summary

A clinical study of belzutifan in people with advanced cancer from adrenal/extra adrenal and pancreas, inherited localized cancers, and certain other advanced solid tumors (MK-6482-015)

Protocol Title: A Phase 2 Study to Evaluate the Efficacy and Safety of Belzutifan (MK-6482, formerly PT2977) Monotherapy in Participants With Advanced Pheochromocytoma/Paraganglioma (PPGL), Pancreatic Neuroendocrine Tumor (pNET), von Hippel-Lindau (VHL) Disease-Associated Tumors, Advanced Gastrointestinal Stromal Tumor (wt GIST), or Advanced Solid Tumors With HIF-2 α related Genetic Alterations

Why is this study needed?

Researchers are looking for new ways to treat people with certain advanced cancers that have a gene mutation (change) that causes HIF-2α to be overactive**. HIF-2α** (hypoxia-inducible factor-2 alpha subunit) is a protein that helps tumors grow and survive when overactive.

Advanced means cancer cannot be removed with surgery or has spread to other parts of the body. This study includes these advanced cancers:

- **Pheochromocytoma/paraganglioma (PPGL)**, which are cancers that start in cells that make hormones or the adrenal glands (small glands on top of each kidney that make hormones)
- **Pancreatic neuroendocrine tumor (pNET)**, which is a rare type of cancer that starts in cells in the pancreas that make hormones, like insulin
- **Gastrointestinal stromal tumor (GIST),** wild type (lacks certain gene mutations), which is a less common type of cancer that starts in the digestive tract
- Other **solid cancers with HIF-2α**, which are cancers that have gene mutations that cause overactive HIF-2α. Solid cancers are mostly in body organs and tissues, not in the blood or other body liquids.

Localized means cancer presents only in the organ where it started and has not spread to other parts of the body. This study includes these localized cancers:

- **Von Hippel-Lindau (VHL) disease tumors**, which are rare cancers caused by a certain gene mutation that is passed down from parents to children

Belzutifan is the study medicine designed to block HIF-2α. The goal of this study is to learn if people with certain cancers who receive belzutifan have the cancer get smaller or go away.

Who will take part in this study?

About 322 people with advanced PPGL, pNET, localized VHL, advanced GIST, or other solid cancers with HIF-2α will be in the study. They will be 12 years old and older (the participants with VHL will be adults only) and:

- Have a tumor sample from a biopsy (doctors take tumor tissue to test in the lab)
- Have a solid tumor with certain gene mutations or biomarkers depending on the cancer type
- Have been treated with systemic therapy and it stopped working, or they did not tolerate systemic therapy or did not have any satisfactory treatment options depending on the cancer type
- Do not have another cancer that was treated or got worse in the past 2 years

What treatments are being given during the study?

All people in the study will take **belzutifan** once a day by mouth as tablets. People will take belzutifan until the cancer gets worse or they don't tolerate treatment with belzutifan.

How is this study designed?

People will be placed into 5 different groups based on the type of cancer they have.

Both the people in the study and the researcher will know which study treatment a person is getting (**open-label study**). During the study, people will give urine and blood samples, have imaging tests, have physical examinations, and answer questions about how they are feeling and their ability to perform daily tasks. A person may be in this study for up to 5 and a half years.

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

Main goal	How it will be measured
To learn about the **objective response rate (ORR)** of people who receive belzutifan	**ORR** is the number of people whose cancer responds to treatment (**responds** means cancer gets smaller or goes away)
Other goals	**How they will be measured**
To learn about the **response** of people who receive belzutifan	Researchers will measure: • **Duration of response (DOR):** the length of time from when the cancer first responds to treatment until the cancer grows or spreads, or death from any cause • **Time to response (TTR):** the length of time from the first dose of belzutifan until cancer responds to treatment • **Progression-free survival (PFS):** the length of time from the first dose of belzutifan until a person's cancer grows or spreads, or death from any cause • **Overall survival (OS):** the length of time from the first dose of belzutifan until death from any cause • **Time to surgery (TTS):** the length of time from the first dose of belzutifan until the first surgery to remove tumors or procedure to shrink tumors. This will be measured in people with VHL tumors.
To learn about the **disease control rate (DCR)** of people who receive belzutifan	**DCR** is the number of people who have the cancer stop growing or get smaller, or show no signs of cancer
To learn if belzutifan is **safe** 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.
More information about the benefits and risks is in the Investigator Brochure, Protocol, and Informed Consent documents.