

## **Gilead Sciences Submits European Marketing Application for Once-Daily Single-Tablet Regimen of Truvada(R) and TMC278 for the Treatment of HIV Infection**

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### ***-- Product Would Be The Second Complete, Fixed-Dose Antiretroviral Regimen --***

FOSTER CITY, Calif., Sep 03, 2010 (BUSINESS WIRE) -- Gilead Sciences, Inc. (Nasdaq:GILD) today announced that it has submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for marketing approval for the fixed-dose combination of Truvada<sup>(R)</sup> (emtricitabine and tenofovir disoproxil (as fumarate)) and Tibotec Pharmaceuticals' investigational non-nucleoside reverse transcriptase inhibitor TMC278 (rilpivirine (as hydrochloride)) for the treatment of HIV-1 infection in adults. Pending approval, the new single-tablet regimen would be only the second product that contains a complete antiretroviral treatment regimen in a single once-daily tablet.

The MAA will be reviewed by the Committee for Medicinal Products for Human Use (CHMP). Review of the MAA will be conducted by the EMA under the centralized licensing procedure, which, when finalized, provides one marketing authorization in all 27 member states of the European Union. An MAA for TMC278 also is being submitted today by Tibotec to the EMA for review.

"The important role of complete, fixed-dose HIV treatment regimens is well established in Europe," said John C. Martin, PhD, Chairman and Chief Executive Officer, Gilead Sciences. "Today, nearly one quarter of HIV patients in the major European countries are taking a one pill, once-daily regimen, and recent updates to the International AIDS Society guidelines support the use of these simplified regimens. We are pleased to work with Tibotec in contributing another potentially important new once-daily, fixed-dose treatment option."

The regulatory application for the fixed-dose combination is supported by 48-week data from two Phase III double-blind, randomized studies (ECHO and THRIVE) evaluating the safety and efficacy of TMC278 in treatment-naïve HIV-1 infected adults and a bioequivalence study conducted by Gilead, which demonstrated that the formulation of the fixed-dose combination of Truvada and TMC278 achieved the same levels of medication in the blood as the component products dosed simultaneously. ECHO (Efficacy Comparison in treatment-naïve HIV-infected subjects Of TMC278 and Efavirenz) evaluated TMC278 (25 mg) combined with a fixed-dose background regimen consisting of emtricitabine (200 mg) and tenofovir disoproxil fumarate (245 mg). THRIVE (TMC278 against HIV, in a once-daily RegImen Versus Efavirenz), evaluated once-daily TMC278 (25 mg) compared to once-daily efavirenz (600 mg) combined with an investigator-selected background regimen consisting of two nucleoside reverse transcriptase inhibitors (abacavir and lamivudine, or emtricitabine and tenofovir disoproxil fumarate, or zidovudine and lamivudine).

Gilead entered into a license and collaboration agreement with Tibotec Pharmaceuticals for the development and commercialization of a single-tablet regimen containing TMC278 and emtricitabine and tenofovir disoproxil fumarate for the treatment of HIV in July 2009. In April 2010, Gilead announced that it had successfully formulated and obtained data supporting bioequivalence of the fixed-dose combination.

### **About TMC278 and the Fixed-Dose Combination**

TMC278 (rilpivirine (as hydrochloride)) is an investigational non-nucleoside reverse transcriptase inhibitor being developed by Tibotec Pharmaceuticals. Tibotec submitted a New Drug Application for U.S. marketing approval of TMC278 on July 23, 2010 for once-daily use with other antiretroviral agents in treatment-naïve HIV-infected adults.

The investigational once-daily single-tablet regimen of Truvada/TMC278 contains 200 mg of emtricitabine and 245 mg of tenofovir disoproxil (as fumarate), both nucleoside reverse transcriptase inhibitors, and 25 mg of rilpivirine (as hydrochloride), a non-nucleoside reverse transcriptase inhibitor.

The fixed-dose single-tablet combination of Truvada/TMC278 is an investigational product and the safety and efficacy have not yet been established.

### **Additional Important Information About Truvada**

Truvada is a fixed-dose combination tablet containing 200 mg of emtricitabine (Emtriva<sup>(R)</sup>) and 245 mg of tenofovir disoproxil (as fumarate) (Viread<sup>(R)</sup>). In the European Union, Truvada is indicated in combination with other antiretroviral agents (such as non-nucleoside reverse transcriptase inhibitors or protease inhibitors) for the treatment of HIV-1 infection in adults.

Truvada should not be administered concomitantly with other medicinal products containing emtricitabine, tenofovir disoproxil (as fumarate) or other cytidine analogs such as lamivudine and zalcitabine. Truvada should not be administered with a third nucleoside analogue.

Emtricitabine and tenofovir are principally eliminated by the kidneys. 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 Truvada and renal function monitored every 4 weeks for the first year and every three months thereafter.

In patients at risk of renal impairment, consideration should be given to more frequent monitoring of renal function.

Dosing interval adjustment and close monitoring of renal function are recommended in all patients with creatinine clearance 30-49 ml/min. Truvada should be avoided with concurrent or recent use of a nephrotoxic agent.

Coadministration of Truvada and didanosine is not recommended. Co-administration of tenofovir disoproxil fumarate and didanosine results in a 40-60 percent increase in systemic exposure to didanosine that may increase the risk of didanosine-related adverse reactions. Rare cases of pancreatitis and lactic acidosis, sometimes fatal, have been reported. Patients on atazanavir/ritonavir and lopinavir/ritonavir plus Truvada should be monitored for tenofovir-associated adverse events and Truvada should be discontinued if these occur.

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. If bone abnormalities are suspected then appropriate consultation should be obtained. Cases of osteomalacia (associated with proximal renal tubulopathy and which may contribute to fractures) have been reported in association with the use of Viread.

Changes in body fat have been observed in patients taking anti-HIV medicines. Immune Reconstitution Syndrome has been reported in patients treated with combination therapy, including Viread and Emtriva, and may necessitate further evaluation and treatment.

Most common adverse reactions (incidence greater-than or equal to 10 percent) are hypophosphatemia, dizziness, headache, diarrhea, nausea, vomiting, elevated creatine kinase, asthenia and rash.

The parent compound of Viread was discovered through 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. The inventors of Viread have agreed to waive their right to a royalty on sales of Viread and Truvada in Gilead Access Program countries to ensure the product can be offered at a no-profit price in parts of the world where the HIV/AIDS epidemic has hit the hardest.

For complete prescribing information for Truvada, visit the EMA website.

## **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.

## **Forward-Looking Statement**

This press release includes forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995, which are subject to risks, uncertainties and other factors, including risks related to Gilead's ability to successfully commercialize the fixed-dose combination of Truvada/TMC278. The EMA, FDA or other regulatory agencies may not approve

TMC278 or the fixed-dose combination of Truvada/TMC278 for the treatment of HIV-infection in treatment-naïve adults, and any marketing approval, if granted, may have significant limitations on its use. 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 first and second quarters of 2010, 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 Truvada is available at [www.Truvada.com](http://www.Truvada.com).*

*U.S. full prescribing information for Viread is available at [www.Viread.com](http://www.Viread.com).*

*U.S. full prescribing information for Emtriva is available at [www.GileadHIV.com](http://www.GileadHIV.com).*

*EU Summary of Product Characteristics for Truvada, Viread and Emtriva are available at [http://www.ema.europa.eu/ema/index.jsp?curl=/pages/home/Home\\_Page.jsp](http://www.ema.europa.eu/ema/index.jsp?curl=/pages/home/Home_Page.jsp)*

*Truvada, Viread and Emtriva are registered trademarks of Gilead Sciences, Inc.*

*For more information on Gilead Sciences, please visit the company's website at [www.gilead.com](http://www.gilead.com) or call Gilead Public Affairs at 1-800-GILEAD-5 or 1-650-574-3000.*

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