Merck’s Letermovir, an Investigational Antiviral Medicine for Prevention of Cytomegalovirus (CMV) Infection in Bone Marrow Transplant Recipients, Highly Effective Through Week 24 Post-Transplant in Pivotal Phase 3 Study

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Letermovir Prophylaxis Associated with Lower All-Cause Mortality Through Week 24 Post-Transplant

Company Plans to Submit New Drug Applications for Letermovir in U.S. and EU in 2017

KENILWORTH, N.J.--(BUSINESS WIRE)--Merck & Co., Inc. (NYSE:MRK), known as MSD outside the United States and Canada, today announced results of the pivotal Phase 3 clinical study of letermovir, an investigational antiviral medicine for the prevention of clinically-significant cytomegalovirus (CMV) infection in adult (18 years and older) CMV-seropositive recipients of an allogeneic hematopoietic stem cell transplant (HSCT), also known as bone marrow transplant (BMT). The study met its primary efficacy endpoint, showing that significantly fewer patients with undetectable CMV DNA at the start of study treatment developed clinically significant CMV infection through Week 24 post-HSCT (using a non-complete equals failure approach, in which patients who discontinued from the study prior to Week 24 post-transplant or had a missing outcome at Week 24 post-transplant were counted as failures). In the study, letermovir prophylaxis was associated with lower all-cause mortality through Week 24 post-HSCT. Based on these results, Merck plans to submit regulatory applications for the approval of letermovir in the United States and European Union (EU) in 2017.

Results from the study were presented for the first time at the BMT Tandem Meetings, the combined annual meetings of the Center for International Blood & Marrow Transplant Research (CIBMTR) and the American Society for Blood and Marrow Transplantation (ASBMT), in Orlando, Fla., Feb. 22-26.

“These results showed that letermovir prophylaxis beginning after HSCT and continuing through Day 100 post-transplant significantly reduced CMV infection requiring preemptive antiviral therapy through Week 24 post-transplant,” said Dr. Francisco M. Marty, associate professor of medicine at Harvard Medical School and attending physician in transplant and oncology infectious diseases at Dana-Farber Cancer Institute and Brigham and Women’s Hospital, who presented the data. “In this study, letermovir was associated with lower all-cause mortality. Based on these findings, letermovir as primary prophylaxis of CMV infection represents a potential new strategy for the prevention of CMV in this high-risk patient population.”

CMV is the most common clinically significant viral infection in allogeneic HSCT recipients. HSCT is a medical procedure in the field of hematologic oncology, most often performed for the treatment of patients with certain cancers of the blood or bone marrow, such as leukemia and lymphoma. While preemptive therapy (treatment when CMV DNA is detected in the blood) with antiviral medicines can reduce the incidence of CMV disease, CMV reactivation post-HSCT is associated with higher mortality despite the use of preemptive therapy.

“There is an unmet need for therapeutic options in the prevention of CMV infection in hematopoietic stem cell transplant recipients,” said Dr. Nicholas Kartsonis, vice president, infectious disease clinical research, Merck Research Laboratories. “As part of Merck’s long-standing commitment to developing innovative approaches in the fight against infectious diseases, we look forward to submitting regulatory applications for letermovir this year.”

About the pivotal Phase 3 study
CMV seropositive HSCT recipients 18 years or older who had undetectable plasma CMV DNA within 5 days of randomization were eligible for the study. Patients were randomized in a 2:1 ratio to receive either letermovir or placebo administered once daily, either in oral tablet or intravenous formulation, through Week 14 (Day 100) post-HSCT. Letermovir was dosed at 480

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mg/day (or 240 mg/day if the patient was on the immunosuppressant medication cyclosporine). Letermovir was started after HSCT; as early as on the day of transplant and no later than 28 days post-transplant. Patients were assessed weekly through Week 14 and biweekly through Week 24 for the primary efficacy endpoint of clinical significant CMV infection. Patients who developed clinically significant CMV infection, defined as the onset of CMV disease or initiation of anti-CMV preemptive therapy based on documented viremia (as measured by the central laboratory) and the clinical condition of the patient, discontinued study drug and received anti-CMV preemptive therapy. Patients continued to be followed for safety every other month through Week 48 post-HSCT.

The primary endpoint of the study was the proportion of patients with clinically significant CMV infection through Week 24 post-HSCT among patients with undetectable CMV DNA at the start of study treatment. Patients who discontinued the study early for any reason or who had missing data at Week 24 post-HSCT were considered study failures. All adverse events were analyzed through 14 days after the last dose of study drug.

The study met its primary efficacy endpoint, showing that of 495 treated patients who had undetectable CMV DNA at the start of study treatment, significantly fewer patients developed clinically significant CMV infection in the letermovir arm (37.5%, n=122/325) compared to the placebo arm (60.6%, n=103/170) through Week 24 post-HSCT [treatment difference: -23.5 (95% confidence interval -32.5 to -14.6), one-sided p<0.0001].

Efficacy was consistently demonstrated across patient subgroups. Letermovir demonstrated significant benefit compared to placebo in time to clinically significant CMV infection through Week 24 post-HSCT in both patients at higher risk and lower risk for CMV disease at baseline (log-rank two-sided p<0.0001 for both groups).

In addition, a secondary endpoint evaluating the end-of-treatment period (at Week 14 post-HSCT) showed that significantly fewer patients developed clinically significant CMV infection in the letermovir arm (19.1%, n=62/325) compared to the placebo arm (50.0%, n=85/170) through Week 14 (Day 100) post-HSCT [treatment difference: -31.3 (95% confidence interval -39.9 to -22.6), one-sided p<0.0001].

In this study, letermovir was associated with lower all-cause mortality through Week 24 post-HSCT (9.8%, n=32/325) compared to placebo (15.9%, n=27/170), log-rank two-sided p=0.0317.

The most common adverse events of any severity reported for the letermovir and placebo arms, respectively, were: graft-versus-host disease (GVHD) (39.1%, 38.5%), diarrhea (26.0%, 24.5%) and nausea (26.5%, 23.4%). Common adverse events that were reported more frequently in the letermovir arm than the placebo arm included: vomiting (18.5%, 13.5%), cough (14.2%, 10.4%) and peripheral edema (14.5%, 9.4%). The most common serious adverse events reported for the letermovir and placebo arms, respectively, were: infection (20.6%, 18.6%), GVHD (9.9%, 10.4%) and acute kidney injury (1.3%, 4.7%). Letermovir was not associated with myelotoxicity or nephrotoxicity.

About letermovir

Letermovir is an investigational once-daily antiviral medicine under development for the prevention of CMV infection and disease. It is a member of a new class of non-nucleoside CMV inhibitors (3,4 dihydro-quinazolines) and inhibits viral replication by specifically targeting the viral terminase complex. Letermovir has no activity against other viruses. Letermovir has been granted orphan designation by the European Medicines Agency, the U.S. Food and Drug Administration (FDA) and the Japanese Ministry of Health, Labour and Welfare for the prevention of CMV infection and disease in at-risk populations. Letermovir also has been granted Fast Track designation by the FDA.

Under an agreement signed in 2012, Merck (through a subsidiary) purchased worldwide rights to develop and commercialize letermovir from AiCuris GmbH & Co KG (www.aicuris.com).

About CMV infection

CMV is a common virus that infects people of all ages. Many adults in the United States are CMV seropositive, meaning they have CMV antibodies in their blood, indicating a previous exposure or primary infection to CMV. People with normal immune systems rarely develop CMV symptoms after initial infection, with the virus typically remaining inactive or latent in the body for life. A weakened immune system may give the virus a chance to reactivate, potentially leading to symptomatic disease or a secondary infection due to other pathogens. CMV disease can lead to end-organ damage, including gastrointestinal tract disease, pneumonia or retinitis. Transplant recipients who develop CMV infection post-transplant are at increased risk for injury to a transplanted organ. In severely immunocompromised patients, CMV infection can be life-threatening.

About Merck

For over a century, Merck has been a global health care 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 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. For more information, visit www.merck.com and connect with us on Twitter, Facebook, YouTube and LinkedIn.

Forward-Looking Statement

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
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 2015 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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