European Commission Approves Viread(R) for Chronic Hepatitis B

April 25, 2008 9:24 AM ET

Important New Treatment Option for Millions of Europeans Affected by Life-Threatening Disease

FOSTER CITY, Calif.--(BUSINESS WIRE)--April 25, 2008--Gilead Sciences, Inc. (NASDAQ:GILD) today announced that the European Commission has granted marketing authorisation for Viread(R) (tenofovir disoproxil fumarate) for the treatment of chronic hepatitis B in all 27 member states of the European Union.

A once-daily tablet, Viread works by blocking hepatitis B virus (HBV) DNA polymerase, the enzyme that is necessary for the virus to replicate in liver cells. Viread has been approved in the European Union for use in adult chronic HBV patients with compensated liver disease, with evidence of active viral replication, persistently elevated serum alanine aminotransferase (ALT) levels and histological evidence of active inflammation and/or fibrosis. The product was recently approved for the treatment of chronic hepatitis B in Turkey and New Zealand, and marketing applications are currently pending regulatory review in the United States, Canada and Australia.

"Hepatitis B is a significant problem in Europe, where approximately 20,000 people die of complications from the disease each year," said Patrick Marcellin, MD, PhD, Professor of Hepatology at the University of Paris and Head of the Viral Hepatitis Research Unit (INSERM) at the Hopital Beaujon in Clichy, France. "As a physician and researcher who has studied this drug extensively in large-scale clinical trials, I believe Viread is an important treatment option for patients who are just starting therapy, as well as for those who may have had previous experience with other medications, including lamivudine."

Today's approval is based primarily on data from two ongoing Phase III clinical trials, Studies 102 and 103, in patients (n = 375) chronically infected with HBV who were new to HBV therapy (treatment-naive). Some patients (n=51) in the Phase III trials have had previous experience with lamivudine (treatment-experienced). These studies evaluate the efficacy, safety and tolerability of Viread compared to Hepsera(R) (adefovir dipivoxil). Positive data from these studies were presented in late-breaker presentations at the annual meeting of the American Association for the Study of Liver Diseases in Boston, Massachusetts, November 2007. Additional 72-week data from these studies were presented at the annual meeting of the European Association for the Study of the Liver in Milan, Italy, April 23-27.

"Data from studies 102 and 103 demonstrate that Viread has many of the preferred qualities of an antiviral treatment: rapid and profound viral suppression, a well-established safety profile with more than one million years of patient experience, and convenient once-daily administration," said Kevin Young, Executive Vice President, Commercial Operations at Gilead Sciences. "Now that Viread is approved for chronic hepatitis B in Europe, our top priority is working to ensure that all individuals who need the medication have access to it as quickly as possible."

Viread represents Gilead's second once-daily antiviral for the treatment of chronic hepatitis B; the first, Hepsera, is currently widely used as a treatment for chronic hepatitis B in Europe. In addition, the company is also developing small molecule compounds for the treatment of hepatitis C and a hepatoprotectant for hepatitis-related liver fibrosis.

Viread has been available in Europe as a part of combination therapy for HIV infection in adults since 2002. Its active ingredient, tenofovir disoproxil, is the most widely prescribed molecule for the treatment of HIV infection in several European Union nations.

About Chronic Hepatitis B

Chronic hepatitis B is a common and potentially fatal liver disease caused by the hepatitis B virus, which is up to 100 times more easily transmitted than HIV. Chronic hepatitis B can produce no symptoms in its earlier stages, meaning many individuals are unaware that they are infected until they have advanced liver disease. Complications commonly associated with chronic hepatitis B include scarring of the liver (cirrhosis), liver failure and liver cancer. More than 400 million people

are estimated to be chronically infected with HBV worldwide and, without treatment, up to one quarter of those will ultimately die of liver disease.

About Viread (tenofovir disoproxil fumarate) for HIV

In the United States, Viread is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection.

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues alone or in combination with other antiretrovirals. Viread is not approved for the treatment of HBV infection and the safety and efficacy of Viread have not been established in patients coinfected with HBV and HIV. Severe acute exacerbations of hepatitis B have been reported in patients who have discontinued Viread. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are co-infected with HIV and HBV and discontinue Viread. If appropriate, initiation of anti-hepatitis B treatment may be warranted.

It is important for patients to be aware that anti-HIV medicines including Viread do not cure HIV infection or AIDS, and do not reduce the risk of transmitting HIV to others.

Renal impairment, including cases of acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), has been reported in association with the use of Viread. It is recommended that creatinine clearance be calculated in all patients prior to initiating therapy with Viread and as clinically appropriate during therapy. Routine monitoring of calculated creatinine clearance and serum phosphorous should be performed in patients at risk for renal impairment. Dosing interval adjustment and close monitoring of renal function are recommended in all patients with creatinine clearance less than 50mL/min. Viread should be avoided with concurrent or recent use of a nephrotoxic agent.

The U.S. package insert advises that co-administration of Viread and didanosine should be undertaken with caution. Patients should be monitored closely for didanosine-associated adverse events and didanosine should be discontinued if these occur. Patients on atazanavir and lopinavir/ritonavir plus Viread should be monitored for Viread-associated adverse events and Viread should be discontinued if these occur. When co-administered with Viread, it is recommended that atazanavir be given with ritonavir 100 mg. Atazanavir without ritonavir should not be co-administered with Viread.

Decreases in bone mineral density (BMD) at the lumbar spine and hip have been seen with the use of Viread. The effect on long-term bone health and future fracture risk is unknown. Cases of osteomalacia (associated with proximal renal tubulopathy) have been reported in association with the use of Viread.

Changes in body fat have been observed in patients taking anti-HIV medicines. The mechanism and long-term health effect of these changes are unknown. Immune Reconstitution Syndrome has been reported in patients treated with combination therapy, including Viread.

The most common adverse events among patients receiving Viread with other antiretroviral agents in a pivotal clinical study (Study 903) were mild to moderate gastrointestinal events and dizziness. Moderate to severe adverse events occurring in more than 5 percent of patients receiving Viread included rash (rash, pruritis, maculopapular rash, urticaria, vesiculobullous rash and pustular rash), headache, pain, diarrhea, depression, back pain, fever, nausea, abdominal pain, asthenia (weakness) and anxiety. In another pivotal study (Study 907), less than 1 percent of patients discontinued participation because of gastrointestinal events.

For full prescribing information outside of the United States physicians should consult their local product labeling.

About Hepsera (adefovir dipivoxil)

In the United States, Hepsera is indicated for the treatment of chronic hepatitis B in patients 12 years of age and older with evidence of active viral replication and either evidence of persistent elevations in serum aminotransferases (ALT or

AST) or histologically active disease. Hepsera is not recommended for use in children less than 12 years of age.

Severe acute exacerbations of hepatitis have been reported in patients who have discontinued anti-hepatitis B therapy, including Hepsera. Hepatic function should be closely monitored in both clinical and laboratory follow-up for at least several months in patients who discontinue hepatitis B therapy. If appropriate, resumption of therapy may be warranted. In patients at risk of having underlying renal dysfunction, chronic administration of Hepsera may result in nephrotoxicity. These patients should be monitored closely for renal function and may require dose adjustment. Dose adjustment is recommended in patients with serum creatinine less than 50 mL/min. HIV resistance may emerge in chronic hepatitis B patients with unrecognized or untreated HIV infection treated with anti-hepatitis B therapies, such as therapy with Hepsera, that may have activity against HIV. Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs alone and in combination with other antiretrovirals.

Adverse reactions identified from placebo-controlled and open label studies include the following: asthenia, headache, abdominal pain, diarrhea, nausea, dyspepsia, flatulence, increased creatinine, and hypophosphatemia. Additional adverse reactions observed from an open-label study in pre- and post-transplant patients include abnormal renal function, renal failure, vomiting, rash and pruritus.

For full prescribing information outside of the United States, physicians should consult their local product labeling.

Viread and Hepsera are the result of a collaborative research effort between Dr. Antonin Holy, Institute for Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic (IOCB) in Prague and Dr. Erik DeClercq, Rega Institute for Medical Research, Katholic University in Leuven, Belgium.

About Gilead Sciences

Gilead Sciences is a biopharmaceutical company that discovers, develops and commercializes innovative therapeutics in areas of unmet medical need. The company's mission is to advance the care of patients suffering from life-threatening diseases worldwide. Headquartered in Foster City, California, Gilead has operations in North America, Europe and Australia.

U.S. full prescribing information for Viread is available at www.Viread.com

U.S. full prescribing information for Hepsera is available at www.Hepsera.com

Viread and Hepsera are registered trademarks of Gilead Sciences, Inc.

For more information on Gilead, please call the Gilead Public Affairs Department at 1-800-GILEAD-5 (1-800-445-3235) or visit www.gilead.com.

CONTACT: Gilead Sciences, Inc.
Patrick O'Brien, 650-522-1936 (Investors)
Cara Miller, 650-522-1616 (Media)
SOURCE: Gilead Sciences, Inc.