Merck Presents New Data from Ongoing Phase 2b Clinical Trial Evaluating Efficacy and Safety of Investigational Islatravir in Combination With Doravirine Through 144 Weeks for HIV-1 Treatment at EACS 2021

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Islatravir Combined with Doravirine Continued to Maintain Viral Suppression for People Who Had Not Previously Received Treatment

KENILWORTH, N.J.--(BUSINESS WIRE)-- Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced Week 144 data from the Phase 2b dose-ranging study evaluating the antiretroviral activity, tolerability, and safety of islatravir in combination with doravirine compared to doravirine/lamivudine/tenofovir disoproxil fumarate (DOR/3TC/TDF) in antiretroviral treatment-naïve adults with HIV-1. Phase 2b data through 144 weeks demonstrated that islatravir combined with doravirine continued to maintain viral suppression, as measured by the number of study participants achieving HIV-1 RNA levels <50 copies/mL, similar to DOR/3TC/TDF. The data further characterized the tolerability and safety profile of islatravir in combination with doravirine. The Week 144 results are a follow-up to the Week 96 results and safety data presented at the virtual 2020 International Congress on Drug Therapy in HIV Infection (HIV Glasgow 2020) and the virtual International AIDS Society Conference on HIV Science (IAS 2021), respectively. The Week 144 data were consistent with the Week 96 results in the 0.75 mg dose group (the selected Phase 3 dose), and were shared as an oral presentation during the 18th European AIDS Conference (EACS 2021) in London, U.K.

“We are encouraged by the Week 144 findings presented at EACS, which further support the potential of a two-drug
doravirine/islatravir regimen for the treatment of HIV-1,” said Dr. Joan Butterton, vice president, global clinical development, infectious diseases, Merck Research Laboratories. “As we advance the ILLUMINATE clinical development program, we look forward to continuing to study this investigational treatment across diverse patient populations.”

Initial data from two pivotal ILLUMINATE Phase 3 clinical trials evaluating a combination product of doravirine/islatravir in virologically suppressed adults with HIV-1 switching from a stable antiretroviral regimen were also recently shared.

Islatravir is currently being evaluated 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. An overview of the islatravir treatment and prevention development program is available here.

**Week 144 Efficacy and Safety Results from Phase 2b Study of Investigational Islatravir with Doravirine**

In this international, multicenter clinical trial (NCT03272347), treatment-naïve adult participants with HIV-1 were randomly assigned (1:1:1:1) to one of four once-daily oral treatment groups: islatravir 0.25 mg (n=29), 0.75 mg (n=30), or 2.25 mg (n=31) in combination with doravirine (100 mg) and 3TC (300 mg) compared to DOR/3TC/TDF (n=31; Part 1). After a minimum of 24 weeks of treatment, participants in the islatravir treatment groups with HIV-1 RNA <50 copies/mL were transitioned to a two-drug regimen consisting of doravirine and islatravir, without 3TC (Part 2). Participants in the islatravir treatment groups then transitioned to 0.75 mg islatravir (the selected Phase 3 dose) plus doravirine between Weeks 60 to 84, and they continued the combination therapy through Week 144 (Part 3). At Week 144, participants switched to the fixed-dose combination of the selected dose of islatravir and doravirine as open-label treatment until the end of the trial at Week 192 (Part 4).

At Week 144, at all dose levels, islatravir combined with doravirine maintained virologic suppression as measured by the proportion of study participants achieving HIV-1 RNA levels <50 copies/mL: 72.4% (n=21/29), 83.3% (n=25/30), and 61.3% (n=19/31) of participants maintained virologic suppression in the 0.25 mg, 0.75 mg, and 2.25 mg islatravir combined with doravirine groups, respectively. Overall, 72.2% (n=65/90) of the combined islatravir with doravirine groups had HIV-RNA levels <50 copies/mL, which was similar to 77.4% (n=24/31) of the DOR/3TC/TDF group. Through Week 144, seven participants met the criteria for protocol-defined virologic failure (PDVF) (confirmed HIV-1 RNA ≥50 copies/mL) and discontinued treatment, all of whom had HIV-1 RNA levels <80 copies/mL. No participants met the criteria for clinically significant confirmed viremia (HIV-1 RNA ≥200 copies/mL) or viral drug resistance analysis.

The proportion of participants experiencing at least one adverse event (AE) at Week 144 was similar between the
islatravir combined with doravirine and DOR/3TC/TDF groups. At Week 144, 89.7% (n=26/29), 90.0% (n=27/30), and 77.4% (n=24/31) of participants experienced AEs in the 0.25 mg, 0.75 mg, and 2.25 mg islatravir combined with doravirine groups, respectively. Additionally, 85.6% (n=77/90) of the combined islatravir combined with doravirine groups experienced AEs, as compared to 87.1% (n=27/31) in the DOR/3TC/TDF group. The most common drug-related AEs for the combined islatravir combined with doravirine groups versus DOR/3TC/TDF were diarrhea (1.1% [n=1/90] vs. 12.9% [n=4/31]), nausea (3.3% [n=3/90] vs. 9.7% [n=3/31]), headache (2.2% [n=2/90] vs. 3.2% [n=1/31]), and abnormal dreams (2.2% [n=2/90] vs. 0% [n=0/31]). No additional islatravir combined with doravirine participants reported drug-related AEs after Week 48. The rate of discontinuations due to drug-related AEs was 2.2% (n=2/90) for the combined islatravir with doravirine groups and 3.2% (n=1/31) for DOR/3TC/TDF, all occurring before Week 48. There were no deaths or serious-drug-related AEs in the islatravir combined with doravirine groups.

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 in the 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 Ilatravir (MK-8591)**

Ilatravir (MK-8591) is Merck’s investigational nucleoside reverse transcriptase translocation inhibitor under evaluation in more than 10 clinical trials. For treatment, ilatravir is being evaluated in combination with other antiretrovirals, including the ILLUMINATE clinical trials program for a once-daily regimen. In the IMPOWER clinical trials, ilatravir 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](http://www.merck.com) and
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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