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New AVERROES Data Demonstrate Investigational Apixaban Superior to Aspirin in Reducing Stroke and Systemic Embolism in Patients with Atrial Fibrillation Unsuitable for Warfarin Therapy

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(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE:BMY - News) and Pfizer Inc. (NYSE:PFE - News) today announced the publication of the full results of the AVERROES study of apixaban in *The New England Journal of Medicine.* Conducted in 36 countries, the study was coordinated by the Population Health Research Institute (PHRI) at McMaster University and at Hamilton Health Sciences in Canada. The study demonstrated that, for patients with atrial fibrillation (AF) who were expected or demonstrated to be unsuitable for a vitamin K antagonist (VKA) therapy such as warfarin, apixaban was statistically superior to aspirin in reducing the composite of stroke or systemic embolism, without a significant increase in major bleeding, fatal bleeding or intracranial bleeding. Importantly, there were no significant differences in the risk of hemorrhagic stroke between apixaban and aspirin. The study results also showed that apixaban demonstrated superiority for its secondary efficacy endpoint in reducing the composite of stroke, systemic embolism, myocardial infarction or vascular death for patients with AF when compared with aspirin.

Aspirin has remained a treatment option in patients for whom warfarin or other VKAs have been demonstrated or predicted to carry unacceptable bleeding risks. This study was designed to address whether a more favorable option might exist for this patient population.

Atrial fibrillation is the most common sustained cardiac arrhythmia, affecting approximately 5.1 million people in the U.S. and more than 6 million in Europe. [1, 2] The lifetime risk of AF is estimated to be approximately one in four for individuals 40 years of age or older.[3] The underlying threat of AF is the increased risk of stroke, which is five times higher in people with AF than those without AF. In fact, 15 percent of all strokes are attributable to AF in the U.S.[4]

Apixaban is an investigational, 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. Preliminary results of AVERROES were first presented in August 2010, at the European Society of Cardiology annual meeting in Stockholm, Sweden. Full results will also be presented today at the International Stroke Conference in Los Angeles.

“The risk of stroke or systemic embolism is of great concern for patients with atrial fibrillation, especially because AF-related strokes can be particularly devastating,” said Stuart Connolly, MD, professor of medicine at McMaster University in Hamilton, Canada, and lead investigator of the study. “We are encouraged by the AVERROES data, which demonstrated that apixaban is more effective than aspirin without a significantly increased risk of major bleeding. Given the significant number of patients who are not eligible for treatment with vitamin K antagonists, it is especially important to have potential new treatment options that are both safe and effective.”

About AVERROES

AVERROES (Apixaban Versus Acetylsalicylic Acid to Prevent Strokes), a randomized, double-blind, multicenter, head-to-head trial, included 5,599 patients with atrial fibrillation at risk for stroke who were expected or demonstrated to be unsuitable for therapy with a vitamin K antagonist such as warfarin. The mean CHADS2 risk score for the study population was 2.0. Patients were randomized to receive either apixaban 5mg twice daily or aspirin 81mg to 324mg once daily.

Apixaban demonstrated superiority ($P<0.001$) for the primary efficacy endpoint, composite of stroke or systemic embolism, compared with aspirin. The relative risk reduction was 55 percent with annual event rates of 1.6 percent for apixaban and 3.7 percent for aspirin in an intention to treat analysis.

The key secondary efficacy endpoint was defined as the composite of stroke, systemic embolism, myocardial infarction or vascular death. The relative risk reduction was 34 percent with annual event rates of 4.2 percent for apixaban and 6.4 percent for aspirin. There was also a statistically significant reduction in cardiovascular hospitalization for apixaban compared with aspirin (12.6 percent versus 15.9 percent, $P<0.001$).

Results from AVERROES also demonstrated that there were no significant differences in major bleeding, fatal bleeding or intracranial bleeding for apixaban compared with aspirin. The annual event rates for major bleeding were 1.4 percent for apixaban and 1.2 percent for aspirin, which was not statistically significant ($P=0.57$) in an intention to treat analysis; the event rates in an on-treatment analysis were 1.4 percent and 0.9 percent, respectively, also not statistically different ($P=0.07$).

In this study, apixaban had a significantly lower discontinuation rate than aspirin ($P=0.03$). There was also no evidence of hepatotoxicity associated with apixaban.

About Management of Atrial Fibrillation

In addition to treatments for heart rate and rhythm, treatment guidelines recommend that AF patients at high risk of stroke receive anticoagulation therapy with a vitamin K antagonist (VKA), such as warfarin.[5] However, surveys of practice patterns in developed countries demonstrate that 40 percent to 50 percent of patients with AF who are at moderate or high risk for stroke do not receive vitamin K antagonist.[6] The most common reason for not treating AF patients with a vitamin K antagonist appears to be concern about bleeding. Difficulties managing and maintaining therapeutic warfarin dosing, as well as the use of other prescription drugs that interfere with warfarin therapy are additional concerns.[6] Currently, guidelines for the management of patients with AF recommend the use of aspirin for those who cannot take VKA.[5]

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 3 trials, including AVERROES.

The AVERROES trial is one of two Phase 3 clinical trials exploring the efficacy and safety of apixaban for stroke prevention in patients with AF. The ongoing ARISTOTLE trial is investigating apixaban compared with warfarin in 18,206 patients with AF. Data from this trial are expected to be presented at a major medical meeting later this year.

In addition to prevention of stroke and other thromboembolic events in patients with atrial fibrillation, apixaban is in Phase 3 trials studying the prevention and treatment of venous thromboembolism.

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. 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.

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, or follow us on Twitter at http://twitter.com/bmsnews.

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At Pfizer, we apply science and our global resources to improve health and well-being at every stage of life. We strive to set the standard for quality, safety and value in the discovery, development and manufacturing of medicines for people and animals. Our diversified global health care portfolio includes human and animal biologic and small molecule medicines and vaccines, as well as nutritional products and many of the world's best-known consumer products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as the world's leading biopharmaceutical company, we also collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, Pfizer has worked to make a difference for all who rely on us. To learn more about our commitments, please visit us at www.pfizer.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. No forward-looking statement can be guaranteed. Among other risks, there can be no guarantee that apixaban will receive regulatory approval or, if approved, that it will become a commercially successful product. 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, 2009, in our Quarterly Reports on Form 10-Q and our 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.

PFIZER DISCLOSURE NOTICE:

The information contained in this release is as of February 10, 2011. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about potential indications for a product candidate, apixaban, including their potential benefits, that involves substantial risks and uncertainties. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet anticipated clinical trial completion dates and regulatory submission dates; decisions by regulatory authorities regarding whether and when to approve any drug applications that may be filed for such indications as well as their decisions regarding labeling and other matters that could affect their 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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