European Medicines Agency Validates Gilead's Marketing Application for Tenofovir Alafenamide (TAF) for the Treatment of Chronic Hepatitis B

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– High Rates of Viral Suppression and Improved Renal and Bone Safety Parameters Compared to Viread in Phase 3 Studies –

FOSTER CITY, Calif.--(BUSINESS WIRE)--Feb. 25, 2016-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced that the company's Marketing Authorization Application (MAA) for tenofovir alafenamide (as fumarate) (TAF) 25 mg – an investigational, once-daily treatment for adults with chronic hepatitis B virus (HBV) infection – has been fully validated and is now under assessment by the European Medicines Agency (EMA).

TAF is a novel, targeted prodrug of tenofovir that has demonstrated high antiviral efficacy similar to Gilead's Viread® 245 mg of tenofovir disoproxil (as fumarate) (TDF) at one-tenth of the dose. TAF also demonstrated improvements in surrogate laboratory markers of renal and bone safety compared to TDF in clinical trials.

"Chronic hepatitis B infection is a major health concern in Europe, with 14 million people living with the disease and more than 1 million Europeans newly infected with the virus each year," said Norbert Bischofberger, PhD, Executive Vice President, Research and Development and Chief Scientific Officer, Gilead Sciences. "The validation of this application represents the latest step in our continued efforts to advance the care of people living with progressive liver diseases like HBV."

The MAA for TAF is supported by 48-week data from two Phase 3 studies which met their primary objective of non-inferiority in efficacy (HBV DNA < 29 IU/mL at week 48) compared to TDF among treatment-naïve and treatment-experienced adults with HBeAg-negative and HBeAg-positive chronic HBV. In both studies, treatment with TAF showed a statistically significant increase in serum alanine aminotransferase normalization relative to the TDF arms when using the American Association for the Study of Liver Disease criteria. Changes in renal and bone laboratory safety parameters favored the TAF treatment regimen. Overall, patients receiving TAF experienced a significantly smaller mean percentage decrease from baseline in hip and spine bone mineral density at week 48 compared to patients receiving TDF. Additionally, the overall median change in serum creatinine from baseline to week 48 favored TAF. Rates of discontinuations due to adverse events and the most commonly reported adverse events were similar in patients receiving TAF or TDF.

TAF for the treatment of HBV will be reviewed by the EMA under the centralized licensing procedure which, if authorized, provides marketing authorization in all 28 member states of the European Union, Norway and Iceland. Gilead also submitted a New Drug Application to the U.S. Food and Drug Administration (FDA) for TAF on January 11, 2016.

TAF as a single agent treatment for HBV is an investigational product and its safety and efficacy have not been established.

Important Safety Information About Viread

Please refer to the Viread individual Summary of Product Characteristics for full prescribing information

Presentation:

Viread film-coated tablet containing 245 mg of tenofovir disoproxil (as fumarate), equivalent to 300 mg of tenofovir disoproxil fumarate, or 136 mg of tenofovir. Viread is also available as 33 mg/g granules.

Indications:

1) The treatment of chronic hepatitis B (CHB), in adults 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. 2) Evidence of lamivudine-resistant hepatitis B virus. 3) Treatment of CHB in adults with decompensated liver disease. 4) Treatment of CHB in adolescents 12 to < 18 years of age with compensated liver disease and evidence of immune active disease, i.e. active viral replication, persistently elevated serum ALT levels and histological evidence of active inflammation and/or fibrosis.

Dosage & Administration:

Adults: One tablet (245 mg) once daily taken with food. Viread is available as 33 mg/g granules for the treatment of CHB in adults for whom a solid dosage form is not appropriate. No dose modification is necessary in patients with mild to moderate liver disease. Optimal duration of treatment is unknown. Children and adolescents: for the treatment of CHB in adolescents aged 12 to < 18 years and weighing ≥ 35 kg, recommended dose is one tablet (245 mg) once daily taken with food. The safety and efficacy of Viread in children with CHB aged 2 to < 12 years or weighing < 35 kg have not been established. Viread is also available as 33 mg/g granules for the treatment of CHB in adolescents aged 12 to < 18 years for whom a solid dosage form is not appropriate. Not recommended in paediatric patients with renal impairment. No dose adjustment is required in patients with hepatic impairment. Elderly: Insufficient data are available on which to make dose recommendations for patients over the age of 65 years – caution should be exercised.

Contraindications:

Known hypersensitivity to tenofovir, tenofovir disoproxil fumarate, or any of the excipients.

Warnings and Precautions:

Renal: If Viread is co-administered with a non-steroidal anti-inflammatory drug (NSAID), renal function should be monitored adequately. A higher risk of renal impairment has been reported in patients receiving Viread in combination with a ritonavir or cobicistat boosted protease inhibitor. A close monitoring of renal function is required in these patients. Renal failure and impairment, elevated creatinine, hypophosphataemia and proximal tubulopathy (including Fanconi syndrome) have been reported with the use of Viread in clinical practice. It is recommended that creatinine clearance (CrCl) is calculated in all patients prior to therapy initiation and renal function monitored after two to four weeks of treatment, after three months of treatment and every three to six months thereafter in patients without renal risk factors. In patients at risk of renal impairment, a more frequent monitoring of renal function is required. There are limited data on the safety and efficacy of Viread in adult patients with impaired renal function. Viread should only be used in these patients if the potential benefits outweigh the risks. Interrupting treatment with Viread should be considered in case of progressive decline of renal function when no other cause has been identified. For adult patients with moderate (CrCl < 30-49 ml/min) or severe (CrCl < 30 ml/min) renal impairment including haemodialysis patients, daily dose adjustment using Viread 33 mg/g granules is recommended. For adult patients with moderate and severe renal impairment who are unable to use the granules formulation, and with no alternative treatments available, prolonged dose intervals using Viread 245 mg film-coated tablets may be used. Viread is not recommended in paediatric patients with renal impairment. Viread should be discontinued in paediatric patients who develop renal impairment during therapy.

Exacerbations of Hepatitis: Flares on treatment: Spontaneous exacerbations in CHB are relatively common. Patients with cirrhosis may be at higher risk for hepatic exacerbations and therefore should be monitored closely. However it also should be noted that increase in ALT can be part of HBV clearance during therapy with Viread. Flares after treatment discontinuation: Acute exacerbations of hepatitis have also been reported in patients who have discontinued hepatitis B therapy. Hepatic function should be monitored at repeated intervals with both clinical and laboratory follow-up for at least 6 months after discontinuation of therapy. Treatment discontinuation is not recommended in patients with advanced liver disease or cirrhosis, since post-treatment exacerbations of hepatitis may lead to hepatic decompensation.

Hepatic Decompensation: There are limited data on the safety and efficacy of Viread in HBV-infected patients with decompensated liver disease and who have a Child Pugh Turcotte (CPT) score > 9. These patients may be at higher risk of

experiencing serious hepatic or renal adverse reactions. Therefore, hepatobiliary and renal parameters should be closely monitored in this patient population.

Hepatic Disease: Safety and efficacy data are very limited in liver transplant patients.

Bone: Viread may cause a reduction in bone mineral density (BMD). The effects of Viread-associated changes in BMD on long term bone health and future fracture risk are unknown. If bone abnormalities are detected/suspected in paediatric patients, consult an endocrinologist and/or nephrologist. Bone abnormalities (infrequently contributing to fractures) may be associated with proximal renal tubulopathy.

HIV Co-infection: HIV antibody testing should be offered to all CHB patients before initiating Viread therapy. Due to the risk of development of HIV resistance, Viread should only be used as part of an appropriate antiretroviral combination regimen in HIV/hepatitis B virus (HBV) co-infected patients. Patients must be advised Viread has not been proven to prevent the risk of transmission of HIV or HBV to others through sexual contact or contamination with blood and appropriate precautions must be used.

Co-infection with Hepatitis C or D: There are no data on the efficacy of Viread in patients co-infected with hepatitis C or D virus.

Use in Pregnancy and Lactation: The use of Viread may be considered during pregnancy. Viread should not be used during breast feeding.

Drug Interactions:

Viread has a low potential for CYP450 mediated interactions with other medicinal products. Viread should not be administered concomitantly with other medicinal products containing tenofovir disoproxil fumarate or adefovir dipivoxil, nephrotoxic agents or medicinal products that reduce renal function or compete for active tubular secretion. Monitor renal function if Viread administered with tacrolimus. Co-administration with didanosine is not recommended as it may result in a 40-60% increase in systemic exposure to didanosine which may increase the risk of didanosine-related adverse events. Co-administration with 400 mg daily didanosine has been associated with significant decreases in CD4 cell counts. A reduced dose of 250 mg didanosine administered with Viread has been associated with reports of high rates of virological failure. Co-administration with lopinavir/ritonavir; 30% increase in tenofovir AUC. Co-administration with atazanavir/ritonavir decreased atazanavir concentrations, but increased exposure to tenofovir. Higher tenofovir concentrations could potentiate tenofovir associated adverse events including renal disorders. Food has been shown to enhance the bioavailability of Viread.

Adverse Reactions:

Very commonly reported adverse events (≥ 1/10): hypophosphataemia*, dizziness, diarrhoea, vomiting, nausea, rash, asthenia. Common (≥ 1/100 to < 1/10): flatulence, headache, abdominal pain, abdominal distension, fatigue, increased transaminases. Uncommon (≥ 1/1,000 to < 1/100): hypokalaemia*, pancreatitis, rhabdomyolysis*, muscular weakness, increased creatinine. Rare (≥ 1/10,000, < 1/1,000): lactic acidosis, hepatic steatosis, hepatitis, angioedema, osteomalacia*, myopathy*, renal failure, acute renal failure, proximal renal tubulopathy including Fanconi syndrome, acute tubular necrosis, nephritis, nephrogenic diabetes insipidus. The side effects marked * may occur as a consequence of proximal renal tubulopathy. In patients with CHB, exacerbations of hepatitis during treatment may arise. Refer to SmPC for full information on adverse events.

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. Gilead has operations in more than 30 countries worldwide, with headquarters in Foster City, California.

Forward-Looking Statement

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 risk that the European Commission or other regulatory agencies, including the FDA, may not approve TAF for the treatment of chronic hepatitis B and that any marketing approvals, if granted, may have significant limitations on its use. As a result, Gilead may not be able to successfully commercialize TAF for chronic hepatitis B. 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 Annual Report on Form 10-K for the year ended December 31, 2015, 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.

The European SmPC for Viread is available from the EMA website at www.ema.europa.eu

Viread is a registered trademark of Gilead Sciences, Inc.

For more information on Gilead Sciences, please visit the company's website at www.gilead.com, follow Gilead on Twitter (@GileadSciences) or call Gilead Public Affairs at +44 (208) 587-2477.

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