First Patient Enrolled in New Phase 3 Trial Program Investigating a Once-Daily Dosing Regimen of ISENTRESS® (raltegravir)

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ONCEMRK Study Globally Enrolling Treatment-Naïve Adults with HIV-1

Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced that the first patient has been enrolled in the company's global Phase 3 clinical trial, ONCEMRK. ONCEMRK is assessing a once-daily investigational formulation of ISENTRESS® (raltegravir), known as reformulated raltegravir, as part of combination HIV therapy for treatment-naïve HIV-1-infected adults. ISENTRESS film-coated tablets are currently administered twice daily in accordance with the approved Prescribing Information.

"ISENTRESS has been a significant component of first-line HIV-1 treatment for more than six years, as a twice-daily component of antiretroviral therapy," said Jürgen Rockstroh, M.D., University of Bonn, Bonn-Venusberg, Germany, a clinical investigator on this study. “We look forward to advancing our understanding of this new formulation of once-daily raltegravir with this new trial.”

ISENTRESS is an integrase inhibitor indicated in combination with other antiretroviral (ARV) agents for the treatment of HIV-1 infection in patients four weeks of age and older. The use of other active agents with ISENTRESS is associated with a greater likelihood of treatment response. Severe, potentially life-threatening and fatal skin reactions have been reported with ISENTRESS. Additionally, during the initial phase of combination ARV treatment, immune reconstitution syndrome may occur. (See Important Selected Safety Information below).

The ONCEMRK trial is a multicenter, double-blind, randomized, active-controlled study evaluating the safety,
efficacy, tolerability and pharmacokinetics of reformulated raltegravir 1200 mg (dosed as two 600 mg tablets) once daily, compared with ISENTRESS 400 mg twice daily, both in combination with once-daily tenofovir/emtricitabine over 96 weeks. The primary endpoint of the non-inferiority study is the proportion of patients achieving viral suppression (<40 copies/mL) at Week 48, which the company estimates will occur in the first half of 2016. Each patient in the study will receive treatment for approximately 96 weeks. To learn more about the ONCEMRK trial, contact Merck at 1-888-577-8839 or visit www.merck.com/clinical-trials. Additional details can also be found online at www.clinicaltrials.gov/ct2/show/NCT02131233.

“We remain dedicated to investigating new applications for ISENTRESS and to further expanding our knowledge of this HIV-1 treatment,” said Peter Sklar, M.D., M.P.H., director, Clinical Research, Merck Research Laboratories. “Merck is proud to mark this notable milestone in the development of once-daily raltegravir and we look forward to continued patient enrollment worldwide over the coming months.”

More than 160 centers in more than 25 countries are expected to participate in the ONCEMRK trial in the coming months. Merck is planning for the program to include approximately 750 patients worldwide.

Investigations of Raltegravir Once Daily

Reformulated raltegravir is a novel non-polyolamser based formulation. Based on the results of several Phase 1 studies, reformulated raltegravir has shown the potential to be investigated further for once daily use.

Data from the previous Phase 3 trial of raltegravir once daily, QDMRK, have contributed to the understanding of raltegravir pharmacokinetics and pharmacodynamics. QDMRK evaluated the long-term safety, tolerability and efficacy of a once-daily 800 mg ISENTRESS dose in a combination regimen compared with a twice-daily 400 mg ISENTRESS dose in combination. The once-daily arm of QDMRK studied the ISENTRESS polyolamser formulation given as two 400 mg tablets simultaneously. Results showed the primary endpoint of non-inferiority was not met, with 83 percent of treatment-naïve adult HIV-1 infected patients achieving viral suppression (<50 copies/mL at Week 48) with the dosing regimen of 800 mg raltegravir once daily, compared with 89 percent of patients treated with ISENTRESS 400 mg twice daily. The safety and tolerability profiles of the two regimens were generally similar in the study and similar to the Prescribing Information for ISENTRESS.

Important Selected Safety Information

ISENTRESS does not cure HIV-1 infection or AIDS.

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 develop 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 (UGT1A1) 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 (DDIs) must be considered prior to and during therapy. Co-administration or staggered administration of aluminum and/or magnesium hydroxide-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 co-administration of ISENTRESS with rifampin in patients below 18 years of age.

The most commonly reported (≥2%) drug-related clinical adverse reactions of moderate to severe intensity in treatment-naïve adult patients receiving ISENTRESS compared with efavirenz were insomnia (4% vs 4%), headache (4% vs 5%), nausea (3% vs 4 %), fatigue (2% vs 3%), and dizziness (2% vs 6%), 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 to 4 creatine kinase laboratory abnormalities were observed in patients treated with ISENTRESS. Myopathy and rhabdomyolysis have been reported. Use with caution in patients at increased risk of myopathy or rhabdomyolysis, such as patients receiving concomitant medications known to cause these conditions and patients with a history of rhabdomyolysis, myopathy or increased serum creatine kinase.

ISENTRESS should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. There are no adequate and well-controlled studies in pregnant women. In addition, there have been no pharmacokinetic studies conducted in pregnant women. To monitor maternal-fetal outcomes of pregnant patients...
exposed to ISENTRESS, an Antiretroviral Pregnancy Registry has been established. Physicians are encouraged to register patients by calling 1-800-258-4263.

About ISENTRESS

ISENTRESS is Merck’s integrase inhibitor for the treatment of HIV-1 infection in adult and pediatric patients ages four weeks and older and weighing at least 3 kg as part of combination HIV therapy. ISENTRESS works by inhibiting the insertion of HIV-1 DNA into human DNA by the integrase enzyme and has demonstrated rapid antiviral activity. Inhibiting integrase from performing this essential function limits the ability of the virus to replicate and infect new cells. ISENTRESS is now approved as part of combination therapy in more than 76 countries for use in treatment-naïve adult patients with HIV-1 and in more than 114 countries for use in treatment-experienced adult patients with HIV-1. ISENTRESS, in combination therapy, for use in children and adolescents with HIV-1 ages two years and older has also been approved for use in 35 countries, and ISENTRESS oral suspension for infants at least four weeks of age is approved for use in the U.S. Merck is continuing to move forward with filings of ISENTRESS for oral suspension in additional countries around the world.

To assist patients taking ISENTRESS, Merck offers the SUPPORT™ program, which provides personal support and patient advocacy regarding individual reimbursement issues. For more information about the SUPPORT™ program, please visit www.merckhelps.com or call 1-800-850-3430.

About Merck

Today’s Merck is a global healthcare leader working to help the world be well. Merck is known as MSD outside the United States and Canada. Through our prescription medicines, vaccines, biologic therapies, and consumer care 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 healthcare through far-reaching policies, programs and partnerships. For more information, visit www.merck.com and connect with us on Twitter, Facebook and YouTube.

Forward-Looking Statement

This news release includes “forward-looking statements” within the meaning of the safe harbor provisions of the United States Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of Merck’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
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; Merck'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 Merck's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

Merck 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 Merck's 2013 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).


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