



# ELIQUIS® (apixaban) Demonstrates Consistent Reductions in Stroke and Systemic Embolism, Major Bleeding and Mortality Compared to Warfarin in Patients with Nonvalvular Atrial Fibrillation at Varying Risk for Stroke and Bleeding

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Subanalysis from Phase 3 ARISTOTLE Study Published Today in The Lancet

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(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE: BMY) and Pfizer Inc. (NYSE: PFE) today announced that the reductions in stroke or systemic embolism, major bleeding and mortality demonstrated with ELIQUIS® compared to warfarin in the ARISTOTLE trial were consistent across a wide range of stroke and bleeding risk scores in patients with nonvalvular atrial fibrillation. These results of a subanalysis from the ARISTOTLE clinical trial were published today in The Lancet.

Stroke and bleeding risk were based on the CHADS2, CHA2DS2VASc, and HAS-BLED scores, which are patient assessment tools used by physicians to help predict the risk of

stroke and of bleeding in patients with atrial fibrillation. Physicians can use these risk scores to help inform decisions regarding the selection of anticoagulation therapy.

The ARISTOTLE trial evaluated the efficacy and safety of ELIQUIS, an investigational compound for the prevention of stroke or systemic embolism in patients with nonvalvular atrial fibrillation, compared with warfarin. This subanalysis evaluated data from 18,201 patients in the ARISTOTLE trial, based on patients' risk of stroke (CHADS<sub>2</sub> 1, 2, or  $\geq 3$ , or CHA<sub>2</sub>DS<sub>2</sub>VASc 1, 2, or  $\geq 3$ ) or risk of bleeding (HAS-BLED 0-1, 2, or  $\geq 3$ ). Across prespecified and post-hoc analyses that evaluated CHADS<sub>2</sub>, CHA<sub>2</sub>DS<sub>2</sub>VASc, or HAS-BLED categories, this subanalysis demonstrated that irrespective of a patient's risk of stroke or bleeding, treatment with ELIQUIS resulted in a consistent reduction in stroke or systemic embolism and mortality, compared to warfarin. There were also consistently lower rates of major bleeding and of intracranial bleeding with ELIQUIS compared with warfarin across all evaluated CHADS<sub>2</sub>, CHA<sub>2</sub>DS<sub>2</sub>VASc, and HAS-BLED score categories. These findings are consistent with the primary results of the ARISTOTLE trial, which demonstrated that ELIQUIS, as compared with warfarin, significantly reduced the risk of stroke or systemic embolism, major bleeding, and mortality. In addition, results of this subanalysis showed that, in patients with nonvalvular atrial fibrillation, the reduction in intracranial bleeding with ELIQUIS compared to warfarin tended to be greater in patients who had the highest risk of bleeding (HAS-BLED score  $\geq 3$ ) than the reduction in patients with the lowest risk of bleeding (HAS-BLED score of 0-1).

"It's encouraging to see that the findings of ARISTOTLE are consistent across patients with atrial fibrillation and different risks of stroke and bleeding," said study lead author Dr. Renato Lopes of Duke University Medical Center in Durham, North Carolina. "These findings suggest that, due to the consistent benefit of apixaban versus warfarin, current risk-scoring systems for selecting anticoagulation therapy may be less relevant when using apixaban than they are for warfarin, at least for patients with CHADS<sub>2</sub> scores  $\geq 1$ ."

#### About ARISTOTLE

The ARISTOTLE study was designed to demonstrate the efficacy and safety of ELIQUIS versus warfarin for the prevention of stroke or systemic embolism. In ARISTOTLE, 18,201 patients were randomized (9,120 patients to ELIQUIS and 9,081 to warfarin). ARISTOTLE was an active-controlled, randomized, double-blind, multi-national trial in patients with nonvalvular atrial fibrillation or atrial flutter, and at least one additional risk factor for stroke. Patients were randomized to treatment with ELIQUIS 5 mg orally twice daily (or 2.5 mg twice daily in selected patients, representing 4.7 percent of all patients) or warfarin (target INR range 2.0-3.0), and followed for a median of 1.8 years.

## About Atrial Fibrillation

Atrial fibrillation is the most common cardiac arrhythmia (irregular heart beat). It is estimated that more than 5.8 million Americans and 6 million individuals in Europe have atrial fibrillation. The lifetime risk of developing atrial fibrillation is estimated to be approximately 25 percent for individuals 40 years of age or older. One of the most serious medical concerns for individuals with atrial fibrillation is the increased risk of stroke, which is five times higher in people with atrial fibrillation than those without atrial fibrillation. In fact, 15 percent of all strokes are attributable to atrial fibrillation in the U.S. Additionally, strokes due to atrial fibrillation are more burdensome than strokes due to other causes. Atrial fibrillation-related strokes are more severe than other strokes, with an associated 30-day mortality of 24 percent and a 50 percent likelihood of death within one year in patients who are not treated with an antithrombotic.

## About ELIQUIS

ELIQUIS is the approved trade name for apixaban in Europe and the proposed trade name in the U.S. ELIQUIS is not approved for the prevention of stroke or systemic embolism in patients with atrial fibrillation in any country. In May 2011, Bristol-Myers Squibb and Pfizer announced the first regulatory approval for ELIQUIS in the 27 countries of the European Union plus Iceland and Norway for the prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery.

The companies continue to progress the ELIQUIS application for stroke prevention in atrial fibrillation based on the ARISTOTLE and AVERROES studies. On September 21, 2012, Bristol-Myers Squibb and Pfizer Inc. announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending that ELIQUIS be granted approval for the prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation and with one or more risk factors for stroke. On September 26, 2012, The U.S. Food and Drug Administration (FDA) acknowledged receipt of the ELIQUIS (apixaban) New Drug Application (NDA) resubmission to reduce the risk of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation. The FDA has deemed the resubmission a complete response to its June 22, 2012 Complete Response Letter (CRL) that requested additional information on data management and verification from the ARISTOTLE trial. The FDA Prescription Drug User Fee Act (PDUFA) date is March 17, 2013.

ELIQUIS is also being investigated in Phase 3 trials for the treatment of VTE.

## About the Bristol-Myers Squibb/Pfizer Collaboration

In 2007, Pfizer and Bristol-Myers Squibb entered into a worldwide collaboration to develop and commercialize ELIQUIS, 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 <http://www.bms.com> or follow us on Twitter at <http://twitter.com/bmsnews>.

## Pfizer Inc.: Working together for a healthier world™

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 <http://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 for an indication in stroke

prevention in patients with atrial fibrillation. There is also no guarantee that, if approved in this indication, apixaban 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, 2011, 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 October 1, 2012. 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 various potential indications for ELIQUIS (apixaban), including their potential benefits, that involves substantial risks and uncertainties. Such risks and uncertainties include, among other things, (i) the uncertainties inherent in research and development; (ii) decisions by the U.S. Food and Drug Administration, the European Commission and regulatory authorities in other jurisdictions regarding whether and when to approve drug applications that have been or may be filed for such indications as well as their decisions regarding labeling and other matters that could affect the availability or commercial potential of such indications; and (iii) 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, 2011 and in its reports on Form 10-Q and Form 8-K.

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