MERCK

Advancing HIV Research

At Merck, we are building on our legacy of invention by advancing HIV treatment and prevention options.

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:

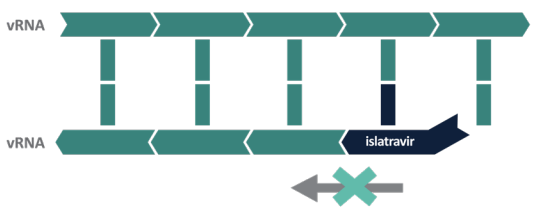
- **Once-Daily Oral Treatment:**
  - **MK-8591A:** combination of doravirine and islatravir (DOR/ISL)
- **Once-Weekly Oral Treatment:**
  - **MK-8591D*:** combination of islatravir and lenacapavir (ISL/LEN)
  - **MK-8591B:** combination of islatravir and ulonivirine, our investigational NNRTI (ISL/ULO)
- **Once-Monthly Oral Pre-exposure Prophylaxis (PrEP):**
  - **MK-8527:** an investigational, novel candidate for HIV pre-exposure prophylaxis (PrEP) with the same mechanisms of action as islatravir

*Collaboration with Gilead

Islatravir: Multiple Mechanisms of Action

Islatravir has multiple mechanisms of action, including immediate and delayed chain termination:

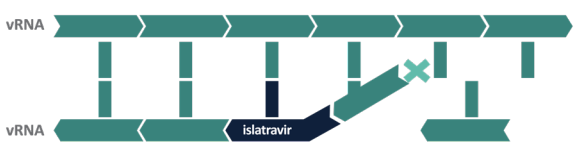
Translocation Inhibition



Islatravir 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



Islatravir 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 islatravir in the vDNA prevent further nucleotide incorporation, resulting in delayed chain termination.

✖ = HIV reverse transcriptase (RT)

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
A Clinical Study of Islatravir and Ulonivirine for People With HIV-1 Who Have Not Been Treated Before (MK-8591B-062)	Phase 2/3	NCT07266831
PrEP		
MK-8527		
Safety and Pharmacokinetic Study of MK-8527 to Prevent Human Immunodeficiency Virus Type 1 (HIV-1) (MK-8527-010)*	Phase 3	NCT07071623
A Clinical Study of MK-8527 to Prevent Human Immunodeficiency Virus Type 1 (HIV-1) (MK-8527-011)**	Phase 3	NCT07044297

*In collaboration with the Gates Foundation and the International Clinical Research Center within the University of Washington Department of Global Health, in partnership with the University of Alabama at Birmingham
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