



## **Bristol-Myers Squibb and Gilead Announce Data Supporting Bioequivalence for Single-Pill Fixed-Dose Regimen of Sustiva(R) (efavirenz) and Truvada(R) (emtricitabine and tenofovir disoproxil fumarate)**

January 9, 2006

NEW YORK & FOSTER CITY, Calif.--(BUSINESS WIRE)--Jan. 9, 2006-- Companies Anticipate Filing New Drug Application in Second Quarter of 2006

Bristol-Myers Squibb Company (NYSE:BMJ) and Gilead Sciences, Inc. (Nasdaq:GILD) today announced they have obtained data supporting bioequivalence of a new formulation of the fixed-dose combination of Bristol-Myers Squibb's Sustiva(R) (efavirenz) and Gilead's Truvada(R) (emtricitabine and tenofovir disoproxil fumarate) with the components that make up the new combination. The new fixed-dose regimen is intended for the treatment of HIV-1 infection in adults.

The fixed-dose regimen was developed using a bi-layer technology to co-formulate Sustiva and Truvada as individually formulated layers combined in one tablet. In August of 2005, Gilead announced that the companies were proceeding with the evaluation of three new formulations in parallel, based on bi-layer technology.

A bioequivalence study is required to demonstrate that a co-formulated product results in the same levels of medication in the blood as achieved when the individual products are dosed simultaneously as separate pills. Gilead and Bristol-Myers Squibb anticipate filing a New Drug Application with the U.S. Food and Drug Administration (FDA) in the second quarter of 2006.

"Tremendous progress has been made in the fight against HIV/AIDS, yet there is still work that needs to be done," said Anthony C. Hooper, President, U.S. Pharmaceuticals, Bristol-Myers Squibb. "Together with our partner Gilead, Bristol-Myers Squibb will continue advancing the development of this potential innovative treatment option for HIV patients."

"The advancement of our fixed-dose regimen represents an important step forward in the further simplification of HIV treatment," said John C. Martin, PhD, President and Chief Executive Officer, Gilead Sciences. "Gilead and Bristol-Myers Squibb share a commitment to the treatment of HIV, a disease for which significant unmet medical need continues to exist, and we look forward to working with regulatory authorities."

In December 2004, Gilead and Bristol-Myers Squibb announced the establishment of a U.S. joint venture to co-formulate the antiretrovirals Truvada and Sustiva in a fixed-dose regimen. If approved by the FDA, the new product would be the first complete Highly Active Antiretroviral Therapy (HAART) treatment regimen for HIV available in a fixed-dose combination tablet taken once daily. Fixed-dose combinations contain multiple medicines formulated together and may help simplify HIV therapy for patients and providers. The joint venture established by the two companies is the first of its kind in the field of HIV therapy.

Guidelines issued by the U.S. Department of Health and Human Services (DHHS) list the combination of emtricitabine, tenofovir disoproxil fumarate and efavirenz as one of the preferred non-nucleoside reverse transcriptase inhibitor (NNRTI)-based treatments for use in appropriate patients that have never taken anti-HIV medicines before. Efavirenz should not be used during the first trimester of pregnancy due to the potential harm to the fetus. Pregnancy should be avoided in women receiving efavirenz. It is important that patients be aware that individual HIV medications must be taken as part of combination regimens, and that they do not cure HIV infection or prevent passing HIV to others.

### **Important Information About SUSTIVA(R) (efavirenz)**

SUSTIVA is a prescription medicine used in combination with other medicines to treat people who are infected with the human immunodeficiency virus type 1 (HIV-1). SUSTIVA does not cure HIV or help prevent passing HIV to others. SUSTIVA should not be taken with Hismanal(R) (astemizole), Propulsid(R) (cisapride), Versed(R) (midazolam), Halcion(R) (triazolam), ergot medicines (for example, Wigraine(R) and Cafergot(R)), or Vfend(R) (voriconazole). This list of medicines is not complete. Patients should discuss all prescription and non-prescription medicines, vitamin and herbal supplements, or other health preparations (particularly St. John's wort) they are taking or plan to take with their healthcare provider.

Patients taking SUSTIVA should tell their doctor right away if they have any side effects or conditions including: severe depression, strange thoughts, or angry behavior, which have been reported in a small number of patients. A few reports of suicide have been made, but it is not known if SUSTIVA was the cause. Dizziness, trouble sleeping, drowsiness, trouble concentrating, and/or unusual dreams are common. These feelings tend to go away after taking SUSTIVA for a few weeks.

Women should not become pregnant or breastfeed while taking SUSTIVA. Serious birth defects have been seen in children of women treated with SUSTIVA during pregnancy. Women must use a reliable form of barrier contraception, such as a condom, even if they also use other methods of birth control. Patients should tell their doctor if they have a history of mental illness or are using drugs or alcohol. Rash is a common side effect that usually goes away without any change in treatment. Rash may be a serious problem in some children. If a child develops a rash, their doctor should be contacted right away. Patients with liver disease, a history of seizures, or taking medicine for seizures, may require the healthcare provider to check the liver or check drug levels in the blood.

Changes in body fat have been seen in some patients taking HIV medicines, however, the cause and long-term effects of these changes are not known at this time. Other common side effects include: tiredness, upset stomach, vomiting and diarrhea. SUSTIVA should be taken on an empty stomach, preferably at bedtime, which may make some side effects less bothersome. SUSTIVA and other anti-HIV medicines should be taken exactly as instructed by healthcare providers. United States Full Prescribing Information for SUSTIVA is available at [www.SUSTIVA.com](http://www.SUSTIVA.com).

### **About Truvada**

Truvada combines Emtriva(R) (emtricitabine) and Viread(R) (tenofovir disoproxil fumarate) in one tablet taken once a day in combination with other antiretroviral agents. 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. Safety and efficacy studies using Truvada tablets or using Emtriva and Viread in combination are ongoing.

Emtriva and Viread have each been studied as part of multi-drug regimens and have been found to be safe and effective. In clinical study 303 Emtriva and lamivudine (3TC) demonstrated comparable efficacy, safety and resistance patterns as part of multidrug regimens. These data, and those from study 903, in which lamivudine and tenofovir were used in combination, support the use of Truvada for the treatment of HIV-1 infection in treatment-naive adults. In treatment-experienced patients, the use of Truvada should be guided by laboratory testing and treatment history.

There are no study results demonstrating the effect of Truvada on clinical progression of HIV-1, and it is not recommended that Truvada be used as a component of a triple nucleoside regimen.

Truvada should not be used with Emtriva or Viread, or other drugs containing lamivudine, including Combivir(R), Eпивir(R), Eпивir-HBV(R), Epzicom(TM) or Trizivir(R). Two-hundred eighty-three patients have received combination therapy with Emtriva and Viread with either a non-nucleoside reverse transcriptase inhibitor or protease inhibitor for 24 to 48 weeks in ongoing clinical studies. Based on these limited data, no new patterns of adverse events were identified and there was no increased frequency of established toxicities. For additional safety information about Emtriva or Viread in combination with other antiretroviral agents, please see "About Emtriva" and "About Viread," below.

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

Immune reconstitution syndrome has been reported in patients treated with combination antiretroviral therapy, including Viread and Emtriva. Changes in body fat have been observed in patients taking anti-HIV medicines, including Viread and Emtriva. The cause and long term health effect of these conditions are unknown.

The parent compound of one of the component drugs in Truvada, tenofovir disoproxil fumarate, 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 have agreed to waive their right to a royalty on sales of products containing tenofovir in the developing countries served by the Gilead Access Program to ensure the product can be offered at a no-profit price in parts of the world where the AIDS epidemic has hit the hardest.

#### About Emtriva

In the United States, Emtriva is indicated, in combination with other antiretroviral agents, for the treatment of HIV-1 infection in patients over three months of age. This indication is based on analyses of plasma HIV-1 RNA levels and CD4 cell counts from controlled studies of 48 weeks duration in antiretroviral-naive patients and antiretroviral-treatment-experienced patients who were virologically suppressed on an HIV treatment regimen. In antiretroviral-treatment-experienced patients, the use of Emtriva may be considered for adults with HIV strains that are expected to be susceptible to Emtriva as assessed by genotypic or phenotypic testing. In pediatric patients over three months of age, the safety and efficacy of emtricitabine is supported by data from three open-label, non-randomized clinical studies in which emtricitabine was administered to 169 HIV-1 infected treatment naive and experienced patients between three months and 21 years of age.

Adverse events that occurred in more than five percent of patients receiving Emtriva with other antiretroviral agents in clinical trials include abdominal pain, asthenia (weakness), headache, diarrhea, nausea, vomiting, dizziness and rash (rash, pruritis, maculopapular rash, urticaria, vesiculobullous rash, pustular rash and allergic reaction). Approximately one percent of patients discontinued participation because of these events. All adverse events were reported with similar frequency in Emtriva and control treatment groups with the exception of skin discoloration which was reported with higher frequency in the Emtriva treated group. Skin discoloration, manifested by hyperpigmentation on the palms and/or soles, was generally mild and asymptomatic. The mechanism and clinical significance are unknown. For pediatric patients over three months of age, the adverse event profile observed during clinical trials was similar to that of adult patients, with the exception of anemia and a higher frequency of hyperpigmentation.

#### About Viread

In the United States, Viread is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection. This indication is based on analyses of plasma HIV-1 RNA levels and CD4 cell counts in controlled studies of Viread in treatment-naive adults and in treatment-experienced adults. There are no study results demonstrating the effect of Viread on clinical progression of HIV-1. The use of Viread should be considered for treating adult patients with HIV-1 strains that are expected to be susceptible to tenofovir as assessed by laboratory testing or treatment history.

Drug interactions have been observed when didanosine, atazanavir or lopinavir/ritonavir is co-administered with Viread 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 Viread should be monitored for Viread-associated adverse events which may require discontinuation. When co-administered with Viread, it is recommended that atazanavir 300 mg be given with ritonavir 100 mg. Atazanavir without ritonavir should not be co-administered with Viread.

Renal impairment, including serious cases, has been reported. 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 and increases in biochemical markers of bone metabolism have been seen with the use of Viread. The clinical significance of changes in BMD and biochemical markers is unknown and follow-up is continuing to assess long-term impact. The most common adverse events and those occurring in more than five percent of patients receiving Viread with other antiretroviral agents in clinical trials include asthenia, pain, abdominal pain, headache, nausea, diarrhea, vomiting, rash (rash, pruritis, maculopapular rash, urticaria, vesiculobullous rash and pustular rash), flatulence, dizziness and depression. Less than one percent of patients discontinued participation because of gastrointestinal events.

#### About Bristol-Myers Squibb

Bristol-Myers Squibb is a global pharmaceutical and related healthcare products company whose mission is to extend and enhance human life. For more than a decade, Bristol-Myers Squibb Company has been a global leader in the science of infectious diseases and has invested consistently in innovative research leading to the development of important treatments for people with HIV/AIDS. 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).

#### 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. Among other risks, there can be no guarantee that the combination product will be submitted for regulatory approval, will receive regulatory approval, or, if approved, will be commercially successful. No forward-looking statement can be guaranteed. 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/A for the year ended December 31, 2004 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 contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995. The forward-looking statements include statements regarding approval and licensure of the combination product. These statements involve risks and uncertainties, which may cause results to differ materially from those set forth in the statements, including the risks related to regulatory requirements to support approval of the combination product, and the willingness of regulatory authorities to grant regulatory approval for the combination product based on available data. No forward-looking statement can be guaranteed, and actual results may differ materially from those projected. Gilead 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 Gilead's business, particularly those mentioned in the cautionary statements in the company's Form 10-K for the year ended December 31, 2004, and in periodic reports on Form 10-Q and Form 8-K.

Sustiva is a registered trademark of Bristol-Myers Squibb Pharma Company.

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

All other trademarks are the property of third parties.

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