

## **Gilead Sciences and Merck Establish Agreement for Distribution of ATRIPLA(TM) in Developing Countries**

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FOSTER CITY, Calif. & WHITEHOUSE STATION, N.J.--(BUSINESS WIRE)--Aug. 11, 2006--Gilead Sciences, Inc. (Nasdaq: GILD) and Merck & Co., Inc. (NYSE: MRK) today announced that the companies have established an agreement for the distribution of ATRIPLA(TM) (efavirenz 600 mg/ emtricitabine 200 mg/ tenofovir disoproxil fumarate 300 mg), a once-daily, single tablet regimen for the treatment of HIV-1 infection in adults, in developing countries around the world.

ATRIPLA contains 600 mg of efavirenz, a non-nucleoside reverse transcriptase inhibitor (NNRTI), 200 mg of emtricitabine and 300 mg of tenofovir disoproxil fumarate, both nucleoside reverse transcriptase inhibitors (NRTIs). Efavirenz is marketed by Merck under the tradename Stocrin(R) in all territories outside of the United States, Canada and certain European countries (where it is commercialized by Bristol-Myers Squibb under the tradename Sustiva(R)). Emtricitabine and tenofovir disoproxil fumarate are commercialized by Gilead Sciences under the tradenames Emtriva(R) and Viread(R), respectively. The compounds are commonly prescribed together as a once-daily, fixed-dose tablet, marketed under the tradename Truvada(R) for use as part of combination therapy.

ATRIPLA was approved by the U.S. Food and Drug Administration (FDA) on July 12, 2006. In the United States, the product is commercialized by Bristol-Myers Squibb and Gilead Sciences through the companies' joint venture. The FDA also granted approval of an alternate tradename of ATRIPLA for developing countries, where ATRIPLA will be made available as a white-colored tablet to distinguish it from the salmon-colored version currently available in the United States. Gilead and Merck plan to pursue registration of the product with individual country health authorities. The component therapies are already registered, or in the process of being registered, in many of these countries.

"The FDA's rapid review and approval of ATRIPLA will help to expedite access for adults infected with HIV-1 living in resource-limited parts of the world," said John C. Martin, PhD, President and CEO, Gilead Sciences. "As a once-daily, single tablet regimen, ATRIPLA may help to simplify therapy for patients, and we recognize the urgent need to ensure access for people living in parts of the world where the epidemic is taking the greatest toll."

"Merck has long been a leader in efforts to broaden access to medicines and vaccines around the world," said Merck Chief Executive Officer and President Richard T. Clark. "This new single-tablet regimen is the latest example of how we are working to fulfill our mission to put patients first. We look forward to collaborating with Gilead and national health authorities to deliver ATRIPLA to those who need it as soon as possible."

Under the terms of the agreement, Gilead will manufacture ATRIPLA using efavirenz supplied by Merck. Merck in turn will handle distribution of the product in the countries covered by the agreement.

### **Important Safety Information About ATRIPLA, Truvada, Viread and Emtriva**

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. ATRIPLA, Truvada, Viread and Emtriva are not indicated for the treatment of chronic hepatitis B virus (HBV) infection and the safety and efficacy of these drugs have not been established in patients co-infected with HBV and HIV. Severe acute exacerbations of hepatitis B have been reported in patients who have discontinued Emtriva or Viread (components of ATRIPLA and Truvada). Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue ATRIPLA, Truvada, Emtriva or Viread and are co-infected with HIV and HBV. If appropriate, initiation of anti-hepatitis B therapy may be warranted.

### **Additional Important Information About ATRIPLA**

ATRIPLA is indicated for use alone as a complete regimen or in combination with other antiretroviral agents for the

treatment of HIV-1 infection in adults.

It is important for patients to be aware that ATRIPLA does not cure HIV infection or AIDS. ATRIPLA has not been shown to reduce the risk of transmission of HIV to others through sexual contact or blood contamination.

ATRIPLA is contraindicated for use with astemizole, cisapride, midazolam, triazolam, ergot derivatives, or voriconazole. Concomitant use of ATRIPLA and St. John's wort (*Hypericum perforatum*) or St. John's wort-containing products is not recommended. Since ATRIPLA contains efavirenz, emtricitabine and tenofovir disoproxil fumarate, it should not be coadministered with efavirenz, Emtriva, Viread, or Truvada. Due to similarities between emtricitabine and lamivudine, ATRIPLA should not be coadministered with drugs containing lamivudine, including Combivir, Epivir(R), Epivir-HBV(R), Epzicom(TM), or Trizivir(R).

Serious psychiatric adverse experiences, including severe depression (2.4%), suicidal ideation (0.7%), nonfatal suicide attempts (0.5%), aggressive behavior (0.4%), paranoid reactions (0.4%) and manic reactions (0.2%) have been reported in patients treated with efavirenz. In addition to efavirenz, factors identified in a clinical study that were associated with an increase in psychiatric symptoms included a history of injection drug use, psychiatric history and use of psychiatric medication. There have been occasional reports of suicide, delusions, and psychosis-like behavior, but it could not be determined if efavirenz was the cause. Patients with serious psychiatric adverse experiences should be evaluated immediately to determine whether the risks of continued therapy outweigh the benefits. Fifty-three percent of patients reported central nervous system symptoms including dizziness (28.1%), insomnia (16.3%), impaired concentration (8.3%), somnolence (7.0%), abnormal dreams (6.2%) and hallucinations (1.2%) when taking efavirenz compared to 25% of patients receiving control regimens. These symptoms usually begin during the first or second day of therapy and generally resolve after the first two to four weeks of therapy. After four weeks of therapy, the prevalence of central nervous system symptoms of at least moderate severity ranged from 5% to 9% in patients treated with regimens containing efavirenz. Nervous system symptoms are not predictive of the less frequent psychiatric symptoms.

ATRIPLA should not be given to patients with creatinine clearance below 50 mL/min. 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 tenofovir disoproxil fumarate, most often in patients with underlying systemic or renal disease, or in patients taking concomitant nephrotoxic agents. Some cases have occurred in patients with no identified risk factors. ATRIPLA should be avoided with concurrent or recent use of a nephrotoxic agent.

ATRIPLA may cause fetal harm when administered during the first trimester to a pregnant woman. Women should not become pregnant or breastfeed while taking ATRIPLA. Barrier contraception must always be used in combination with other methods of contraception such as oral or other hormonal contraceptives. If the patient becomes pregnant while taking ATRIPLA, she should be apprised of the potential harm to the fetus.

Mild to moderate rash is a common side effect of efavirenz. In controlled clinical trials, 26% of patients treated with efavirenz experienced new-onset skin rash compared with 17% of patients treated in control groups. Skin discoloration, associated with emtricitabine, may also occur. ATRIPLA should be discontinued in patients developing severe rash associated with blistering, desquamation, mucosal involvement, or fever. Liver enzymes should be monitored in patients with known or suspected hepatitis B or C and when ATRIPLA is administered with ritonavir or other medications associated with liver toxicity. Decreases in bone mineral density have been seen with tenofovir disoproxil fumarate. Use ATRIPLA with caution in patients with a history of seizures. Convulsions have been observed in patients receiving efavirenz, generally in the presence of known medical history of seizures. Redistribution and/or accumulation of body fat have been observed in patients receiving antiretroviral therapy. Immune reconstitution syndrome has been reported in patients treated with combination antiretroviral therapy, including the components of ATRIPLA.

Coadministration of ATRIPLA and atazanavir is not recommended due to concerns regarding decreased atazanavir concentrations. Patients on lopinavir/ritonavir plus ATRIPLA should be monitored for tenofovir-associated adverse events. ATRIPLA should be discontinued in patients who develop tenofovir-associated adverse events. Coadministration

of ATRIPLA and didanosine should be undertaken with caution. Patients receiving this combination should be monitored closely for didanosine-associated adverse events. See full prescribing information for complete list of drug-drug interactions.

In a large controlled clinical trial (Study 934), adverse events observed in greater than or equal to 5% of patients in the Viread/Emtriva/efavirenz group include dizziness, nausea, diarrhea, fatigue, headache, and rash.

The dose of ATRIPLA is one tablet once daily taken orally on an empty stomach. Dosing at bedtime may improve the tolerability of nervous system symptoms.

#### Important Information About Efavirenz

Efavirenz combination with other antiretroviral agents is indicated for the treatment of HIV-1 infection. This indication is based on two clinical trials of at least one year duration that demonstrated prolonged suppression of HIV RNA.

Coadministration with astemizole, cisapride, midazolam, triazolam, ergot derivatives, or voriconazole is contraindicated. Concomitant use of efavirenz and St. John's wort (*Hypericum perforatum*) or St. John's wort-containing products is not recommended. This list of medications is not complete.

Serious psychiatric adverse experiences, including severe depression (2.4%), suicidal ideation (0.7%), nonfatal suicide attempts (0.5%), aggressive behavior (0.4%), paranoid reactions (0.4%) and manic reactions (0.2%) have been reported in patients treated with efavirenz. In addition to efavirenz, factors identified in a clinical study that were associated with an increase in psychiatric symptoms included history of injection drug use, psychiatric history, and use of psychiatric medication. There have been occasional reports of suicide, delusions, and psychosis-like behavior, but it could not be determined if efavirenz was the cause. Patients with serious psychiatric adverse experiences should be evaluated immediately to determine whether the risks of continued therapy outweigh the benefits. Fifty-three percent of patients reported central nervous system symptoms including dizziness (28.1%), insomnia (16.3%), impaired concentration (8.3%), somnolence (7.0%), abnormal dreams (6.2%) and hallucinations (1.2%) when taking efavirenz compared to 25% of patients receiving control regimens. These symptoms usually begin during Days 1-2 of therapy and generally resolve after the first 2-4 weeks of therapy. After four weeks of therapy, the prevalence of central nervous system symptoms of at least moderate severity ranged from 5% to 9% in patients treated with regimens containing efavirenz. Nervous system symptoms are not predictive of the less frequent serious psychiatric symptoms.

Efavirenz may cause fetal harm when administered during the first trimester to a pregnant woman. Women should not become pregnant or breastfeed while taking efavirenz. Barrier contraception must always be used in combination with other methods of contraception (e.g. oral or other hormonal contraceptives). If the patient becomes pregnant while taking efavirenz, she should be apprised of the potential harm to the fetus.

Mild to moderate rash is a common side effect of efavirenz. In controlled clinical trials, 26% of patients treated with efavirenz experienced new-onset skin rash compared with 17% of patients treated in control groups. Efavirenz should be discontinued in patients developing severe rash associated with blistering, desquamation, mucosal involvement, or fever. Rash is more common and often more severe in pediatric patients.

Liver enzymes should be monitored in patients with known or suspected hepatitis B or C, in patients treated with other medications associated with liver toxicity, and when efavirenz is administered with ritonavir. Use efavirenz with caution in patients with a history of seizures. Convulsions have been observed in patients receiving efavirenz, generally in the presence of known medical history of seizures. Redistribution and/or accumulation of body fat have been seen in patients receiving antiretroviral therapy. A causal relationship has not been established. Immune reconstitution syndrome has been reported in patients treated with combination antiretroviral therapy, including efavirenz.

It is recommended that efavirenz be taken on an empty stomach, preferably at bedtime. The increased concentrations following administration of efavirenz with food may lead to an increase in frequency of adverse events. Dosing at bedtime

may improve the tolerability of nervous system symptoms.

#### Additional Important Information About Truvada

Truvada is a fixed-dose combination product that combines 200 mg of Emtriva(R) (emtricitabine) and 300 mg of Viread(R) (tenofovir disoproxil fumarate) in one tablet, taken once a day. In the United States, 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 coadministered with Emtriva, Viread or lamivudine-containing products and it is not recommended that Truvada be used as a component of a triple nucleoside regimen. In treatment-experienced patients, the use of Truvada should be guided by laboratory testing and treatment history.

Clinical Study 934 supports the use of Truvada tablets for the treatment of HIV-1 infection. Additional data in support of the use of Truvada are derived from Study 903, in which Viread and lamivudine were used in combination in treatment-naïve adults, and clinical Study 303, in which Emtriva and lamivudine demonstrated comparable efficacy, safety and resistance patterns as part of multidrug regimens.

No drug interaction studies have been conducted using Truvada. Drug interactions have been observed when didanosine, atazanavir, or lopinavir/ritonavir are co-administered with Viread, a component of Truvada, and dose adjustments may be necessary. Data are not available to recommend a dose adjustment of didanosine for patients weighing less than 60 kg. Patients on atazanavir or lopinavir/ritonavir plus Truvada should be monitored for Truvada-associated adverse events that may require discontinuation. When co-administered with Truvada, it is recommended that atazanavir 300 mg be given with ritonavir 100 mg. Atazanavir without ritonavir should not be co-administered with Truvada.

Four-hundred and forty-seven HIV-1 infected patients have received combination therapy with Emtriva and Viread with either a non-nucleoside reverse transcriptase inhibitor (Study 934) or protease inhibitor for 48 weeks in clinical studies. Adverse events observed in Study 934 were generally consistent with those seen in other studies in treatment-experienced or treatment-naïve patients receiving Viread and/or Emtriva. Adverse events observed in more than 5% of patients in the Viread/Emtriva group in Study 934 include diarrhea, nausea, fatigue, headache, dizziness and rash.

Renal impairment, including cases of acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), has been reported among patients taking Viread, a component of Truvada (emtricitabine and tenofovir disoproxil fumarate). Renal impairment occurred most often in patients with underlying systemic or renal disease or in patients taking concomitant nephrotoxic agents, though some cases have appeared in patients without identified risk factors. Decreases in bone mineral density (BMD) at the lumbar spine and hip have been seen with the use of Viread. Redistribution and/or accumulation of body fat have been observed in patients receiving antiretroviral therapy. Immune reconstitution syndrome has been reported in patients treated with combination antiretroviral therapy including Truvada, Viread and Emtriva.

The effects of Viread-associated changes in BMD and biochemical markers on long-term bone health and future fracture risk are unknown. Skin discoloration, manifested by hyperpigmentation on the palms and/or soles, has been reported with the use of Emtriva, a component of Truvada. Skin discoloration was generally mild and asymptomatic and its mechanism and clinical significance are unknown.

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.

#### 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. Visit Gilead on the World Wide Web at [www.gilead.com](http://www.gilead.com).

## About Merck

Merck & Co., Inc. is a global research-driven pharmaceutical company dedicated to putting patients first. Established in 1891, Merck currently discovers, develops, manufactures and markets vaccines and medicines to address unmet medical needs. The Company devotes extensive efforts to increase access to medicines through far-reaching programs that not only donate Merck medicines but also help deliver them to the people who need them. Merck also publishes unbiased health information as a not-for-profit service. For more information, visit [www.merck.com](http://www.merck.com).

## Forward-Looking Statements

### Gilead 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 physicians and regulatory agencies may not see advantages of ATRIPLA over other antiretrovirals and may therefore be reluctant to prescribe the product. 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 the Gilead Annual Report on Form 10-K for the year ended December 31, 2005, 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.

### Merck Forward-Looking Statement

This press release contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995. These statements are based on management's current expectations and involve risks and uncertainties, which may cause results to differ materially from those set forth in the statements. The forward-looking statements may include statements regarding product development, product potential or financial performance. No forward-looking statement can be guaranteed, and actual results may differ materially from those projected. Merck undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Merck's business, particularly those mentioned in the cautionary statements in Item 1 of Merck's Form 10-K for the year ended Dec. 31, 2005, and in its periodic reports on Form 10-Q and Form 8-K, which the Company incorporates by reference.

Full prescribing information for ATRIPLA is available at [www.atripla.com](http://www.atripla.com).

Full prescribing information for Stocrin is available at <http://www.emea.eu.int/humandocs/Humans/EPAR/Stocrin/Stocrin.htm>

Full prescribing information for Truvada, Viread and Emtriva is available at [www.gilead.com](http://www.gilead.com)

ATRIPLA is a trademark of Bristol-Myers Squibb & Gilead Sciences, LLC.

Stocrin is a registered trademark of Merck & Co., Inc.

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

Sustiva is a registered trademark of Bristol-Myers Squibb.

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