Merck Announces Positive Top-Line Results from Pivotal Phase 3 Trials Evaluating Investigational, Once-Daily Oral Fixed Dose Combination of Doravirine/Islatravir for the Treatment of People with HIV-1 Infection

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Week 48 Data Met Safety and Efficacy Endpoints in Adults with HIV-1 Infection Currently on Antiretroviral Therapy

KENILWORTH, N.J.--(BUSINESS WIRE)-- Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced positive top-line results from two pivotal Phase 3 trials of the investigational, once-daily oral fixed dose combination pill of doravirine/islatravir (DOR/ISL) in adults with HIV-1 infection who are virologically suppressed on different antiretroviral therapy regimens (ART; ILLUMINATE SWITCH A) or bictegravir/emtricitabine/tenofovir (BIC/FTC/TAF; ILLUMINATE SWITCH B). 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 ART (ILLUMINATE SWITCH A) and between DOR/ISL and BIC/FTC/TAF (ILLUMINATE SWITCH B). The safety and tolerability profile of DOR/ISL during the trials to date are consistent with the previously reported Phase 2 studies. Doravirine is approved for the treatment of adults with HIV-1 in combination with other antiretrovirals, as a single agent (PIFELTRO) and a component of a single-tablet regimen (DELSTRIGO; DOR/3TC/TDF). Islatravir is Merck's investigational nucleoside reverse transcriptase translocation inhibitor under evaluation for the treatment of people living with HIV-1 infection in combination with other antiretrovirals. Detailed findings from these studies will be presented at a future scientific congress and will form the basis of global regulatory applications.
“Merck is committed to investigating potential treatment options to help address the evolving needs of people living with HIV,” said Dr. Joan Butterton, vice president, global clinical development, infectious diseases, Merck Research Laboratories. “We are encouraged by the results from the Phase 3 ILLUMINATE SWITCH A and B trials, in which the DOR/ISL dual regimen efficacy was comparable to certain commonly used three-drug regimens. We will continue to study doravirine/islatravir in diverse populations of people living with HIV and look forward to sharing data from these trials.”

The ILLUMINATE clinical trial program is evaluating DOR/ISL in a broad patient population, which includes people with HIV-1 who are virologically suppressed on ART, those who are heavily treatment experienced and those who are new to HIV treatment. The clinical trial program also includes pediatric participants with HIV-1 weighing at least 35 kg who are virologically suppressed and have not previously been treated. Merck is committed to enrolling diverse people in our HIV-1 clinical trials, especially among communities who may be disproportionately impacted by HIV, such as women and those within the Black and Latinx communities.

Indications and Usage for 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 ILLUMINATE SWITCH A

The ILLUMINATE SWITCH A (MK-8591A-017) (NCT04223778) Study is a Phase 3, randomized, active-controlled, open-
label clinical trial to evaluate a switch from antiretroviral therapy (ART) to investigational, oral, once-daily DOR/ISL
(100 mg/0.75 mg) (MK-8591A), in adults with HIV-1 who are virologically suppressed. Participants (n=672) were
randomized 1:1 to either switch to DOR/ISL or continue with their current baseline ART regimen through Week 48.
At Week 48, all participants receive DOR/ISL through Week 96 of the trial. The primary efficacy (percentage of
participants with HIV-1 RNA levels ≥50 copies/mL) and safety (number of participants experiencing adverse events
(AEs) and discontinuing study intervention due to AEs) endpoints were assessed at Week 48.

About ILLUMINATE SWITCH B

The ILLUMINATE SWITCH B (MK-8591A-018) (NCT04223791) Study is a Phase 3, randomized, double-blind clinical
trial to evaluate a switch from BIC/FTC/TAF to investigational, oral, once-daily DOR/ISL (100 mg/0.75 mg), in adults
with HIV-1 who are virologically suppressed. Participants (n=641) were randomized 1:1 to either switch to DOR/ISL
or continue on BIC/FTC/TAF through Week 144. The primary efficacy (percentage of participants with HIV-1 RNA
levels ≥50 copies/mL) and safety (number of participants experiencing AEs and discontinuing study intervention due
to AEs) endpoints were assessed at Week 48.

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. An overview of the islatravir treatment and prevention development program is available here.

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 
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Please see Prescribing Information for DELSTRIGO (doravirine/3TC/TDF) at: 

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