Pfizer’s Bosutinib Receives Positive Opinion For Conditional Marketing Authorization From The Committee For Medicinal Products For Human Use For The Treatment Of Ph+ Chronic Myelogenous Leukemia With Resistance Or Intolerance To Prior Therapy In Europe

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--(BUSINESS WIRE)--Pfizer Inc. announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion regarding the conditional marketing authorization of bosutinib in the European Union (EU) for the treatment of adult patients with chronic phase (CP), accelerated phase (AP), and blast phase (BP) Philadelphia chromosome positive chronic myelogenous leukemia (Ph+ CML) previously treated with one or more tyrosine kinase inhibitor(s) (TKIs) and for whom imatinib, nilotinib and dasatinib are not considered appropriate treatment options.

The positive opinion for bosutinib was based on data from Study 200, a global, single-arm, open-label, multi-cohort, Phase 1/2 study of bosutinib in more than 500 patients

with Ph+ CML with separate cohorts for chronic, accelerated and blast phase disease previously treated with one or more prior TKIs.

Conditional approvals in the EU are granted to medicinal products with a positive benefit/risk assessment that address unmet medical needs and whose availability would result in a significant public health benefit.

CML accounts for 15 percent of all leukemia cases.1 Despite the availability of existing treatments for CML, there remains a need for additional treatment options. During the course of initial treatment some patients may never respond, may develop drug-resistant disease or may not be able to tolerate their therapy.2,3

"We are very pleased with this positive recommendation on bosutinib by the CHMP. We believe that bosutinib, if approved by the European Commission, would represent an important option for patients with CML who have progressed on prior treatment and are not candidates for alternative treatments. The development of bosutinib is evidence of our commitment to bringing meaningful new medicines to patients with hematologic cancers,"said Mace Rothenberg, MD, senior vice president of Clinical Development and Medical Affairs, Pfizer Oncology Business Unit. "We believe many doctors and CML patients will find this treatment, if approved, to be a welcome addition, offering a distinct adverse event profile and a convenient once-daily dosing regimen."

The CHMP's positive opinion will be reviewed by the European Commission, which has the authority to approve medicines for the EU. Pfizer anticipates a decision from the Commission in the coming months.

About Bosutinib

Bosutinib is an oral, once-daily, kinase inhibitor, which limits cancer cell growth by inhibiting the Abl and Src signaling pathways.4 Bosutinib was first approved as BOSULIF® in the United States (U.S.) in September 2012 for the treatment of adult patients with chronic, accelerated, or blast phase Ph+ CML with resistance, or intolerance to prior therapy. Bosutinib is an investigational agent under review in other markets.

Bosutinib (BOSULIF®) U.S. Important Safety Information

Contraindication: Hypersensitivity to BOSULIF. Anaphylactic shock occurred in less than 0.2% of treated patients.

Gastrointestinal Toxicity: Diarrhea, nausea, vomiting, and abdominal pain can occur. In the clinical trial, median time to onset for diarrhea was 2 days, median duration was 1

day, and median number of episodes per patient was 3 (range 1-221). Monitor and manage patients using standards of care, including antidiarrheals, antiemetics, and/or fluid replacement. Withhold, dose reduce, or discontinue BOSULIF as necessary.

Myelosuppression: Thrombocytopenia, anemia, and neutropenia can occur. A complete blood count should be performed weekly for the first month and then monthly or as clinically indicated. Withhold, dose reduce, or discontinue BOSULIF as necessary.

Hepatic Toxicity: Twenty percent of patients experienced an increase in either alanine aminotransferase (ALT) or aspartate aminotransferase (AST). Liver enzyme elevation usually occurs early in treatment. Perform monthly hepatic enzyme tests for the first 3 months and as clinically indicated. In patients with transaminase elevations, monitor liver enzymes more frequently. Drug-induced liver injury has occurred. Withhold, dose reduce, or discontinue BOSULIF as necessary.

Fluid Retention: Fluid retention can occur and may cause pericardial effusion, pleural effusion, pulmonary edema, and/or peripheral edema. Monitor and manage patients using standards of care. Interrupt, dose reduce, or discontinue BOSULIF as necessary.

Embryofetal Toxicity: BOSULIF may cause fetal harm when administered to a pregnant woman. Women of childbearing potential should be advised of potential hazard to the fetus and to avoid becoming pregnant while receiving BOSULIF.

Adverse Reactions: The most common adverse reactions observed in greater than 20% of patients in the Phase 1/2 safety population (N=546) were diarrhea, nausea, thrombocytopenia, vomiting, abdominal pain, rash, anemia, pyrexia, and fatigue.

The most common Grade 3/4 adverse reactions and laboratory abnormalities observed in greater than 10% of patients were thrombocytopenia, anemia, and neutropenia.

Drug Interactions: Avoid concurrent use with strong or moderate CYP3A inhibitors or inducers.

Proton Pump Inhibitors (PPIs): Consider using short-acting antacids or H2 blockers instead of PPIs. Separate antacid or H2 blocker dosing and BOSULIF dosing by more than 2 hours.

Substrates of P-glycoprotein: BOSULIF may increase the plasma concentrations of drugs that are P-gp substrates, such as digoxin.

Nursing Mothers: Given the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or BOSULIF.

Hepatic Impairment: Treat with a dose of 200 mg daily in patients with any baseline hepatic impairment.

For more information and full prescribing information, please visit www.BOSULIF.com.

About Pfizer Oncology

Pfizer Oncology is committed to the discovery, investigation and development of innovative treatment options to improve the outlook for cancer patients worldwide.

Hematologic cancers are a complex group of diseases, with over 70 different types of lymphomas, leukemias or myelomas. While there have been significant advancements in the treatment of some hematologic cancers, there continues to be a need for additional therapeutic options. Pfizer Oncology is committed to improving outcomes for patients living with hematologic malignancies like CML. Pfizer Oncology has a robust hematology pipeline, with biologics and small molecules in clinical development across a number of hematologic malignancies. We are advancing technologies as well as working to identify new and innovative options that address specific hematologic cancers, molecular subtypes, gene over-expression and mechanisms of resistance.

For more information, please visit www.Pfizer.com.

DISCLOSURE NOTICE: The information contained in this release is as of January 18, 2013. 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 that involves substantial risks and uncertainties about an oncology product candidate, bosutinib, including its potential benefits, that is under review by regulatory authorities in the EU and various other jurisdictions. Such risks and uncertainties include, among other things, whether and when the European Commission and regulatory authorities in such other jurisdictions will approve drug applications that have been or may be filed for bosutinib 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, 2011 and in its reports on Form 10-Q and Form 8-K.

1 Jabbour E et al. Targeted Therapy in Chronic Myeloid Leukemia. Expert Review of Anticancer Therapy. 2008; 8: 99-110.

2 Steegman J.L et al. Off-target effects of BCR-ABL1 inhibitors and their potential long-term implications in patients with chronic myeloid leukemia. Leukemia & Lymphoma. 2012; Early Online: 1-11.

3 Cortes J, Kantarjian H. Resistance in Chronic Myeloid Leukemia: Still an Issue? American Society of Clinical Oncology. 2011; 270-274.

4 Konig H. Effects of Dasatinib on Src Kinase Activity and Downstream Intracellular Signaling in Primitive Chronic Myelogenous Leukemia Hematopoietic Cells. Cancer Research. 2008; 68: 9624-9633.

Pfizer Inc. Media: Victoria Davis, (+1) 347-558-3455 or Investors: Jennifer Davis, (+1) 212-733-0717