Protocol Plain Language Summary

A clinical study of people with HIV-1 who switch their treatment to a combination of doravirine and islatravir (MK-8591A-052)

Protocol title: A Phase 3, Randomized, Active-Controlled, Double-Blind Clinical Study to Evaluate a Switch to Doravirine/Islatravir (DOR/ISL 100 mg/0.25 mg) Once-Daily in Participants With HIV-1 Who Are Virologically Suppressed on Bictegravir/Emtricitabine/Tenofovir Alafenamide (BIC/FTC/TAF)

Why is this study needed?

Researchers are looking for new treatments for all people living with **HIV-1** (Human Immunodeficiency Virus Type 1). HIV-1 is the most common type of HIV, which is a virus that attacks cells of the immune system.

HIV-1 treatments, called **ART** (antiretroviral therapy), involve taking medicines to lower the amount of HIV-1 virus in the body. **Standard ART** helps people live longer but includes up to three medicines and may affect other health problems. New ART is needed that is safe and works well. In addition, new ART is needed that can be taken for a long time without creating or worsening other medical conditions and that does not interact with other medicine a person takes. The **study ART** combines 2 medicines and is taken once a day.

The purpose of this study is to learn if switching treatment from a **standard ART** to **study ART** works as well or better to treat HIV-1 than continuing to take a **standard ART**.

Who will take part in this study?

About 501 people with HIV-1 will take part in this study. They will be at least 18 years old and:

- Currently taking a standard ART called **BIC/FTC/TAF** (bictegravir, emtricitabine, and tenofovir alafenamide)
- Not have HIV-2

How is this study designed?

This study has 2 treatment groups. People will be assigned by chance to Group 1 or Group 2:

- **Group 1** will take the **study ART** for 96 weeks (about 2 years)
- **Group 2** will continue to take **BIC/FTC/TAF** for 96 weeks (about 2 years)

Twice as many people will be assigned to Group 1 than Group 2. A person will be in the study for about 2 years. Neither the people in the study nor the researchers will know which treatment a person is taking (double-blind study).

A person will give urine samples, have blood tests and physical examinations, and answer sets of questions during the study.

What treatments are being given during this study?

During this study, people will be assigned by chance to:

- **Switch to the study ART** – 2 medicines combined in a single pill called **DOR/ISL** (doravirine and islatravir)
- **Keep taking BIC/FTC/TAF** – 3 medicines combined in a single pill called **BIC/FTC/TAF**

People will take their assigned treatment by mouth once a day.

All people in the study will also take a **placebo** that looks like the other treatment but does not contain any medicine. This way, the person and the researchers will not know which group a person is assigned to. Using a placebo helps researchers better understand the real effects of the study medicine.

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

Main goal	How it will be measured
To compare if study ART works as well as or better than BIC/FTC/TAF to treat HIV-1	At Week 48, the number of people who have a HIV-1 viral load of 50 copies or more in a milliliter (mL) of blood. A lower viral load of HIV-1 in the blood is better. The viral load is measured as the number of "**copies**" in a small amount of blood (1 mL).
To learn about the **safety** and how well people **tolerate** the study ART compared to BIC/FTC/TAF	By Week 48, the number of people who: • Had an **adverse event (AE).** An AE is a health problem that happens or worsens during a study • Stopped ART due to an AE
Other goals	**How they will be measured**
To compare if study ART works as well as or better than BIC/FTC/TAF to treat HIV-1	At Week 96, the number of people who have a HIV-1 viral load of 50 or more copies
To learn how well study ART works to treat HIV-1 compared to BIC/FTC/TAF	At Weeks 48 and 96, the number of people who have a HIV-1 viral load of: • less than 200 copies • less than 50 copies
To learn if the number of immune system cells called **CD4+ T-cells** has changed during the study. **CD4+ T-cells** help fight HIV-1 infection	The average change in the number of CD4+ T-cells in the blood from before treatment to: • Week 48 • Week 96
To learn if study ART or BIC/FTC/TAF stops working for people	The number of people who are changed from their ART because the ART stops working for them, measured at Week 48 and Week 96
To learn about the safety and how well people tolerate the study ART compared to BIC/FTC/TAF	The number of people who: • Had an AE by Week 102 • Stopped the study ART or BIC/FTC/TAF due to an AE by Week 96

What are the possible benefits and risks?

People may or may not benefit from the treatment received during the study. This study has a Data Monitoring Committee that oversees the study's overall risk and benefit. If this committee 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.