



NEWS RELEASE

Merck's HIV Therapy DELSTRIGO™ (doravirine / lamivudine / tenofovir disoproxil fumarate) Meets Primary Efficacy Endpoint in Phase 3 DRIVE-SHIFT Study Evaluating Switch to DELSTRIGO from Other Antiretroviral Treatment Regimens

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New Data on Patients Who Were Virologically Suppressed Switching to DELSTRIGO to be Presented as Late-Breaker Oral Presentation at IDWeek 2018

KENILWORTH, N.J.--(**BUSINESS WIRE**)--Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced the first presentation of data from the Phase 3 DRIVE-SHIFT trial evaluating a switch of medication to DELSTRIGO™, a once-daily fixed-dose combination tablet of doravirine (100 mg), lamivudine (3TC, 300 mg) and tenofovir disoproxil fumarate (TDF, 300 mg), in adults with HIV-1 infection who demonstrated virological suppression for at least six months on a stable antiretroviral treatment regimen. The study met its primary endpoint of non-inferior efficacy as measured by the proportion of participants who switched to DELSTRIGO and had plasma HIV-1 RNA levels <50 copies/mL at Week 48 compared to the proportion of participants who continued on their baseline regimen and had HIV-1 RNA levels <50 copies/mL at Week 24. These study results will be presented today as a late-breaking oral presentation at **IDWeek 2018** taking place Oct. 3-7, 2018, in San Francisco.

"These data build on the existing clinical profile of DELSTRIGO as seen in treatment-naïve patients, and suggests its potential to address a broader population," said Dr. Princy Kumar, Chief, Division of Infectious Diseases and Tropical Medicine at MedStar Georgetown University Hospital and Professor of Medicine and Microbiology,

Georgetown University School of Medicine, Washington, D.C. "Data from this trial support another possible future option for people living with HIV, many of whom may require a change to a different treatment regimen."

Data from DRIVE-SHIFT

In the DRIVE-SHIFT study, 670 participants who demonstrated virological suppression (undetectable HIV-1 RNA) on an antiretroviral regimen for at least six months were randomized to begin treatment with DELSTRIGO (doravirine/3TC/TDF) immediately on Day 1 (immediate switch group, ISG; N=447) or after 24 weeks (delayed switch group, DSG; N=223). The primary endpoint was the proportion of participants with HIV-1 RNA <50 copies/mL, with the primary comparison between the DELSTRIGO ISG at Week 48 and baseline regimen DSG at Week 24, and a secondary comparison between the DELSTRIGO ISG and baseline regimen DSG at Week 24.

In the study, DELSTRIGO-receiving participants in the ISG maintained virologic control at the 48-week timepoint:

- 90.8 percent (406/447) of participants who switched to DELSTRIGO on Day 1 (ISG) had HIV-1 RNA <50 copies/mL at Week 48; in comparison, 94.6 percent (211/223) of participants who continued on their baseline regimen (DSG) had HIV-1 RNA <50 copies/mL at Week 24 (treatment difference: -3.8%, 95% confidence interval: -7.9, 0.3).
- 1.6 percent in the DELSTRIGO ISG group had HIV-1 RNA ≥50 copies/mL at Week 48 compared to 1.8 percent in the baseline regimen DSG group at Week 24 (treatment difference: -0.2%, 95% confidence interval: -2.5, 2.1).

Secondary comparisons were also made at Week 24 for both treatment groups. DELSTRIGO-receiving participants in the ISG also maintained virologic control at this earlier (Week 24) timepoint:

- 93.7 percent (419/447) of participants who switched to DELSTRIGO on Day 1 (ISG) had HIV-1 RNA <50 copies/mL, compared with 94.6 percent (211/223) of those who continued on their baseline regimen (DSG) (treatment difference: -0.9%; 95% confidence interval: -4.7, 3.0).
- 1.8 percent in both treatment groups had HIV-1 RNA ≥50 copies/mL at Week 24 (treatment difference: 0.0%; 95% confidence interval: -2.3, 2.3).

No genotypic or phenotypic resistance to any study drug was observed in participants taking DELSTRIGO through 48 weeks of treatment.

At Week 24, participants who switched to DELSTRIGO on Day 1 showed statistically significant decreases in fasting LDL-cholesterol (LDL-C) and non-HDL-cholesterol (non-HDL-C) compared to those who continued on a boosted protease inhibitor regimen (LDL-C: -16.5 mg/dL vs. -1.9 mg/dL, treatment difference: -14.7, 95% confidence interval: -18.9, -10.4, p<0.0001; non-HDL-C: -24.7 mg/dL vs. -1.3 mg/dL, treatment difference: -23.0, 95% confidence interval: -28.0, -18.1, p<0.0001). At this timepoint, DELSTRIGO (doravirine/3TC/TDF) also showed decreases in cholesterol and

triglyceride levels (cholesterol: -26.2 mg/dL vs. 0.5 mg/dL, treatment difference: -25.8, 95% confidence interval: -31.0, -20.7; triglycerides: -43.2 mg/dL vs. 0.9 mg/dL, treatment difference: -42.9, 95% confidence interval: -59.1, -26.7).

The most common adverse events (>5% incidence in any group) in the DELSTRIGO ISG group through Week 24, the baseline regimen DSG group through Week 24, and the DSG group after the delayed switch to DELSTRIGO (Week 24 to Week 48) were nasopharyngitis (7.4%; 5.4%; 4.3%, respectively) and headache (6.5%; 2.2%; 6.7%, respectively). The most common drug-related adverse event (>2% incidence in any group) was headache (1.6%; 0.4%; 2.4%, respectively). The rates of discontinuation of therapy due to adverse events through Week 24 were 2.5% in the DELSTRIGO ISG group and 0.4% in the baseline regimen DSG group.

"Merck's dedication over the past several decades to improving HIV treatment and care has always been focused on addressing unmet needs. People living with HIV need new treatment options," said Dr. George Hanna, vice president and therapeutic area head of infectious diseases, global clinical development, Merck Research Laboratories. "The data from DRIVE-SHIFT suggest the clinical potential of DELSTRIGO to serve as a new fixed-dose combination option for those considering a change in their HIV antiretroviral treatment regimen."

About DRIVE-SHIFT

DRIVE-SHIFT is a Phase 3 multicenter, open-label, randomized, active-controlled, non-inferiority clinical trial evaluating a switch to DELSTRIGO compared with continuation of current therapy in adults with HIV-1 infection who were virologically suppressed (undetectable plasma HIV-1 RNA levels <40 copies/mL) for at least six months on a stable regimen of two nucleoside reverse transcriptase inhibitors (NRTIs) plus a boosted protease inhibitor, boosted elvitegravir, or NNRTI. Participants with screening HIV-1 RNA <40 copies/mL, no history of virologic failure on any regimen, and no resistance to DELSTRIGO were randomized (2:1) to start DELSTRIGO on Day 1 (ISG) or after 24 weeks (DSG). The primary endpoint was the proportion of participants with HIV-1 RNA <50 copies/mL, with the primary comparison between the DELSTRIGO ISG at Week 48 and baseline regimen DSG at Week 24 and a secondary comparison between the treatment groups at Week 24. For further information regarding DRIVE-SHIFT please visit www.clinicaltrials.gov clinical trial registry number NCT02397096.

On Aug. 30, 2018, DELSTRIGO (doravirine/3TC/TDF) was approved by the U.S. Food and Drug Administration for the treatment of HIV-1 infection in adult patients with no prior antiretroviral treatment experience and is 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 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.

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

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 coinfecte^d with HIV-1 and HBV and have discontinued products containing 3TC or TDF, which are components of DELSTRIGO. Patients coinfecte^d 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 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 (doravirine/3TC/TDF) 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 $\geq 5\%$, 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.

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

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