NEWS RELEASE

Merck Provides Update on Phase 2 Clinical Trial of Once-Weekly Investigational Combination of MK-8507 and Islatravir for the Treatment of People Living with HIV-1

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KENILWORTH, N.J.--(BUSINESS WIRE)-- Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced an update regarding the Phase 2 IMAGINE-DR clinical trial (MK-8507-13), which is evaluating the investigational combination of MK-8507, a non-nucleoside reverse transcriptase inhibitor, and islatravir (ISL), a nucleoside reverse transcriptase translocation inhibitor, as a once-weekly oral treatment for HIV-1 infection. MK-8507 and islatravir, alone and in combination, are investigational and not approved for use.

Decreases in total lymphocyte and CD4+ T-cell counts were observed in study participants randomized to receive ISL+MK-8507. A review by the external Data Monitoring Committee (eDMC) determined that this effect was related to treatment with the combination of ISL+MK-8507; the greatest decreases were seen in the arms of the study receiving the highest doses of MK-8507 (200 mg and 400 mg). At the recommendation of the eDMC, Merck is stopping dosing in the trial, with continued monitoring of study participants. The company has notified investigators and paused development of MK-8507. Merck remains confident in islatravir's overall profile and is continuing with development of islatravir across a range of settings including in treatment of patients living with HIV and in pre-exposure prophylaxis (PrEP). None of these other programs combine islatravir with MK-8507.

"Merck remains resolute in its commitment to help address the unmet needs of people living with HIV and continue to do our part in the global efforts to help end the HIV pandemic, which includes the ongoing development of islatravir," said Dr. Joan Butterton, vice president, infectious diseases, Global Clinical Development, Merck Research

Laboratories. “All clinical studies provide important learnings to help us in the fight against HIV, and we are grateful to the patients and investigators for their contributions.”

In light of the findings from the MK-8507-013 study, Merck conducted a review of trends in total lymphocyte and CD4+ T-cell counts in company-sponsored clinical trials of ISL across all indications and dosing regimens. A dose-dependent decrease in lymphocyte counts was observed in an ongoing Phase 2 trial (MK-8591-016), which is evaluating monthly ISL (60 mg and 120 mg) for PrEP in participants at low-risk of HIV-1 infection. In this population of HIV-1 uninfected participants, the mean decreases were in the normal range and there was no increase in clinical adverse events (AEs) related to infection. In addition, a small, treatment related mean decrease in CD4+ T-cell counts was observed through Week 48 in two Phase 3 trials, ILLUMINATE SWITCH A and ILLUMINATE SWITCH B (MK-8591A-017 and MK-8591A-018), which are evaluating doravirine 100 mg in combination with ISL 0.75 mg daily (DOR/ISL) in HIV-1 virologically suppressed participants. There was no increased incidence of AEs related to infections in participants receiving DOR/ISL relative to comparators through Week 48. Investigators for these trials have been informed and the trials are continuing. Full results from ILLUMINATE SWITCH A and ILLUMINATE SWITCH B will be presented at an upcoming medical meeting.

Merck has an expansive HIV clinical development program evaluating islatravir across a variety of dosing regimens, for both the treatment of HIV-1 in combination with other antiretroviral agents and for the prevention of HIV-1 as a monotherapy. Merck recently announced positive **topline results** from the ILLUMINATE SWITCH A and ILLUMINATE SWITCH B Phase 3 clinical trials. As previously reported, at 48 weeks, both trials met their primary efficacy endpoint of percentage of participants with HIV-1 RNA levels ≥50 copies/mL, demonstrating that antiviral efficacy was comparable between DOR/ISL and different antiretroviral therapy regimens (ILLUMINATE SWITCH A) and between DOR/ISL and bictegravir/emtricitabine/tenofovir (ILLUMINATE SWITCH B).

About IMAGINE-DR

The IMAGINE-DR clinical trial was a Phase 2, randomized, controlled, double-blind, dose-ranging study, designed to evaluate a switch to MK-8507 and ISL in combination as a once-weekly oral treatment in adults with HIV-1 who have been virologically suppressed for greater than or equal to six months on bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) once-daily. The study had been fully enrolled with 161 participants and was ongoing.

About PIFELTRO™ and DELSTRIGO™

PIFELTRO ™ (doravirine, 100 mg) is indicated in combination with other antiretroviral (ARV) agents for the treatment of HIV-1 infection in adult patients with no prior ARV treatment history or to replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable ARV regimen with no history of treatment failure and no known substitutions associated with resistance to doravirine.

DELSTRIGO™ (doravirine 100 mg/lamivudine 300 mg/tenofovir disoproxil fumarate 300 mg) is indicated as a complete regimen for the treatment of HIV-1 infection in adult patients with no prior ARV treatment history or to replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable ARV regimen with no history of treatment failure and no known substitutions associated with resistance to the individual components of DELSTRIGO. DELSTRIGO contains a boxed warning regarding post-treatment acute exacerbations of hepatitis B (HBV) infection. See Selected Safety Information below.

Selected Safety Information about PIFELTRO and DELSTRIGO

Warning: Posttreatment Acute Exacerbation of Hepatitis B (HBV)

All patients with HIV-1 should be tested for the presence of HBV before initiating ARV therapy. Severe acute exacerbations of HBV have been reported in patients who are coinfected with HIV-1 and HBV and have discontinued products containing lamivudine or tenofovir disoproxil fumarate (TDF), which are components of DELSTRIGO. Patients coinfected with HIV-1 and HBV who discontinue DELSTRIGO should be monitored with both clinical and laboratory follow-up for at least several months after stopping DELSTRIGO. If appropriate, initiation of anti-HBV therapy may be warranted.

PIFELTRO and DELSTRIGO are contraindicated when co-administered with drugs that are strong cytochrome P450 (CYP)3A enzyme inducers (including the anticonvulsants carbamazepine, oxcarbazepine, phenobarbital, and phenytoin; the androgen receptor inhibitor enzalutamide; the antimycobacterials rifampin and rifapentine; the cytotoxic agent mitotane; and the herbal product St. John’s wort (Hypericum perforatum)), as significant decreases in doravirine plasma concentrations may occur, which may decrease the effectiveness of DELSTRIGO and PIFELTRO.

DELSTRIGO is contraindicated in patients with a previous hypersensitivity reaction to lamivudine.

Renal impairment, including cases of acute renal failure and Fanconi syndrome, have been reported with the use of TDF. DELSTRIGO should be avoided with concurrent or recent use of a nephrotoxic agent (eg, high-dose or multiple NSAIDs). Cases of acute renal failure after initiation of high-dose or multiple NSAIDs have been reported in patients with risk factors for renal dysfunction who appeared stable on TDF.

Prior to or when initiating DELSTRIGO, and during treatment, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, also assess serum phosphorus. Discontinue DELSTRIGO in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome. Discontinue DELSTRIGO if estimated creatinine clearance declines below 50 mL/min.

In clinical trials in HIV-1 infected adults, TDF was associated with slightly greater decreases in bone mineral density (BMD) and increases in biochemical markers of bone metabolism. Serum parathyroid hormone levels and 1,25 Vitamin D levels were also higher. Cases of osteomalacia associated with proximal renal tubulopathy have been reported with the use of TDF.

Immune reconstitution syndrome can occur, including the occurrence of autoimmune disorders with variable time to onset, which may necessitate further evaluation and treatment.

Because DELSTRIGO is a complete regimen, co-administration with other antiretroviral medications for the treatment of HIV-1 infection is not recommended.

Co-administration of PIFELTRO with efavirenz, etravirine, or nevirapine is not recommended.

If DELSTRIGO is co-administered with rifabutin, take one tablet of DELSTRIGO once daily, followed by one tablet of doravirine (PIFELTRO) approximately 12 hours after the dose of DELSTRIGO.

If PIFELTRO is co-administered with rifabutin, increase PIFELTRO dosage to one tablet twice daily (approximately 12 hours apart).

Consult the full Prescribing Information prior to and during treatment for more information on potential drug-drug interactions.

Because DELSTRIGO is a fixed-dose combination tablet and the dosage of lamivudine and TDF cannot be adjusted, DELSTRIGO is not recommended in patients with estimated creatinine clearance less than 50 mL/min.

The most common adverse reactions with DELSTRIGO (incidence ≥5%, all intensities) were dizziness (7%), nausea (5%), and abnormal dreams (5%). The most common adverse reactions with PIFELTRO (incidence ≥5%, all intensities) were nausea (7%), dizziness (7%), headache (6%), fatigue (6%), diarrhea (6%), abdominal pain (5%), and abnormal dreams (5%).

By Week 96 in DRIVE-FORWARD, 2% of adult subjects in the PIFELTRO group and 3% in the DRV+r group had adverse events leading to discontinuation of study medication.

By Week 96 in DRIVE-AHEAD, 3% of adult subjects in the DELSTRIGO group and 7% in the EFV/FTC/TDF group had adverse events leading to discontinuation of study medication.

In DRIVE-FORWARD, mean changes from baseline at Week 48 in LDL-cholesterol (LDL-C) and non-HDL-cholesterol

(non-HDL-C) were pre-specified. LDL-C: -4.6 mg/dL in the PIFELTRO group vs 9.5 mg/dL in the DRV+r group. Non-HDL-C: -5.4 mg/dL in the PIFELTRO group vs 13.7 mg/dL in the DRV+r group. The clinical benefits of these findings have not been demonstrated.

In DRIVE-AHEAD, mean changes from baseline at Week 48 in LDL-cholesterol (LDL-C) and non-HDL-cholesterol (non-HDL-C) were pre-specified. LDL-C: -2.1 mg/dL in the DELSTRIGO group vs 8.3 mg/dL in the EFV/FTC/TDF group. Non-HDL-C: -4.1 mg/dL in the DELSTRIGO group vs 12.7 mg/dL in the EFV/FTC/TDF group. The clinical benefits of these findings have not been demonstrated.

In DRIVE-SHIFT, mean changes from baseline at Week 48 in LDL-cholesterol (LDL-C) and non-HDL-cholesterol (non-HDL-C) were pre-specified. LDL-C: -16.3 mg/dL in the DELSTRIGO group vs -2.6 mg/dL in the PI + ritonavir group. Non-HDL-C: -24.8 mg/dL DELSTRIGO group vs -2.1 mg/dL in the PI + ritonavir group. The clinical benefits of these findings have not been demonstrated.

In DRIVE-AHEAD, neuropsychiatric adverse events were reported in the three pre-specified categories of sleep disorders and disturbances, dizziness, and altered sensorium. Twelve percent of adult subjects in the DELSTRIGO group and 26% in the EFV/FTC/TDF group reported neuropsychiatric adverse events of sleep disorders and disturbances; 9% in the DELSTRIGO group and 37% in the EFV/FTC/TDF group reported dizziness; and 4% in the DELSTRIGO group and 8% in the EFV/FTC/TDF group reported altered sensorium.

The safety of DELSTRIGO in virologically-suppressed adults was based on Week 48 data from subjects in the DRIVE-SHIFT trial. Overall, the safety profile in virologically-suppressed adult subjects was similar to that in subjects with no ARV treatment history.

There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to PIFELTRO or DELSTRIGO during pregnancy. Healthcare providers are encouraged to register patients by calling the Antiretroviral Pregnancy Registry (APR) at 1-800-258-4263.

Mothers infected with HIV-1 should be instructed not to breastfeed if they are receiving PIFELTRO or DELSTRIGO due to the potential for HIV-1 transmission.

About Islatravir (MK-8591)

Islatravir (MK-8591) is Merck's investigational nucleoside reverse transcriptase translocation inhibitor under evaluation in more than 10 clinical trials. For treatment, islatravir is being evaluated in combination with other antiretrovirals, including the ILLUMINATE clinical trials program for a once-daily regimen. In the IMPOWER clinical trials, islatravir is also being studied for pre-exposure prophylaxis (PrEP) of HIV-1 infection as a single agent across a

variety of formulations, including an oral once-monthly regimen.

Our Commitment to HIV

For more than 35 years, Merck has been committed to scientific research and discovery (R&D) in HIV. Today, we are developing a series of antiviral options designed to help people manage HIV and protect people from HIV, with the goal of reducing the growing burden of infection worldwide. We remain committed to working hand-in-hand with our partners in the global HIV community to address the complex challenges that impede progress toward ending the epidemic.

About Merck

For over 130 years, Merck, known as MSD outside the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases in pursuit of our mission to save and improve lives. We demonstrate our commitment to patients and population health by increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to prevent and treat diseases that threaten people and animals – including cancer, infectious diseases such as HIV and Ebola, and emerging animal diseases – as we aspire to be the premier research-intensive biopharmaceutical company in the world. For more information, visit **www.merck.com** and connect with us on **Twitter**, **Facebook**, **Instagram**, **YouTube** and **LinkedIn**.

Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of the global outbreak of novel coronavirus disease (COVID-19); the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market

conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2020 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (**www.sec.gov**).

Please see Prescribing Information for PIFELTRO (doravirine) at: **https://www.merck.com/product/usa/pi_circulars/p/pifeltro/pifeltro_pi.pdf**; and Patient Information for PIFELTRO (doravirine) at: **https://www.merck.com/product/usa/pi_circulars/p/pifeltro/pifeltro_ppi.pdf**

Please see Prescribing Information for DELSTRIGO (doravirine/3TC/TDF) at: **https://www.merck.com/product/usa/pi_circulars/d/delstrigo/delstrigo_pi.pdf** and Patient Information for DELSTRIGO (doravirine/3TC/TDF) at: **https://www.merck.com/product/usa/pi_circulars/d/delstrigo/delstrigo_ppi.pdf**

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