ADVANCE-2 Study Results Demonstrate Investigational Anticoagulant Apixaban Was Statistically Superior To Enoxaparin In The Prevention Of Venous Thromboembolism Following Knee Replacement Surgery

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Phase III Data Published in The Lancet also Demonstrate Comparable Rates of Bleeding with Apixaban Versus Enoxaparin

(BUSINESS WIRE)--Apixaban, an oral anticoagulant being developed by Bristol-Myers Squibb Company (NYSE: BMY) and Pfizer Inc. (NYSE: PFE), was statistically superior to 40 mg once daily enoxaparin in reducing the incidence of venous thromboembolism in patients undergoing elective total knee replacement surgery, according to the ADVANCE-2 study results published today in The Lancet. The study results also showed numerically lower rates of major and clinically relevant non-major bleeding in patients treated with apixaban compared with those treated with enoxaparin. These results did not meet statistical significance.

Apixaban is a novel, oral, highly selective Factor Xa inhibitor, part of a class of agents being studied for their potential to prevent and treat blood clots in the veins and arteries. Results of ADVANCE-2 were first presented in July 2009 at the 22nd Congress of the International Society on Thrombosis and Haemostasis in Boston.

Patients undergoing major orthopedic surgery, including total knee replacement, are at high risk for venous thromboembolism. In fact, venous thromboembolism occurs in 40 to 60 percent of patients undergoing orthopedic surgery who do not receive preventive care. With an estimated 400,000 people worldwide undergoing total knee replacement surgery each year, the threat of venous thromboembolism and its associated morbidity and mortality risk represent a growing challenge to physicians.

“One of the major concerns for orthopedic surgeons using oral anticoagulants for venous thromboembolism prevention in knee surgery is the significant risk of bleeding,” said Michael Rud Lassen, M.D., Hoersholm Hospital in Copenhagen, Denmark, lead investigator for the study. “We are encouraged by the ADVANCE-2 data, which demonstrated better antithrombotic effect and comparable bleeding rates for apixaban compared with enoxaparin.”

About ADVANCE-2

ADVANCE-2, a randomized, double-blind, multicenter, head-to-head trial was designed to evaluate the efficacy and safety of oral, twice daily apixaban 2.5 mg compared with subcutaneous enoxaparin 40 mg once daily, over a 10-to-14 day treatment period for reducing the risk of venous thromboembolism in patients undergoing elective total knee replacement surgery. Of the 3,221 patients from 27 countries (Europe, Asia/Pacific, Latin America, Africa) enrolled in the study, 1,973 patients were eligible for the analysis of the primary efficacy endpoint defined as the composite of asymptomatic and symptomatic deep vein thrombosis, non-fatal pulmonary embolism, and death from any cause during study treatment. The statistical plan for the study required testing non-inferiority of apixaban before testing for superiority.

When apixaban was compared with enoxaparin, the primary efficacy endpoint occurred in 15.1 percent of patients in the apixaban group and 24.4 percent of patients in the enoxaparin group, demonstrating a statistically significant relative risk reduction for apixaban of 38 percent ($p<0.0001$).

The secondary efficacy outcome of major venous thromboembolism occurred in 1.1 percent of patients in the apixaban group compared with 2.2 percent in the enoxaparin group, demonstrating a statistically significant relative risk reduction for apixaban of 50 percent (one-sided $p=0.02$).

The primary safety measure of major bleeding occurred in 0.6 percent of patients who received apixaban, and in 0.9 percent of patients who received enoxaparin, not reaching statistical significance ($p=0.30$). The composite outcome of major bleeding and clinically

relevant non-major bleeding occurred in 3.5 percent and 4.8 percent of patients in the apixaban and enoxaparin groups, respectively, and did not reach statistical significance (p=0.09).

The overall safety profiles of apixaban and enoxaparin were similar in ADVANCE-2. During the treatment and follow-up periods, liver alanine transaminase (ALT) and liver aspartate transaminase (AST) elevations greater than three times the upper limit of normal were reported in 2 percent of patients in the apixaban and enoxaparin groups. Discontinuations due to adverse events in the apixaban and enoxaparin patient groups were similar.

About Venous Thromboembolism

Venous thromboembolism encompasses two serious conditions: deep vein thrombosis, a blood clot in a vein, usually in the leg that partially or totally blocks the flow of blood; and pulmonary embolism, a blood clot blocking a vessel in the lungs. Deep vein thrombosis causes multiple symptoms including pain, swelling and redness and, more importantly, can progress to pulmonary embolism, which carries the risk of sudden death.

About the Apixaban Clinical Trial Program

Apixaban is being investigated within the EXPANSE Clinical Trials Program, which is projected to include nearly 60,000 patients worldwide across multiple indications and patient populations and includes a total of nine completed or ongoing, randomized, double-blind Phase III trials, including ADVANCE-2.

The dose and regimen for apixaban were informed by Phase I and II apixaban clinical trial data and data modeling results. Dosing apixaban twice daily appeared to reduce fluctuations in Factor Xa inhibition over the dosing interval and lower the peak-to-trough ratio for apixaban blood levels compared with once-daily dosing.

In addition to prevention of venous thromboembolism, apixaban is in Phase III trials studying the prevention of stroke and other thromboembolic events in patients with atrial fibrillation, the treatment of venous thromboembolism and in patients with acute coronary syndrome.

About the Bristol-Myers Squibb/Pfizer Collaboration

In 2007, Pfizer and Bristol-Myers Squibb entered into a worldwide collaboration to develop and commercialize apixaban, an investigational oral anticoagulant discovered by Bristol-Myers Squibb being studied for the prevention and treatment of a broad range of venous

and arterial thrombotic conditions. This global alliance combines Bristol-Myers Squibb's long-standing strengths in cardiovascular drug development and commercialization with Pfizer’s global scale and expertise in this field to maximize the potential benefits of apixaban for patients.

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information, please visit www.bms.com.

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the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2009, its Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise.

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This release contains forward-looking information about a product candidate, apixaban, including its potential benefits, that involves substantial risks and uncertainties. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development; decisions by regulatory authorities regarding whether and when to approve any drug applications that may be filed for apixaban as well as their decisions regarding labeling and other matters that could affect its availability or commercial potential; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer’s Annual Report on Form 10-K for the fiscal year ended December 31, 2009 and in its reports on Form 10-Q and Form 8-K.

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