ENILWORTH, N.J., May 30, 2017 – Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced that the U.S. Food and Drug Administration (FDA) has approved ISENTRESS HD, a new 1200 mg once-daily dose of the company’s integrase inhibitor, ISENTRESS® (raltegravir), to be administered orally as two 600 mg film-coated tablets with or without food, in combination with other antiretroviral agents, for the treatment of HIV-1 infection in adults, and pediatric patients weighing at least 40 kg, who are treatment-naïve or whose virus has been suppressed on an initial regimen of ISENTRESS 400 mg given twice daily.

“ISENTRESS has been used as a component of treatment regimens for patients diagnosed with HIV-1 for almost a decade,” said Dr. Michael S. Saag, associate dean for global health, and director of the Center for AIDS Research at the University of Alabama at Birmingham School of Medicine. “The addition of a convenient once-daily version with a comparable efficacy and safety profile at 48 weeks to the existing twice-daily version of ISENTRESS provides physicians with a new therapeutic option for some patients with HIV-1 infection.”

ISENTRESS and ISENTRESS HD do 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 or ISENTRESS HD 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. For more information, see “Selected Safety Information” below.
The FDA approval of once-daily ISENTRESS® HD (raltegravir) is supported by data from the pivotal Phase 3 ONCEMRK trial. Through 48 weeks of treatment, 89 percent (N=531) of treatment-naïve HIV-1 infected patients receiving ISENTRESS HD 1200 mg (2 x 600 mg) once a day achieved viral suppression of HIV-1 RNA <40 copies/mL compared to 88 percent (N=266) of patients receiving ISENTRESS 400 mg twice a day, each in combination therapy with emtricitabine + tenofovir disoproxil fumarate, with a treatment difference of 0.5 percent, and a 95 percent confidence interval of -4.2, 5.2. This was consistent across demographic groups at initiation of therapy and a variety of patient populations, including those with high viral load (HIV-1 RNA >100,000 copies/mL).

“Because of improvements in the effectiveness of antiretroviral therapies and with appropriate access to care, HIV infection can now be managed as a chronic disease,” said Carl Schmid, deputy executive director of the AIDS Institute. “For people living with HIV, having a wide range of effective therapies is important because it provides options to fit patients’ individual needs and lifestyles.”

In ONCEMRK, through 48 weeks, the rate of discontinuation of therapy due to adverse events was low (1 percent in patients receiving ISENTRESS HD 1200 mg once daily and 2 percent in patients receiving ISENTRESS 400 mg twice daily). There were no drug-related clinical adverse reactions of moderate to severe intensity occurring in ≥2 percent of patients in either treatment group. Clinical adverse reactions of all intensities (mild, moderate, and severe) occurring in ≥2 percent of patients on ISENTRESS HD or ISENTRESS included abdominal pain, diarrhea, vomiting, and decreased appetite. Treatment-emergent viral mutations leading to any drug resistance were detected in less than 1 percent (4/531) of those treated with ISENTRESS HD once daily.
ISENTRESS® HD (raltegravir) can be co-administered with a wide range of antiretroviral agents and non-antiretroviral agents. The potential for drug-drug interactions must be considered prior to and during therapy. The co-administration of ISENTRESS HD with aluminum and/or magnesium-containing antacids, calcium carbonate antacids, rifampin, tipranavir/ritonavir, etravirine, and other strong inducers of drug metabolizing enzymes (e.g., carbamazepine, phenobarbital, and phenytoin) is not recommended.

"ISENTRESS HD exemplifies Merck’s unwavering commitment to innovation in HIV therapy, and we are pleased to be able to offer this option to a broad range of appropriate adult and pediatric patients weighing at least 40 kg who are living with HIV," said Dr. Eliav Barr, senior vice president, global clinical development, infectious diseases and vaccines, Merck Research Laboratories.

The price of ISENTRESS HD will be the same as ISENTRESS twice daily. Merck anticipates ISENTRESS HD to be available in pharmacies in approximately four weeks.

About ONCEMRK

The ONCEMRK study is an ongoing Phase 3 multicenter, double-blind, randomized, active comparator-controlled clinical trial designed to evaluate the efficacy and safety of once-daily ISENTRESS HD 1200 mg, given as two 600 mg oral tablets, compared to twice-daily ISENTRESS 400 mg, each in combination therapy with emtricitabine + tenofovir disoproxil fumarate in previously untreated adults with HIV-1 infection with HIV-1 RNA ≥1000 copies/mL. The primary efficacy objective was the proportion of patients achieving HIV-1 RNA <40 copies/mL at Week 48.
Selected Safety Information About ISENTRESS® HD (raltegravir) and ISENTRESS (raltegravir)

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

Co-administration of ISENTRESS or ISENTRESS HD 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 hydroxide-containing antacids and ISENTRESS or ISENTRESS HD is not recommended. Co-administration of ISENTRESS HD with calcium carbonate antacids, tipranavir/ritonavir, or etravirine is also not recommended.

During co-administration with rifampin, the recommended dosage of ISENTRESS in adults is 800 mg twice daily. Rifampin, a strong inducer of UGT1A1, reduces plasma concentrations of ISENTRESS. There are no data to guide co-administration of ISENTRESS with rifampin in patients below 18 years of age.

Co-administration with rifampin is not recommended with ISENTRESS HD.

The impact of other strong inducers of drug metabolizing enzymes on raltegravir is unknown (e.g., carbamazepine, phenobarbital, and phenytoin). Co-administration of ISENTRESS or ISENTRESS HD with other strong inducers is not recommended.
About ISENTRESS® (raltegravir)

Approved in 2007, ISENTRESS was the first integrase inhibitor developed for the treatment of HIV-1 infection. ISENTRESS is one of the regimen options recommended by the Department of Health and Human Services – in combination with other antiretroviral agents – as a first-line therapy in treatment-naïve HIV-1 infected adults. ISENTRESS chewable tablets and oral suspension, each in combination therapy, are approved to treat pediatric patients aged at least four weeks of age, and weighing less than 20 kg.

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 approved as part of combination therapy in 112 countries for treatment of HIV-1 infection in adult patients. ISENTRESS, in combination therapy, for use in children and adolescents with HIV-1 aged two years and older has also been approved for use in 69 countries, and ISENTRESS oral suspension for infants at least four weeks of age is approved for use in 33 countries.

Selected Safety Information About ISENTRESS HD (raltegravir) and ISENTRESS (raltegravir) Continued

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 headache (4% vs. 5%), insomnia (4% vs. 4%), nausea (3% vs. 4%), dizziness (2% vs. 6%), and fatigue (2% vs. 3%), respectively. The most commonly reported (≥2%) clinical adverse reactions of all intensities (Mild, Moderate, and Severe) in treatment-naïve adult patients receiving ISENTRESS HD compared with ISENTRESS through 48 weeks included abdominal pain, diarrhea, vomiting, and decreased appetite. Intensities were defined as follows: Mild (awareness of sign or symptom, but easily tolerated); Moderate (discomfort enough to cause interference with usual activity); or Severe (incapacitating with inability to work or do usual activity).

Grade 2–4 creatine kinase laboratory abnormalities were observed in subjects treated with ISENTRESS or ISENTRESS HD. Myopathy and rhabdomyolysis have been reported with ISENTRESS. 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.

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ISENTRESS or ISENTRESS HD 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 or ISENTRESS HD 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 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 2016 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).


###