NEWS RELEASE

European Commission Approves Merck's DELSTRIGO™ (doravirine / lamivudine / tenofovir disoproxil fumarate), a Once-Daily Fixed-Dose Combination Tablet as a Complete Regimen and PIFELTRO™ (doravirine), an NNRTI, Both for the Treatment of HIV-1 in...

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Approvals Based on Findings from the Pivotal Phase 3 DRIVE-AHEAD and DRIVE-FORWARD Trials Evaluating the Efficacy and Safety of DELSTRIGO and PIFELTRO Through 96 Weeks

KENILWORTH, N.J.--(**BUSINESS WIRE**)--Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced that the European Commission has approved DELSTRIGO™ and PIFELTRO™ for the treatment of HIV-1 infection. DELSTRIGO is a new once-daily fixed-dose combination tablet of doravirine (100 mg), lamivudine (3TC, 300 mg) and tenofovir disoproxil fumarate (TDF, 300 mg[1]). It is indicated in the European Union for the treatment of adults with HIV-1 infection without past or present evidence of resistance to the non-nucleoside reverse transcriptase inhibitor (NNRTI) class of antiviral agents, lamivudine or tenofovir. PIFELTRO (doravirine, 100 mg) is a new, once-daily NNRTI indicated (in the EU) in combination with other antiretroviral medicines for the treatment of adults with HIV-1 infection without past or present evidence of resistance to the NNRTI class.

In the United States, both DELSTRIGO and PIFELTRO are indicated for the treatment of HIV-1 infection in adults with no prior antiretroviral treatment experience, and are administered orally once daily with or without food. DELSTRIGO contains a boxed warning regarding post-treatment acute exacerbations of hepatitis B (HBV) infection. DELSTRIGO and PIFELTRO do not cure HIV-1 infection or AIDS.

“We are very pleased that the European Commission has approved DELSTRIGO and PIFELTRO, as this approval marks another important milestone in Merck’s unwavering commitment to the global HIV community,” said Dr. George Hanna, vice president and therapeutic area head of infectious diseases, Global Clinical Development, Merck Research Laboratories. “These medicines bring new treatment options with demonstrated efficacy that could potentially address unmet needs for people in Europe living with HIV.”

The approval allows for marketing of DELSTRIGO and PIFELTRO in all 28 European Union member states, plus Iceland, Lichtenstein and Norway, and follows a positive opinion from the Committee for Medicinal Products for Human Use of the European Medicines Agency announced on Sept. 20, 2018. Marketing authorization applications for DELSTRIGO and PIFELTRO are also under review in other countries, including Australia and Switzerland. The U.S. Food and Drug Administration approved DELSTRIGO and PIFELTRO on Aug. 30, 2018. Health Canada approved PIFELTRO on Oct. 12, 2018 and DELSTRIGO on Nov. 9, 2018. Availability for DELSTRIGO and PIFELTRO in the EU is anticipated to begin in the first half of 2019.

“As a practitioner serving people living with HIV, I welcome new medicines that can help us tailor HIV treatment regimens to the needs of the individual,” said Dr. Esteban Martínez, senior consultant and associate professor of medicine, infectious diseases, University of Barcelona, Spain. “The approvals of DELSTRIGO and PIFELTRO bring important new treatment options to market which have shown demonstrated efficacy and low rates of discontinuation.”

Data Supporting the Approvals of DELSTRIGO and PIFELTRO in the European Union

The approval from the European Commission was based on data from two pivotal, randomized, multicenter, double-blind, active controlled Phase 3 trials, DRIVE-AHEAD and DRIVE-FORWARD, evaluating the efficacy and safety of DELSTRIGO and PIFELTRO, respectively, in participants infected with HIV-1 with no prior antiretroviral treatment history. Across both of the studies, 25.4 percent of the participants were based in Europe (379/1494).

In DRIVE-AHEAD, DELSTRIGO met its primary endpoint, demonstrating non-inferior efficacy compared to efavirenz (EFV)/emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF) at 48 weeks (84% in the DELSTRIGO group achieved viral suppression of HIV-1 RNA <40 copies/mL vs. 80% in the EFV/FTC/TDF group; treatment difference: 4.1%, 95% confidence interval: -1.5, 9.7). The Week 96 data were supportive of the Week 48 findings. At Week 96, 76% in the DELSTRIGO group achieved viral suppression of HIV-1 RNA <40 copies/mL vs. 73% in the EFV/FTC/TDF group; treatment difference: 3.3%, 95% confidence interval: -3.1, 9.6. The rate of discontinuation of treatment due to adverse events was lower in the DELSTRIGO treatment group than in the EFV/FTC/TDF treatment group, 3% and 6.6% respectively. Clinical adverse reactions of all grades occurring in ≥5 percent of participants in the DELSTRIGO treatment group included nausea (6%) and headache (5%).

In DRIVE-FORWARD, PIFELTRO met its primary endpoint, demonstrating non-inferior efficacy compared to darunavir + ritonavir (DRV+r), each in combination with FTC/TDF or abacavir (ABC)/3TC at 48 weeks (83% in the PIFELTRO group achieved viral suppression of HIV-1 RNA <40 copies/mL vs. 79% in the DRV+r group; treatment difference: 4.2%, 95% confidence interval: -1.4, 9.7). The Week 96 data were supportive of the Week 48 findings. At week 96, 72% in the PIFELTRO group achieved viral suppression of HIV-1 RNA <40 copies/mL vs. 64% in the DRV+r group; treatment difference: 7.6%, 95% confidence interval: 1.0, 14.2. In a pooled analysis combining data from two clinical trials of treatment-naïve participants (P007 and P021/DRIVE-AHEAD), fewer participants in the combined doravirine (100 mg) treatment groups (2.8%) discontinued due to an adverse event by week 48 compared with the combined EFV treatment group (6.1%) (treatment difference -3.4%, p=0.012). Clinical adverse reactions of all grades occurring in ≥5 percent of participants in the PIFELTRO treatment group included nausea (6%) and headache (5%).

Selected Safety Information about DELSTRIGO (doravirine/3TC/TDF) in the U.S.

Warning: Post treatment Acute Exacerbation of Hepatitis B (HBV)

All patients with HIV-1 should be tested for the presence of HBV before initiating antiretroviral 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 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.

DELSTRIGO is 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. 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, as 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.

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

If 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. The most common adverse reactions with DELSTRIGO (incidence ≥5%, all intensities) were dizziness (7%), nausea (5%) and abnormal dreams (5%).

There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to DELSTRIGO during pregnancy. Healthcare providers are encouraged to register patients by calling the Antiretroviral Pregnancy Registry at 1-800-258-4263. Mothers infected with HIV-1 should be instructed not to breastfeed if they are receiving DELSTRIGO due to the potential for HIV-1 transmission. Because DELSTRIGO is a fixed-dose combination tablet and the components cannot be altered, it is not recommended in patients with estimated creatinine clearance less than 50 mL/min.

Selected Safety Information about PIFELTRO (doravirine) in the U.S.

PIFELTRO is 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 PIFELTRO plasma concentrations may occur, which may decrease the effectiveness of PIFELTRO. Immune reconstitution syndrome can occur, including the occurrence of autoimmune disorders with variable time to onset, which may necessitate further evaluation and treatment. Co-administration of PIFELTRO with efavirenz, etravirine or nevirapine is not recommended. If 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 important potential drug-drug interactions. The safety of PIFELTRO is based on two studies, DRIVE-FORWARD and DRIVE-AHEAD. In DRIVE-FORWARD, the most common adverse reactions (incidence ≥5%, all intensities) were nausea (7%), headache (6%), fatigue (6%), diarrhea (5%) and abdominal pain (5%). In DRIVE-AHEAD, the most common adverse reactions (incidence ≥5%, all intensities) were dizziness (7%), abnormal dreams (5%) and nausea (5%).

There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to PIFELTRO during pregnancy. Healthcare providers are encouraged to register patients by calling the Antiretroviral Pregnancy Registry at 1-800-258-4263. Mothers infected with HIV-1 should be instructed not to breastfeed if they are receiving PIFELTRO due to the potential for HIV transmission.

About Merck

For more than a century, Merck, a leading global biopharmaceutical company known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. 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 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 2017 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 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**

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**

[1] Equivalent to 245 mg of tenofovir disoproxil

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