U.S. FDA Approves Eliquis (apixaban) for the Treatment of Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE), and for the Reduction in the Risk of Recurrent DVT and PE Following Initial Therapy

- *Eliquis demonstrated noninferiority in the primary efficacy endpoint of recurrent symptomatic venous thromboembolism (VTE) or VTE related death versus enoxaparin/warfarin in the AMPLIFY trial*
- *Eliquis demonstrated superiority in the primary safety endpoint of major bleeding versus enoxaparin/warfarin in the AMPLIFY trial*

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Bristol-Myers Squibb Company (NYSE: BMY) and Pfizer Inc. (NYSE: PFE) today announced the U.S. Food and Drug Administration (FDA) has approved a Supplemental New Drug Application (sNDA) for *Eliquis* for the treatment of DVT and PE, and for the reduction in the risk of recurrent DVT and PE following initial therapy. Combined, DVT and PE are known as VTE. It is estimated that every year, approximately 900,000 Americans are affected by DVT and PE.

"We are pleased that *Eliquis* is now available as an effective treatment option for DVT and PE," said Douglas Manion, M.D., Head of Specialty Development, Bristol-Myers Squibb. "*Eliquis* offers oral dosing, no routine coagulation testing, and does not require the use of a parenteral anticoagulant or bridging during initiation."

"DVT, which may lead to PE, can be a serious medical condition, with PE requiring immediate medical attention for treatment. Once a VTE has occurred, approximately 33 percent of patients are at risk of a recurrence within 10 years," said Steve Romano, senior vice president, Head of Medicines Development Group for Global Innovative Pharmaceuticals, Pfizer Inc. "The Bristol-Myers Squibb and Pfizer alliance is committed to delivering important treatment options to patients and physicians."

The full Prescribing Information for *Eliquis* includes Boxed Warnings for the increased risk of thrombotic events in patients who prematurely discontinue *Eliquis*; and for the increased risk of epidural or spinal hematoma, which may cause long-term or permanent paralysis, in patients using *Eliquis* and undergoing spinal epidural anesthesia or spinal puncture.

Eliquis increases the risk of bleeding and can cause serious, potentially fatal, bleeding. Please see the complete Boxed Warnings and additional Important Safety Information in this press release.

The FDA approval of *Eliquis* for the treatment of DVT and PE, and for the reduction in the risk of recurrent DVT and PE following initial therapy, is based on data from the global AMPLIFY and AMPLIFY-EXT studies.

The AMPLIFY study, a randomized, double-blind trial, was designed to demonstrate the efficacy and safety of *Eliquis* for the treatment of DVT and PE, and included patients with confirmed symptomatic DVT or PE (2,609 for *Eliquis* and 2,635 for standard of care, which was initial enoxaparin treatment for at least five days, overlapped by warfarin therapy [International Normalized Ratio (INR) range 2.0-3.0] orally for six months).

In the AMPLIFY study, *Eliquis* 10 mg twice daily for one week followed by 5 mg twice daily for six months demonstrated efficacy comparable to standard of care in treating DVT and PE patients for the primary efficacy composite endpoint of recurrent, symptomatic VTE, or VTE-related death (2.3% vs. 2.7%, relative risk, 0.84; 95% confidence interval [CI], 0.60 to 1.18; P-value<0.0001 for noninferiority).

Eliquis demonstrated superiority in the primary safety endpoint of major bleeding versus standard of care (0.6% vs. 1.8%, relative risk 0.31; 95% CI, 0.17 to 0.55; P<0.0001 for superiority). Major bleeding was defined as clinically overt bleeding that was accompanied by one or more of the following: a decrease in the hemoglobin level of 2 g/dL or more; a transfusion of two or more units of packed red blood cells; bleeding that occurred in at least one of the following critical sites: intracranial, intraspinal, intraocular, pericardial, intra-articular, intramuscular with compartment syndrome, retroperitoneal; or bleeding that was fatal.

For the secondary safety endpoint in the AMPLIFY study, the event rates for clinically relevant nonmajor bleeding (CRNM) were fewer in *Eliquis*-treated patients compared to standard of care-treated patients (3.9% vs. 8.0%). CRNM was defined as overt bleeding that did not meet the criteria for major bleeding but was associated with a medical intervention, contact with a physician, interruption of the study drug, or discomfort or impairment in carrying out daily activities.

In AMPLIFY, the discontinuation rate due to bleeding events was 0.7% in the *Eliquis*-treated patients compared to 1.7% in enoxaparin/warfarin-treated patients.

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