Islatravir (ISL, MK-8591) is the first nucleoside reverse transcriptase translocation inhibitor (NRTTI) in development for the treatment and prevention of HIV-1 infection. Doravirine (DOR) is a next-generation non-nucleoside reverse transcriptase inhibitor (NNRTI) approved for the treatment of HIV-1. The combined attributes of ISL and DOR create the potential for a potent, simple 2-drug regimen that may address some of the long-term safety and toxicity concerns of traditional regimens. Protocol 11 is a Phase 2b dose-ranging trial of DOR + ISL (NCT03272347). – Virologic suppression among participants receiving ISL + DOR was high at Week 48 and maintained through Week 96. – ISL + DOR was generally well tolerated at all doses, with few drug-related AEs; 3 of 90 participants in the combined ISL groups discontinued due to AEs through Week 96. – The 0.75 mg dose of ISL was selected for further clinical development.

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Background

- ISL changes RT/DNA structure such that nucleotide incorporation is prevented
- ISL inhibits viral replication

Results

Figure 4. Albumin/Creatinine Ratio

Conclusions

- No renal safety concerns were found for DOR + ISL in this exploratory analysis from the Phase 2 trial
- Similar changes in serum creatinine and eGFR across all treatment groups
- Similar changes across treatment groups in renal biomarkers: albumin/creatinine, retinol-binding protein/creatinine, and beta-2 microglobulin/creatinine ratio
- No dose-response relationship for renal effects of DOR + ISL
- No discontinuations due to renal adverse events
- Phase 3 clinical trials will provide additional data on the renal safety profile of DOR/ISL.

Figure 5. Retinol-Binding Protein/Creatinine Ratio

Renal Safety Through 96 Weeks in a Phase 2 Trial (P011) of Islatravir and Doravirine in Treatment-Naïve Adults With HIV-1

Methods

Figure 1. Protocol 011: Phase 2 Dose-Ranging Trial of ISL + DOR

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Disclosure

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