Gilead Announces Long-Term Data from Two Pivotal Phase III Studies Evaluating Viread(R) For Chronic Hepatitis B

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No Evidence of Viral Resistance Through Three Years of Treatment

BOSTON--(BUSINESS WIRE)--Oct. 31, 2009-- Gilead Sciences, Inc. (Nasdaq:GILD) today announced the presentation of three-year (144-week) open label data from two pivotal Phase III clinical trials, Studies 102 and 103, evaluating the safety and efficacy of once-daily Viread® (tenofovir disoproxil fumarate) among adult patients with chronic hepatitis B virus (HBV) infection. These data will be presented at the annual meeting of the American Association for the Study of Liver Diseases (The Liver Meeting 2009) being held this week in Boston, October 30-November 3.

These new data show that the majority of patients who received Viread for up to 144 weeks experienced sustained suppression of HBV DNA levels in the blood to below 400 copies/mL (87 percent in Study 102 and 71 percent in Study 103). Additionally, cumulatively over 144 weeks, 8 percent of all patients in Study 103 (HBeAg-positive) experienced “s” antigen (HBsAg) loss, which can contribute to resolution of chronic hepatitis B infection. Notably, no mutations associated with resistance to Viread developed in any patients up to 144 weeks of treatment.

“The development of resistance is a significant challenge for practitioners treating patients with chronic hepatitis B,” said Patrick Marcellin, MD, of Hôpital Beaujon in Clichy, France, and the principal investigator of Study 102. “The robust and comprehensive resistance surveillance in these studies provides important information for the medical community and shows that Viread offers a high barrier to resistance.”

Clinical practice guidelines recommending Viread as a first-line therapy for the treatment of chronic hepatitis B were issued earlier this year by both the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. The U.S. Food and Drug Administration (FDA) approved Viread for chronic hepatitis B in adults in 2008 based on earlier (48-week) results from Studies 102 and 103, and recently approved the inclusion of 96-week data in the product’s label.

“These data underscore the rationale for Viread’s position as a recommended first-line therapy for chronic hepatitis B infection,” said Jenny Heathcote, MD, of the University of Toronto, Canada, and the principal investigator for Study 103. “In particular, the loss of the hepatitis B ‘s’ antigen in 8 percent of patients, which is associated with resolution of HBV infection, is significant from a clinical perspective.”

Nine additional presentations examining the efficacy of Viread across a variety of patient populations, including treatment-experienced patients, patients new to therapy, patients of Asian descent, pregnant women and patients with decompensated liver disease, also will be presented during The Liver Meeting.

About Studies 102 and 103

Studies 102 and 103 were multi-center, randomized, double-blind Phase III clinical trials comparing Viread to Hepsera® (adefovir dipivoxil) among HBeAg-negative presumed pre-core mutant (n=375) and HBeAg-positive (n=266) chronic hepatitis B patients with compensated liver disease, respectively. The majority of patients were treatment-naïve upon study initiation, although some patients were lamivudine-experienced.

Patients originally randomized to Hepsera in both studies rolled over to open-label Viread (n=196) at week 48, while patients originally randomized to Viread continued open-label Viread treatment (n=389). After 72 weeks, patients with confirmed viremia (HBV DNA levels at or above 400 copies/mL on two consecutive visits) had the option of adding emtricitabine treatment by substituting Truvada® (emtricitabine and tenofovir disoproxil fumarate) for Viread. By 144 weeks, 87 percent of patients remained in Study 102 (n=328) and 80 percent of patients remained in Study 103 (n=214).

Study 102 Results (Poster Presentation #481)

HBeAg-negative patients

A long-term evaluation algorithm through 144 weeks showed that 87 percent of patients achieved virologic suppression (HBV DNA levels below 400 copies/mL), and similar efficacy was observed between patients who received Viread monotherapy throughout (206/238, 87 percent) compared to those who initially received Hepsera and then rolled over to Viread (107/121, 88 percent).

Three patients receiving Viread had HBV DNA of 400 copies/mL or more at week 144, and one additional viremic patient discontinued Viread during year three. Three patients in Study 102 added emtricitabine treatment at or after week 72 due to confirmed viremia, and all three achieved HBV DNA levels below 400 copies/mL at week 144.

Levels of alanine aminotransferase (ALT, an enzyme that serves as a measure of liver damage), which had been high at baseline, remained at normal levels through 144 weeks of treatment (overall mean ALT value of 33 U/L).

Viread was well tolerated by study subjects during open-label treatment through 144 weeks. The incidence of serious adverse events considered drug-related was low, with one event (mild renal impairment) reported in the Viread group and none reported in the Hepsera-to-Viread group. The incidence of grade 3-4 laboratory abnormalities was similar between groups; 14 percent for Viread and 15 percent in the Hepsera-to-Viread group. During the study, three patients on Viread discontinued treatment due to adverse events (hepatocellular carcinoma, dizziness/fatigue/lack of concentration and septic shock). No patients experienced a confirmed 0.5 mg/dL increase in serum creatinine or a decrease in creatinine clearance to less than 50 mL/min. There were three deaths during open-label treatment, but the causes (nasopharyngeal cancer, metastatic liver cancer and cervical cancer) were not considered related to study drug.

No resistance to Viread developed among patients who received Viread for up to three years.

Study 103 Results (Poster Presentation #483)

HBeAg-positive patients

Using a long-term evaluation algorithm through 144 weeks, 71 percent of patients achieved HBV DNA levels below 400 copies/mL, with similar response between patients who received Viread monotherapy throughout (118/165, 72 percent) and those who initially received Hepsera and rolled over to Viread (63/89, 71 percent) after week 48.

Five patients on Viread had HBV DNA of 400 copies/mL or more at week 144, and one additional viremic patient discontinued Viread during year three. Thirty-one patients in Study 103 added emtricitabine treatment between 72 and 144 weeks due to confirmed viremia; 17 achieved HBV DNA levels below 400 copies/mL at week 144.

As with Study 102, ALT levels, which had been elevated at baseline in both patient groups, remained stable at near-normal levels by week 144 (mean of 38.6 U/L).

Among all patients who continued Viread treatment to week 144, 34 percent achieved loss of HBeAg and 26 percent experienced HBeAg seroconversion. Seroconversion is defined as both the disappearance of the hepatitis B “e” antigen, a marker of HBV replication (rendering the patient “HBe-antigen negative”), and the detection of antibodies specific for this antigen (making the patient “HBe-antibody positive”). Cumulatively, 8 percent of patients experienced “s” antigen (HBsAg) loss, which contributes to resolution of chronic hepatitis B infection.

As in Study 102, Viread was well tolerated by study subjects during open-label treatment through 144 weeks. The incidence of serious adverse events considered drug-related was low, with two events (increase of ALT and facial spasm) reported in the Viread group and two events (increase of ALT) reported in the Hepsera-to-Viread group. The incidence of grade 3-4 laboratory abnormalities was 12.3 percent in the Viread group and 15.5 percent in the Hepsera-to-Viread group. During the study, one patient on Viread discontinued treatment due to an unconfirmed 0.5 mg/dL increase in creatinine.

Two patients (initially randomized to Hepsera) experienced a confirmed 0.5 mg/dL increase in creatinine. No patients experienced a decrease in confirmed creatinine clearance to less than 50 ml/min.

As with Study 102, no resistance to Viread developed among patients who received Viread for up to three years.

Continued treatment with Viread for 144 weeks in Studies 102 and 103 did not reveal any new adverse reactions and no change in the tolerability profile observed during the first 48 weeks of treatment. The most common adverse reaction (all grades) was nausea, observed in 9 percent of patients taking Viread at week 48. Other treatment-related adverse events observed in greater than 5 percent of patients during the first 48 weeks of Studies 102 and 103 included abdominal pain, diarrhea, headache, dizziness, fatigue, nasopharyngitis, back pain and skin rash.

Important Information About Viread for Chronic Hepatitis B and HIV

Viread (tenofovir disoproxil fumarate) is indicated for the treatment of chronic hepatitis B in adults. This indication is based primarily on data from the treatment of nucleoside-treatment-naïve patients, and a smaller number of patients who had previously received lamivudine or adefovir. Patients were adults with HBeAg-positive and HBeAg-negative chronic hepatitis B with compensated liver disease. The number of patients in clinical trials who had lamivudine- or adefovir-associated substitutions at baseline was too small to reach conclusions of efficacy. Viread has not been evaluated in patients with decompensated liver disease.

Viread is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection. The following points should be considered when initiating therapy with Viread for the treatment of

HIV-1: Viread should not be used in combination with Truvada (emtricitabine/tenofovir disoproxil fumarate) or Atripla® (efavirenz/emtricitabine/tenofovir disoproxil fumarate).

The recommended dose for the treatment of chronic hepatitis B and HIV infection is 300 mg once daily taken orally without regard to food. The dosing interval of Viread should be adjusted in patients with renal impairment.

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleos(t)ide analogs, including Viread, in combination with other antiretrovirals.

Severe acute exacerbations of hepatitis have been reported in HBV-infected patients who have discontinued anti-hepatitis B therapy, including Viread. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue anti-hepatitis B therapy, including Viread. If appropriate, resumption of anti-hepatitis B therapy may be warranted.

New onset or worsening of renal impairment including cases of acute renal failure and Fanconi syndrome has been reported with the use of Viread. It is recommended to assess creatinine clearance (CrCl) before initiating treatment with Viread and monitor CrCl and serum phosphorus in patients at risk, including those who have previously experienced renal events while receiving Hepsera. Administering Viread with concurrent or recent use of nephrotoxic drugs should be avoided.

Viread should not be used with other tenofovir-containing products (e.g. Atripla, Truvada). Viread should not be administered in combination with Hepsera.

HIV antibody testing should be offered to all HBV-infected patients before initiating therapy with Viread. Viread should only be used as part of an appropriate antiretroviral combination regimen in HIV-infected patients with or without HBV coinfection.

Decreases in bone mineral density (BMD) have been observed in HIV-infected patients. It is recommended that BMD monitoring be considered for patients with a history of pathologic fracture or who are at risk for osteopenia. The bone effects of Viread have not been studied in patients with chronic HBV infection.

Redistribution/accumulation of body fat has been observed in HIV-infected patients receiving antiretroviral combination therapy.

Immune reconstitution syndrome has been observed in HIV-infected patients receiving antiretroviral combination therapy, including Viread, which may necessitate further evaluation and treatment.

Early virologic failure has been reported in HIV-infected patients on triple nucleoside-only regimens. Patients on an antiretroviral therapy utilizing a triple nucleoside-only regimen should be carefully monitored and considered for treatment modification.

In controlled clinical trials in patients with chronic hepatitis B, the most common adverse reaction (all grades) was nausea, observed in 9 percent of patients taking Viread at week 48. Other adverse reactions observed at week 48 in greater than 5 percent of patients treated with Viread include abdominal pain, diarrhea, headache, dizziness, fatigue, nasopharyngitis, back pain and skin rash. In HIV-infected patients, the most common adverse reactions (incidence ≥10 percent, grades 2-4) are rash, diarrhea, headache, pain, depression, asthenia and nausea. No significant change in the tolerability profile was observed in patients continuing treatment with Viread for 144 weeks.

Important Information about Hepsera (adefovir dipivoxil)

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. This indication is based on histological, virological, biochemical and serological responses in adult patients with HBeAg-positive and HBeAg-negative chronic hepatitis B with compensated liver function, and with clinical evidence of lamivudine-resistant hepatitis B virus with either compensated or decompensated liver function.

For patients 12 to less than 18 years of age, the indication is based on virological and biochemical responses in patients with HBeAg-positive chronic hepatitis B virus infection with compensated liver function.

The recommended dose for the treatment of chronic hepatitis B is 10 mg once daily taken orally without regard to food. The dosing interval of Hepsera should be adjusted in patients with renal impairment.

Severe acute exacerbations of hepatitis have been reported in patients who have discontinued anti-hepatitis B therapy, including Hepsera. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue anti-hepatitis B therapy. If appropriate, resumption of anti-hepatitis B therapy may be warranted.

In patients at risk of or 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. It is important to monitor renal function for all patients during treatment with Hepsera.

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, which may have activity against HIV.

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleos(t)ide analogs alone or in combination with other antiretrovirals.

HIV antibody testing should be offered to all HBV-infected patients before initiating therapy with Hepsera.

For patients with lamivudine-resistant HBV, adefovir dipivoxil should be used in combination with lamivudine. For all patients, consider modifying treatment in case serum HBV DNA remains above 1000 copies/mL with continued treatment.

Co-administration with drugs that reduce renal function or compete for active tubular secretion may increase serum concentrations of adefovir and/or the co-administered drug. Monitor for Hepsera associated adverse events. The most

common adverse reaction (less than 10 percent) in compensated disease patients is asthenia and in pre- and post-transplantation lamivudine-resistant liver disease patients is increased creatinine.

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.

This press release includes forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995, that are subject to risks, uncertainties and other factors, including the risks that physicians may not prescribe Viread over other existing HBV medications. In addition, as Viread is used over longer periods of time by many patients with underlying health problems, taking numerous other medicines, safety, resistance, drug interaction or other issues may arise, which could reduce the market acceptance of Viread. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. The reader is cautioned not to rely on these forward-looking statements. These and other risks are described in detail in Gilead's Quarterly Report on Form 10-Q for the second quarter of 2009, as filed with the U.S. Securities and Exchange Commission. All forward-looking statements are based on information currently available to Gilead, and Gilead assumes no obligation to update any such forward-looking statements.

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
U.S. full prescribing information for Truvada is available at www.Truvada.com
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Source: Gilead Sciences, Inc.

Gilead Sciences, Inc.
Investors
Susan Hubbard, 650-522-5715
or
Media
Michael Claeys, 650-522-2459