Protocol Plain Language Summary

A clinical study that compares MK-2870 with or without pembrolizumab to chemotherapy in people with breast cancer that cannot be removed with surgery (MK-2870-010)

Protocol Title: An Open-label, Randomized Phase 3 Study of MK-2870 as a Single Agent and in Combination with Pembrolizumab Versus Treatment of Physician's Choice in Participants with HR+/HER2- Unresectable Locally Advanced or Metastatic Breast Cancer

Why is this study needed?

Researchers are looking for new ways to treat people with **metastatic hormone receptor positive (HR+)/ human epidermal growth factor receptor-2 negative (HER2-) breast cancer**. **Metastatic** means the cancer has spread to other parts of the body. This type of cancer is often treated with **hormone therapy**, which is a treatment that blocks the hormones that cancer cells use to grow. Sometimes hormone therapy stops working and the cancer grows or spreads. In these cases, doctors may use **chemotherapy** as a second type of treatment. Chemotherapy uses medicine to shrink or destroy cancer cells.

Researchers want to learn if **MK-2870** (the study medicine), given alone or with pembrolizumab, works to treat HR+/HER2- breast cancer that has already been treated with hormone therapy. MK-2870 is a **targeted therapy**, which is a treatment that works on specific types of cancer cells to stop them from growing. **Pembrolizumab** is an **immunotherapy**, which is a treatment that helps the immune system fight cancer.

The main goal of this study is to learn if people treated with MK-2870 with or without pembrolizumab live longer without the cancer spreading or getting worse than people treated with chemotherapy.

Who will take part in this study?

About 1,200 people with breast cancer will be in this study. They will be age 18 and older and:

- Have metastatic HR+/HER2- breast cancer that cannot be removed with surgery
- Had the cancer grow or spread during treatment with hormone therapy
- Have not received chemotherapy for the metastatic cancer

What treatments are being given during the study?

People in this study will receive 1 or 2 of these treatments:

- **MK-2870**, the study medicine
- **Pembrolizumab**, an immunotherapy
- **Chemotherapy** of the researcher's choice

People will receive MK-2870 through a needle into a vein as an intravenous (IV) infusion every 2 weeks. They will receive pembrolizumab by IV infusion every 6 weeks for about 2 years. They will receive chemotherapy by IV infusion or by mouth, based on the type. Timing of chemotherapy treatments will also depend on type.

People will receive treatment until they cannot tolerate it, the cancer grows or spreads, or they stop the study.

How is this study designed?

People will be assigned by chance to 1 of 3 treatment groups:

- **Group A** will receive **MK-2870 alone**
- **Group B** will receive **MK-2870 and pembrolizumab**

- **Group C** will receive **chemotherapy**

For every 8 people in this study, 3 will be assigned to Group A, 3 to Group B, and 2 to Group C. Both the people in the study and the researcher will know which study treatment a person is getting (open-label study).

People may give urine samples, have blood, tumor, and imaging tests, have physical examinations, and answer sets of questions during the study. A person may be in this study for up to 7 years.

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

Main goal	How it will be measured
To learn if the **progression-free survival (PFS)** of people in Groups A and B is longer than those in Group C	**PFS** is the length of time from the start of the study until a person's cancer grows or spreads (gets worse) or death from any cause

Other goals	How they will be measured
To compare the **overall survival (OS)** of people in Groups A and B to group C, and group A to Group B	**OS** is the length of time that people live from the start of the study until death from any cause
To compare the **PFS** of people in Group B to Group A	**PFS** is the length of time from the start of the study until a person's cancer grows or spreads (gets worse) or death from any cause
To compare the **cancer response** of people in Groups A and B to Group C	Researchers will measure these responses: • **Objective response rate (ORR)** is the number of people whose cancer **responds** to treatment (the cancer gets smaller or goes away) during the study • **Duration of response (DOR)** 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 compare the **health-related quality of life** (**HRQoL**) of people in Groups A and B to Group C	People will answer sets of questions about their overall and emotional health, treatment side effects, and their ability to carry out daily tasks. Researchers will measure: • The change in scores during the study • The length of time from the start of the study until the scores get worse
To learn about **safety** of MK-2870, MK-2870 with pembrolizumab, and chemotherapy and how well people tolerate them	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 who 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.