Merck Announces Week 96 Data from Pivotal Phase 3 DRIVE-AHEAD Study Evaluating DELSTRIGO™ (doravirine / lamivudine / tenofovir disoproxil fumarate) for the Treatment of HIV-1 in Treatment-Naïve Patients

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KENILWORTH, N.J.--(BUSINESS WIRE)--Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced new results from the Phase 3 DRIVE-AHEAD clinical trial evaluating the efficacy and safety of DELSTRIGO™, a once-daily fixed-dose combination tablet of doravirine (100 mg), lamivudine (3TC, 300 mg) and tenofovir disoproxil fumarate (TDF, 300 mg) in treatment-naïve adults with HIV-1 infection. The efficacy findings at Week 96 in DRIVE-AHEAD were consistent with the findings at Week 48 in which DELSTRIGO demonstrated non-inferior efficacy in comparison to a fixed-dose combination of efavirenz (EFV, 600 mg), emtricitabine (FTC, 200 mg) and TDF (300 mg). The pivotal Phase 3, Week 48 data were previously presented at the 9th IAS Conference on HIV Science / IAS 2017.

The new Week 96 findings will be presented today as a late-breaking oral presentation at IDWeek 2018 taking place Oct. 3-7, 2018, in San Francisco.

“Long-term data from this pivotal clinical trial further confirm the efficacy and safety of DELSTRIGO in treatment-naïve patients,” said Dr. Jean-Michel Molina, Professor of Infectious Diseases, University of Paris, and Head of the Infectious Diseases Department at Saint-Louis Hospital in Paris, France. “The data position this fixed-dose combination as a new treatment option that can address the needs of people living with HIV today.”

Data from DRIVE-AHEAD

In DRIVE-AHEAD, 728 participants with no antiretroviral treatment history were randomized and received at least one dose of either DELSTRIGO or EFV/FTC/TDF once daily. In this trial, after 96 weeks of treatment, the proportion of participants achieving plasma HIV-1 RNA levels less than 50 copies/mL was 77.5 percent in the group treated with DELSTRIGO (doravirine/3TC/TDF) and 73.6 percent in the group treated with EFV/FTC/TDF (treatment difference: 3.8%, 95% confidence interval: -2.4, 10.0).

No additional viral drug resistance to doravirine was observed in study participants between Week 48 and Week 96, while two study participants in the EFV/FTC/TDF group developed viral drug resistance to EFV.

At Week 96, the rate of discontinuation of therapy due to adverse events was 3.0 percent (11/364) in the DELSTRIGO group and 7.0 percent (27/364) in the EFV/FTC/TDF group. In addition, the three pre-specified neuropsychiatric endpoints of dizziness, sleep disorders/disturbances and altered sensorium were significantly less frequent in the DELSTRIGO group than in the EFV/FTC/TDF group: dizziness (10.2% vs. 38.2%, treatment difference: -28%, 95% confidence interval: -33.9, -22.1), sleep disorders and disturbances (14.0% vs. 27.5%, treatment difference: -13.5%, 95% confidence interval: -19.3, -7.6) and altered sensorium (4.9% vs. 8.5%, treatment difference: -3.6%, 95% confidence interval: -7.4, 0.1).

The study also reported lower mean changes from baseline in the levels of fasting lipids in the DELSTRIGO group compared with the EFV/FTC/TDF group at Week 96, including LDL-C (-0.6 mg/dL vs. 10.8 mg/dL, treatment difference: -11.1, 95% confidence interval: -14.8, -7.4) and non-HDL-C (-2.1 mg/dL vs. 15.0 mg/dL, treatment difference: -17.0, 95% confidence interval: -21.3, -13.0).

“At Merck, we are committed to continued scientific innovation as we look for new ways to help improve how HIV is treated. The recent U.S. Food and Drug Administration approval of DELSTRIGO represents this ongoing commitment,” said Dr. George Hanna, vice president and therapeutic area head of infectious diseases, global clinical development, Merck Research Laboratories. “We are pleased to see the efficacy results for DELSTRIGO at 96 weeks, which support the initial findings seen in the 48 week data.”

On Aug. 30, 2018, DELSTRIGO and PIFELTRO (doravirine) were approved by the U.S. Food and Drug Administration (FDA). DELSTRIGO was approved as a once-daily fixed-dose combination tablet of doravirine (100 mg), 3TC (300 mg) and TDF (300 mg); and PIFELTRO (100 mg), a new non-nucleoside reverse transcriptase inhibitor (NNRTI), was approved to be administered in combination with other antiretroviral medicines. Both DELSTRIGO and PIFELTRO are indicated for the treatment of HIV-1...
infection in adult patients with no prior antiretroviral treatment experience, and are administered orally once daily with or without food. In the U.S., DELSTRIGO contains a boxed warning regarding post-treatment acute exacerbation of hepatitis B (HBV) infection. DELSTRIGO (doravirine/3TC/TDF) does not cure HIV-1 infection or AIDS. On Sept. 20, 2018, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending granting of marketing authorization for DELSTRIGO (doravirine/3TC/TDF) and PIFELTRO (doravirine).

About DRIVE-AHEAD

DRIVE-AHEAD is a Phase 3 multicenter, double-blind, randomized clinical trial in which 728 participants with no antiretroviral treatment history were randomized and received at least one dose of either DELSTRIGO or efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV 600 mg/FTC 200 mg/TDF 300 mg) once daily. The primary endpoint of the clinical trial was the proportion of participants with HIV-1 RNA copies of less than 50 copies/mL at Week 48. The primary safety endpoint was the proportion of participants with neuropsychiatric adverse events through Week 48 in the following pre-specified categories: dizziness, sleep disorders and disturbances and the inability to think clearly or concentrate (altered sensorium). The trial consists of a 96-week double-blind treatment period (base study) and an open label extension after participants complete the base study. Secondary endpoints include efficacy at Week 96, an evaluation of the effects of DELSTRIGO and EFV/FTC/TDF on fasting serum lipids, change from baseline in CD4+ T-cell count and evaluation of safety and tolerability. For further information regarding DRIVE-AHEAD please visit www.clinicaltrials.gov clinical trial registry number NCT02403674.

Selected Safety Information about DELSTRIGO (doravirine/3TC/TDF)

Warming: 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 3TC 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 (doravirine/3TC/TDF). DELSTRIGO is contraindicated in patients with a previous hypersensitivity reaction to 3TC.

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)

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.

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 to continuing 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, NJ, 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
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_ppi.pdf
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Language:
English

Contact:
Merck
Media:
Pam Eisele
(267) 305-3558
or
Sarra S. Herzog
(908) 740-1871
or
Investors:
Teri Loxam
(908) 740-1986