Protocol Plain Language Summary

A clinical study of MK-1084 in people with advanced solid tumors (MK-1084-001)

Protocol Title: A Phase 1, Open-Label, Multicenter Study to Assess Safety, Tolerability, PK and Efficacy of MK-1084 as Monotherapy and as Part of Various Combination Therapies in Participants With KRAS G12C Mutant Advanced Solid Tumors

Why is this study needed?

Researchers want to learn about new ways to treat advanced cancer with solid tumors that have a gene mutation called KRAS G12C. **Advanced** means that cancer has spread in the body or cannot be removed with surgery. **Solid tumors** are mostly in body organs and tissues, not in the blood or other body liquids. A **gene mutation** is a change in the order of DNA.

Standard treatment for advanced solid tumors is immunotherapy and chemotherapy. **Immunotherapy** is a treatment that helps the immune system fight cancer. **Chemotherapy** is medicine that destroys cancer cells or stops them from growing.

MK-1084, the study medicine, is a targeted therapy designed to treat cancers with the KRAS G12C mutation. A **targeted therapy** is a treatment that works on specific cells to stop them from growing.

The goal of this study is to learn about the safety of giving **MK-1084** alone or with immunotherapy and chemotherapy and how well people tolerate it.

Who will take part in this study?

About 830 people with advanced cancer with solid tumors will be in this study. They will be at least 18 years old and:

- Have cancer with the KRAS G12C gene mutation, such as non-small cell lung cancer (NSCLC) or colorectal cancer
- Have not had treatment for the advanced solid tumor within the past month

What treatments are being given during the study?

Everyone in the study will receive **MK-1084.** They may also receive:

- **Immunotherapy,** which is pembrolizumab or cetuximab
- **Chemotherapy**, which is mFOLFOX6, carboplatin, or pemetrexed

All people will take MK-1084 once or twice a day by mouth as tablets. People may receive immunotherapy, chemotherapy, or both once every 2 or 3 weeks through a needle into a vein as an intravenous (IV) infusion.

How is this study designed?

People will be assigned to 1 of 6 treatment groups based on the type of cancer they have:

- **Group 1**: MK-1084 alone

- **Group 2**: MK-1084 and pembrolizumab
- **Group 3**: MK-1084 alone (as a different type of tablet)
- **Group 4**: MK-1084 and pembrolizumab, carboplatin, and pemetrexed
- **Group 5**: MK-1084 and cetuximab
- **Group 6**: MK-1084 and cetuximab and mFOLFOX6

Researchers will start the study by giving a low dose of MK-1084 to people in Group 1. Researchers will then review the safety and amount of MK-1084 in the blood at different dose levels. This will help the researchers decide if the rest of the people in the study will receive a higher or lower dose of MK-1084.

Both the people in the study and the researchers will know which treatment the person receives because everyone receives MK-1084 (open-label study). During the study, people will give blood, urine, and tumor tissue samples, have imaging tests, and eye and physical examinations. People may be in the study for up to 7 years.

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

Main goals	How they will be measured
To learn about the **dose limiting toxicities (DLTs)** of **MK-1084** alone and with immunotherapy and chemotherapy	Researchers will measure the number of people who had a DLT during the first: • 3 weeks of treatment for Groups 1, 2, 3, and 4 • 4 weeks of treatment for Groups 5 and 6 **DLTs** are medical problems related to study medicine that prevent giving a higher dose
To learn about the **safety** of **MK-1084** and how well people **tolerate** it alone and with immunotherapy and chemotherapy	During the study, the number of people who: • Had an **adverse event (AE)** – An AE is a health problem that happens or worsens • Stopped treatment due to an AE

Other goals	How they will be measured
To learn the **cancer response** of people who receive **MK-1084** alone and with immunotherapy and chemotherapy	Researchers will measure how the **cancer responds** (the cancer gets smaller or goes away) in all people in the study: • **Objective response** is the number of people whose cancer responds to treatment during the study • **Duration of response** is the length of time from when the cancer first responds to treatment until the cancer grows or spreads, or death from any cause
To learn what happens to different doses of **MK-1084** alone and with immunotherapy and chemotherapy in a person's body over time	Researchers will measure the amount of MK-1084 in people's blood samples at different times during the study

What are the possible benefits and risks?

Clinical studies may have benefits and risks. People may benefit because the study treatment may treat cancer or stop it from getting worse. There may be risks because the study treatment may not work or may cause health problems.

More information about the benefits and risks is in the protocol.