Protocol Plain Language Summary

A clinical study of MK-5684 and standard hormone therapy in people with prostate cancer (MK-5684-004)

Protocol Title: A Phase 3, Randomized, Open-label Study of MK-5684 Versus Alternative Abiraterone Acetate or Enzalutamide in Participants with Metastatic Castration-resistant Prostate Cancer (mCRPC) That Progressed On or After Prior Treatment with One Next-generation Hormonal Agent (NHA)

Why is this study needed?

Researchers are looking for new ways to treat people with a type of prostate cancer called **metastatic castration-resistant prostate cancer (mCRPC)**. In mCRPC, the cancer has spread to other parts of the body and got worse or came back after standard hormone therapy. **Standard hormone therapy** is treatment to lower the level of certain hormones in the body to slow the growth and spread of cancer cells. The more recent types of hormone therapy to treat mCRPC are called **next-generation hormonal agents (NHA)**.

MK-5684 is a study medicine designed to treat mCRPC by blocking the body from making steroid hormones. Researchers will give MK-5684 with **hormone replacement therapy (HRT)** because the body needs certain steroid hormones to control body functions such as balancing water and blood pressure.

Researchers want to learn if people who take MK-5684 live longer overall and without the cancer getting worse compared to people who take NHA.

Who will take part in this study?

About 1,500 people with mCRPC will be in this study. They will be at least 18 years old and:

- Have a type of prostate cancer that got worse during or after treatment with no more than 1 NHA
- Have not received certain chemotherapy to treat mCRPC. Chemotherapy is medicine that destroys cancer cells or stops them from growing.

What treatments are being given during the study?

People will have an equal chance of taking one of these treatments by mouth as tablets:

- **MK-5684** with **HRT** (dexamethasone and fludrocortisone)
- **NHA**, either:
    - Abiraterone acetate and prednisone
    - Enzalutamide

People may take MK-5684 or prednisone twice a day. All other treatments will be taken once a day. People will continue their treatment until the cancer gets worse or the person doesn't tolerate treatment.

How is this study designed?

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 and physical examinations, and answer questions about how they are feeling and their ability to carry out daily tasks.

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

Main goals	How they will be measured
To learn if the **radiographic progression-free survival (PFS)** of people who take MK-5684 is longer than those who take NHA	**rPFS** is the length of time from the start of treatment until the cancer grows or spreads (based on imaging tests), or death from any cause
To learn if the **overall survival (OS)** of people who take MK-5684 is longer than those who take NHA	**OS** is the length of time that people live from the start of treatment until death from any cause

Other goals	How they will be measured
To compare the **time to the next treatment (TFST)** of people who take MK-5684 to those who take NHA	**TFST** is the length of time from when a person starts treatment until they switch to a different treatment, or death from any cause
To compare the **cancer response** of people who take MK-5684 to those who take NHA	Researchers will measure responses throughout the study: • **Objective response (OR)**: the number of people whose cancer responds to treatment (gets smaller or goes away). • **Duration of response (DOR)**: the length of time from when the cancer first responds to treatment until the cancer grows, spreads, or death from any cause.
To compare the **levels of prostate specific antigen (PSA)** in people who take MK-5684 to those who take NHA	During the study, researchers will measure: • **PSA progression**: the length of time from the start of treatment until the **PSA** blood level goes up by a certain amount—**PSA** is a protein in the blood that the prostate makes. It may be higher in people with prostate cancer. • **PSA response**: the number of people who have the PSA level go down by at least half.
To learn about the **pain and bone health** of people who take MK-5684 compared to those who take NHA	During the study, researchers will measure the length of time form the start of treatment until: • A person's pain gets worse by a certain amount **(time to pain progression or TTPP)** • Certain bone-related events happen, such as certain treatments, surgeries, or broken bones **(symptomatic skeletal-related events or SSRE)**
To learn the **health-related quality of life (HRQoL)** of people who take MK-5684 or NHA	People will answer sets of questions to measure their **HRQoL**, including questions about their overall health, prostate cancer symptoms, and their ability to carry out daily tasks. Researchers will measure: • The change in the scores during the study • The length of time from when the person starts treatment until their HRQoL gets worse

To learn about the **safety** of MK-5684 and how well people tolerate it	During the study, the number of people who: • Have an **adverse event (AE)** – An AE is a health problem that happens or worsens • Stop treatment due to an AE

What are the possible benefits and risks?

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

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