New Data from Merck’s Expanding HIV Clinical Development Program to be Presented at CROI 2019

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KENILWORTH, N.J., Feb 25, 2019 – Merck (NYSE: MRK), known as MSD outside the United States and Canada, announced today that new data from the company’s HIV clinical development program are scheduled to be presented at the Conference on Retroviruses and Opportunistic Infections (CROI 2019) taking place March 4-7, 2019 in Seattle, WA. Presentations include an integrated efficacy analysis of data from the Phase 3 DRIVE-FORWARD and DRIVE-AHEAD trials that evaluated DELSTRIGO™ (doravirine/lamivudine/tenofovir disoproxil fumarate) and PIFELTRO™ (doravirine) in treatment-naïve adults; data on the safety of ISENTRESS® exposure in pregnancy; and findings from a clinical pharmacokinetic (PK) study of MK-8591, a novel investigational nucleoside reverse transcriptase translocation inhibitor.

“Merck continues to build on our long legacy of research and development in HIV medicines,” said Dr. George Hanna, vice president and therapeutic area head of infectious diseases, global clinical development, Merck Research Laboratories. “These data reflect the extensive nature of our HIV portfolio and pipeline, and our commitment to improving care for people living with HIV.”

Key Abstracts from Merck’s HIV Portfolio and Pipeline at CROI 2019:

- MK-8591 Potency and PK Provide High Inhibitory Quotients at Low Doses QD and QW. Abstract 481. J. Grobler et al.
- InSTI Exposure and Neural-Tube Defects: Data from Antiretroviral Pregnancy Registry. Abstract 747. J. Albano et al.

For more information, including a complete list of abstract titles and presentation dates and times for Merck’s HIV portfolio, please visit the CROI website.

PIFELTRO (doravirine, 100 mg), a once-daily non-nucleoside reverse transcriptase inhibitor (NNRTI) to be administered in combination with other antiretroviral (ARV) medicines, and DELSTRIGO, a once-daily fixed-dose combination tablet of doravirine (100 mg), lamivudine (3TC, 300 mg) and tenofovir disoproxil fumarate (TDF, 300 mg) as a complete regimen, are currently indicated for the treatment of HIV-1 infection in adult patients not previously treated with antiretroviral therapy. DELSTRIGO contains a boxed warning regarding post-treatment acute exacerbations of hepatitis B (HBV) infection. PIFELTRO and DELSTRIGO do not cure HIV-1 infection or AIDS.

Earlier this year, the U.S. Food and Drug Administration (FDA) accepted for review the supplemental New Drug Applications (sNDAs) for PIFELTRO (in combination with other antiretroviral medicines) and DELSTRIGO for use in people living with HIV-1 who are switching from a stable antiretroviral regimen and whose virus is suppressed (HIV-1 RNA <50 copies/mL). The Prescription Drug User Fee Act (PDUFA) date for the sNDAs is Sept. 20, 2019.

Selected Safety Information about PIFELTRO (doravirine)

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 antituberculosis 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 (doravirine).
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 (doravirine/lamivudine (3TC)/tenofovir disoproxil fumarate (TDF)) 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.

Indication for ISENTRESS (raltegravir)

ISENTRESS is indicated in combination with other antiretroviral (ARV) agents for the treatment of HIV-1 infection in adults.

Selected Safety Information about ISENTRESS

Severe, potentially life-threatening and fatal skin reactions have been reported. This includes cases of Stevens-Johnson syndrome, hypersensitivity reaction and toxic epidermal necrolysis. Immediately discontinue treatment with ISENTRESS and other suspect agents if severe hypersensitivity, severe rash, or rash with systemic symptoms or liver aminotransferase elevations develops and monitor clinical status, including liver aminotransferases closely.

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

ISENTRESS chewable tablets contain phenylalanine, a component of aspartame, which may be harmful to patients with phenylketonuria.

Co-administration of ISENTRESS with drugs that are strong inducers of uridine diphosphate glucuronosyltransferase (UGT) 1A1 may result in reduced plasma concentrations of raltegravir. Co-administration of ISENTRESS with drugs that inhibit UGT1A1 may increase plasma levels of raltegravir.

Co-administration of ISENTRESS and other drugs may alter the plasma concentration of raltegravir. The potential for drug-drug interactions must be considered prior to and during therapy. Co-administration or staggered administration of aluminum and/or magnesium-containing antacids and ISENTRESS is not recommended.

Rifampin, a strong inducer of UGT1A1, reduces plasma concentrations of ISENTRESS. Therefore, the dose of ISENTRESS for adults should be increased to 800 mg twice daily during coadministration with rifampin. There are no data to guide coadministration of ISENTRESS with rifampin in patients below 18 years of age.

The impact of other strong inducers of drug metabolizing enzymes on raltegravir is unknown (e.g., Carbamazepine,
Phenobarbital, and Phenytoin). Co-administration of ISENTRESS with other strong inducers is not recommended.

The most commonly reported (≥2%) drug-related clinical adverse reactions of moderate to severe intensity in treatment-naïve adult patients receiving ISENTRESS compared to efavirenz were headache (4% vs 5%), insomnia (4% vs 4%), nausea (3% vs 4%), dizziness (2% vs 6%), and fatigue (2% vs 3%), respectively. In treatment-experienced adult patients receiving ISENTRESS, the most commonly reported (≥2%) drug-related clinical adverse reactions of moderate to severe intensity and at a higher incidence compared with placebo was headache (2% vs <1%). In both studies, intensities were defined as: Moderate (discomfort enough to cause interference with usual activity); or Severe (incapacitating with inability to work or do usual activity). In treatment-experienced pediatric patients 4 weeks through 18 years of age receiving ISENTRESS, the frequency, type and severity of drug-related adverse reactions were comparable to those observed in adults.

Grade 2-4 creatine kinase laboratory abnormalities were observed in subjects treated with ISENTRESS. Myopathy and rhabdomyolysis have been reported. Use with caution in patients at increased risk of myopathy or rhabdomyolisis, such as patients receiving concomitant medications known to cause these conditions and patients with a history of rhabdomyolysis, myopathy or increased serum creatine kinase.

Rash occurred more commonly in treatment-experienced subjects receiving regimens containing ISENTRESS + darunavir/ritonavir compared to subjects receiving ISENTRESS without darunavir/ritonavir or darunavir/ritonavir without ISENTRESS. However, rash that was considered drug related occurred at similar rates for all 3 groups. These rashes were mild to moderate in severity and did not limit therapy; there were no discontinuations due to rash.

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

Women infected with HIV-1 should be instructed not to breastfeed if they are receiving ISENTRESS due to the potential for HIV transmission.

Our Commitment to HIV

For more than 30 years, Merck has been committed to scientific research and discovery in HIV, and we continue to be driven by the conviction that more medical advances are still to come. Our focus is on pursuing research that addresses unmet medical needs and helps people living with HIV and their communities. We remain committed to working hand-in-hand with our partners in the global HIV community to address the complex challenges that hinder continued progress.

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 (darunavir/3TC/TDF) at: https://www.merck.com/product/usa/pi_circulars/d/delstrigo/delstrigo_ppi.pdf; and Patient Information for DELSTRIGO (darunavir/3TC/TDF) at: https://www.merck.com/product/usa/pi_circulars/d/delstrigo/delstrigo_pi.pdf

Please see Prescribing Information for PIFELTRO (darunavir) at: https://www.merck.com/product/usa/pi_circulars/p/pifeltro/pifeltro_ppi.pdf; and Patient Information for PIFELTRO (darunavir) at: https://www.merck.com/product/usa/pi_circulars/p/pifeltro/pifeltro_pi.pdf
Please see Prescribing Information for ISENTRESS (raltegravir) at: https://www.merck.com/product/usa/pi_circulars/i/isentress/isentress_pi.pdf; and Patient Information for ISENTRESS (raltegravir) at: https://www.merck.com/product/usa/pi_circulars/i/isentress/isentress_ppi.pdf;

The Instructions for Use also are available at: http://www.merck.com/product/usa/pi_circulars/i/isentress/isentress_ifu.pdf

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