

**U.S. Food and Drug Administration (FDA) Approves ATRIPLA(TM) (efavirenz 600 mg/ emtricitabine 200 mg/ tenofovir disoproxil fumarate 300 mg), The First Once-Daily Single Tablet Regimen for Adults with HIV-1 Infection**

PRINCETON, N.J. and FOSTER CITY, Calif.--(BUSINESS WIRE)--July 12, 2006--

Product Developed Through U.S. Joint Venture between Bristol-Myers

Squibb and Gilead Sciences, the First of Its Kind in HIV Treatment

Bristol-Myers Squibb Company (NYSE:BMJ) and Gilead Sciences, Inc. (Nasdaq:GILD) today announced the U.S. Food and Drug Administration (FDA) has granted approval of ATRIPLA(TM) (efavirenz 600 mg/ emtricitabine 200 mg/ tenofovir disoproxil fumarate 300 mg) for the treatment of HIV-1 infection in adults. ATRIPLA is the first-ever once-daily single tablet regimen (STR) for HIV intended as a stand-alone therapy or in combination with other antiretrovirals. The product combines SUSTIVA(R) (efavirenz), manufactured by Bristol-Myers Squibb, and Truvada(R) (emtricitabine and tenofovir disoproxil fumarate), manufactured by Gilead Sciences. Truvada itself is a fixed-dose product that contains two of Gilead's anti-HIV medications, Viread(R) (tenofovir disoproxil fumarate) and Emtriva(R) (emtricitabine), in a single once-daily tablet for use as part of combination therapy. ATRIPLA will be available in the United States within seven business days.

"The availability of ATRIPLA marks the culmination of ten years of efforts to simplify dosing while helping to achieve and maintain effective viral suppression for adults infected with HIV-1," said John G. Bartlett, MD, Johns Hopkins University.

The collaboration between Bristol-Myers Squibb and Gilead is the first of its kind in the 25-year history of the AIDS epidemic. On December 20, 2004 the companies established a U.S. joint venture to develop and commercialize the single tablet regimen.

"We appreciate the recognition by the FDA of this important therapeutic advance, and with their approval of ATRIPLA in just over two months, patients will now have rapid access to the first once-daily single tablet regimen for the treatment of HIV-1 infection in adults," said John C. Martin, PhD, President and CEO of Gilead Sciences. "We are proud to have worked closely with Bristol-Myers Squibb in this precedent-setting collaboration to simplify therapy for physicians and patients."

"With the approval of ATRIPLA, Bristol-Myers Squibb continues two decades of progress in the development and commercialization of medications to treat HIV. Partnering with Gilead, we are able to address another area of need for adults infected with HIV-1," said Anthony C. Hooper, President, U.S. Pharmaceuticals, Bristol-Myers Squibb. "ATRIPLA is an important step forward as we continue our focus on discovering, developing and providing innovative treatments for serious diseases."

The once-daily single tablet regimen contains three medicines from two classes of anti-HIV drugs. 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). All three active ingredients work by blocking reverse transcriptase, an enzyme necessary for HIV replication.

Clinical data support the use of the three-drug regimen contained in ATRIPLA in HIV treatment-naive patients. An ongoing randomized, open label, active-controlled, multicenter, non-inferiority study, Study 934, compares a once-daily regimen of Viread, Emtriva and SUSTIVA, the components of ATRIPLA, with twice-daily Combivir(R) (lamivudine and zidovudine) and once-daily SUSTIVA in treatment-naive patients with HIV. Through 48 weeks, 84% of patients in the Viread/Emtriva/SUSTIVA group (n=244) compared to 73% of patients in the Combivir/SUSTIVA group (n=243) achieved and maintained HIV-1 RNA less than 400 copies/mL. This difference largely results from the higher number of discontinuations in the Combivir/SUSTIVA group due to adverse events (9% vs. 4% in the Viread/Emtriva/SUSTIVA group) and other reasons including lost to follow-up, patient withdrawal, non-compliance and protocol violation (14% vs. 10% in the Viread/Emtriva/SUSTIVA group). In addition, 80% and 70% of patients in the Viread/Emtriva/SUSTIVA group and the Combivir/SUSTIVA group, respectively, achieved and maintained HIV-1 RNA less than 50 copies/mL. The mean increase from baseline in CD4 cell count was 190 cells/mm<sup>3</sup> in the Viread/Emtriva/SUSTIVA group and 158 cells/mm<sup>3</sup> in the Combivir/SUSTIVA group. Selected adverse events observed in greater than or equal to 5% of patients in the Viread/Emtriva/SUSTIVA group include dizziness, nausea, diarrhea, fatigue, headache and rash.

Guidelines issued by the U.S. Department of Health and Human Services (DHHS) list efavirenz, emtricitabine and tenofovir disoproxil fumarate among the preferred agents for use in an NNRTI-based treatment regimen in appropriate patients who have never taken anti-HIV medicines. Efavirenz should not be used during the first trimester of pregnancy due to the potential harm to the fetus. Pregnancy should be avoided by women receiving efavirenz.

#### About HIV/AIDS

2006 marks the 25th anniversary of the start of the AIDS epidemic. The first cases of HIV/AIDS were reported by the U.S. Centers for Disease Control and Prevention (CDC) in the June 5, 1981 issue of the Morbidity and Mortality Weekly Report (MMWR). Today, the CDC estimates that more than one million Americans are infected with HIV, the virus that causes AIDS. Of these, approximately 25% are unaware of their infection. Although HIV treatment options have expanded rapidly in recent years, the CDC estimates that 216,000 Americans who are HIV positive and eligible for antiretroviral treatment are currently not receiving it.

#### 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 SUSTIVA, 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/SUSTIVA 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 SUSTIVA

SUSTIVA (efavirenz) in 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 SUSTIVA 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 SUSTIVA. In addition to SUSTIVA, 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 SUSTIVA 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 SUSTIVA 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 SUSTIVA. Nervous system symptoms are not predictive of the less frequent serious psychiatric symptoms.

SUSTIVA may cause fetal harm when administered during the first trimester to a pregnant woman. Women should not become pregnant or breastfeed while taking SUSTIVA. 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 SUSTIVA, she should be apprised of the potential harm to the fetus.

Mild to moderate rash is a common side effect of SUSTIVA. In controlled clinical trials, 26% of patients treated with SUSTIVA experienced new-onset skin rash compared with 17% of patients treated in control groups. SUSTIVA 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 SUSTIVA is administered with ritonavir. Use SUSTIVA 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 SUSTIVA.

It is recommended that SUSTIVA be taken on an empty stomach, preferably at bedtime. The increased concentrations following administration of SUSTIVA 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-naive 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-naive 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, Catholic University in Leuven, Belgium.

#### About Bristol-Myers Squibb

Bristol-Myers Squibb is a global pharmaceutical and related healthcare products company. Visit Bristol-Myers Squibb on the World Wide Web at [www.bms.com](http://www.bms.com).

#### 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).

#### Forward-Looking Statements

##### Bristol-Myers Squibb Forward-Looking Statement

This press release contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding product development. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Among other risks, there can be no guarantee that the combination product will be commercially successful. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb's business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2005 and in our Quarterly Reports on Form 10-Q. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

#### 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.

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

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

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

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