Advancing HIV Research

At MSD, we are building on our legacy of invention by advancing HIV treatment and prevention options based on the nucleoside reverse transcriptase translocation inhibitor (NRTTI) mechanisms of action.

With daily and long-acting oral regimens currently in development, we aim to offer choices that can help people treat and prevent HIV according to their needs and preferences.

Current development programs include:

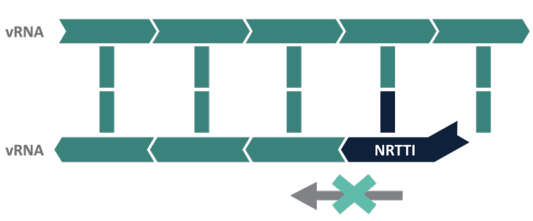
- **Once-Daily Oral Treatment:**
  - **MK-8591A:** combination of doravirine and islatravir (DOR/ISL)
- **Once-Weekly Oral Treatment:**
  - **MK-8591D*:** combination of islatravir and Gilead's lenacapavir (ISL/LEN)
  - **MK-8591B:** combination of islatravir and our novel non-nucleoside reverse transcriptase inhibitor (NNRTI), ulonivirine (ISL/ULO)
- **Once-Monthly Oral Pre-exposure Prophylaxis (PrEP):**
  - **MK-8527:** a novel investigational NRTTI candidate for HIV pre-exposure prophylaxis (PrEP)

*Collaboration with Gilead

NRTTI: Multiple Mechanisms of Action

NRTTIs have multiple mechanisms of actions including immediate and delayed chain termination:

Translocation Inhibition



NRTTI is incorporated into the vDNA strand and blocks RT translocation which prevents further nucleotide incorporation. This results in immediate chain termination.

✖ = HIV reverse transcriptase (RT)

Delayed Chain Termination

NRTTI is incorporated into the vDNA strand and in the event translocation occurs, one additional nucleotide is incorporated in the vDNA strand. Structural changes induced by NRTTI in the vDNA prevent further nucleotide incorporation, resulting in delayed chain termination.

✖ = HIV reverse transcriptase (RT)

Development Program

Development Program	Phase	Study Number & Link
Treatment		
MK-8591A		
A Switch to Doravirine/Islatravir (DOR/ISL) in Participants With Human Immunodeficiency Virus Type 1 (HIV-1) Who Are Virologically Suppressed on Antiretroviral Therapy (ART) (MK-8591A-051)	Phase 3	NCT05631093
A Switch to Doravirine/Islatravir (DOR/ISL) in Participants With Human Immunodeficiency Virus Type 1 (HIV-1) Who Are Virologically Suppressed on Bictegravir/Emtricitabine/Tenofovir Alafenamide (BIC/FTC/TAF) (MK-8591A-052)	Phase 3	NCT05630755
Study of Doravirine/Islatravir (DOR/ISL) compared with Bictegravir/Emtricitabine/Tenofovir Alafenamide (BIC/FTC/TAF) in Treatment-Naïve Participants living with HIV-1 (MK-8591A-053)	Phase 3	NCT05705349
A Study of Doravirine/Islatravir (DOR/ISL, MK-8591A) for the Treatment of Human Immunodeficiency Virus 1 (HIV-1) in Participants Who Previously Received DOR/ISL (MK-8591A-054)	Phase 3	NCT05766501
Open-label, Follow-up of Doravirine/Islatravir for Participants With Human Immunodeficiency Virus -1 (HIV-1) (MK-8591A-033)	Phase 3	NCT04776252
MK-8591D		
Study Evaluating the Safety and Efficacy of Islatravir in Combination With Lenacapavir in Virologically Suppressed People With HIV	Phase 2	NCT05052996 (Gilead is study sponsor)
Study to Compare an Oral Weekly Islatravir/ Lenacapavir Regimen With Bictegravir/ Emtricitabine/ Tenofovir Alafenamide in Virologically Suppressed People With HIV-1 (ISLEND-1)	Phase 3	NCT06630286 (Gilead is study sponsor)
Study to Compare an Oral Weekly Islatravir/ Lenacapavir Regimen With Standard of Care in Virologically Suppressed People With HIV-1 (ISLEND-2)	Phase 3	NCT06630299 (Gilead is study sponsor)
MK-8591B		
A Phase 2b, Randomized, Active-Controlled, Open-Label Clinical Study to Evaluate a Switch to Islatravir (ISL) and Ulonivirine (ULO) Once Weekly in Adults With HIV-1 Virologically Suppressed on Bictegravir/Emtricitabine/Tenofovir Alafenamide (BIC/FTC/TAF) Once Daily	Phase 2	NCT06891066
PrEP		
MK-8527		
A Clinical Study of MK-8527 to Prevent Human Immunodeficiency Virus Type 1 (HIV-1) (MK-8527-011)	Phase 3	NCT07044297