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U.S. Food and Drug Administration Approves BOSULIF® (bosutinib) for Patients with Previously Treated Philadelphia Chromosome-Positive Chronic Myelogenous Leukemia (CML)

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Only Approval With Pivotal Trial That Included CML Patients Treated With Imatinib, Followed By Second Generation Tyrosine Kinase Inhibitor Third Pfizer Cancer Medicine Approved in the U.S. in Last 13 Months

"As the first therapy in our growing hematology portfolio to receive approval by the FDA, BOSULIF exemplifies Pfizer's commitment to bringing meaningful new medicines to patients with hematologic cancers,"

(BUSINESS WIRE)--Pfizer Inc. announced today the U.S. Food and Drug Administration (FDA) has approved BOSULIF® (bosutinib), an Abl and Src kinase inhibitor, for the treatment of adult patients with chronic, accelerated, or blast phase Philadelphia chromosome-positive (Ph+) chronic myelogenous leukemia (CML) with resistance, or intolerance to prior therapy. Patients in the registrational trial included patients who were previously treated with imatinib [Gleevec®] or imatinib plus at least one second generation tyrosine kinase inhibitor (TKI).[1] Once daily BOSULIF represents the only therapy approved with pivotal trial data that included CML patients treated with imatinib followed by a second generation TKI.

"BOSULIF is the third new medicine from Pfizer Oncology's pipeline to be approved by the FDA in just 13 months, a remarkable achievement that reflects our commitment to advancing the science in cancer drug development and delivering on Pfizer's innovative core," said Garry Nicholson, president and general manager, Pfizer Oncology Business Unit. "By focusing our pipeline on those compounds best positioned for advancement, we have been able to bring yet another important therapy to patients who urgently need it."

Chronic myelogenous leukemia is one of the four most common types of leukemia, with more than 5,000 new cases diagnosed per year in the United States.[2] Today, as many as 26,000 Americans are living with CML,[3] a number that is expected to increase tenfold by 2040.[4] While strides have been made in recent years, approximately one-third of patients receiving imatinib as initial therapy do not achieve an optimal response, and of those who ultimately require second generation TKIs, approximately half do not have a good outcome.[5]

"BOSULIF is an important new addition to the CML treatment landscape," said Dr. Jorge E. Cortes, deputy chair and professor of medicine in the Department of Leukemia at The University of Texas MD Anderson Cancer Center, and a lead investigator of the Pfizer-sponsored registrational study. "Despite recent advances, an unmet need remains for many CML patients who are refractory to one or more tyrosine kinase inhibitors."

“As the first therapy in our growing hematology portfolio to receive approval by the FDA, BOSULIF exemplifies Pfizer’s commitment to bringing meaningful new medicines to patients with hematologic cancers,” said Mace Rothenberg, vice president of Clinical Development and Medical Affairs, Pfizer Oncology Business Unit. “We believe many doctors and CML patients will find this treatment to be a welcome addition, offering a distinct adverse event profile and a convenient once-daily dosing regimen.”

BOSULIF is a kinase inhibitor that limits cancer cell growth by inhibiting the Abl and Src signaling pathways.[1,6] The recommended dose of BOSULIF is 500 mg, orally, taken once daily, with food.[1]

BOSULIF Clinical Data

Study 200 is a global, single-arm, open-label, multi-cohort, Phase 1/2 study of more than 500 patients with imatinib-resistant or –intolerant Ph+ CML with separate cohorts for chronic, accelerated and blast phase disease previously treated with one prior TKI (imatinib) or more than one TKI (imatinib followed by dasatinib and/or nilotinib).[1]

The major cytogenetic response (MCyR) at 24 weeks for patients with chronic phase CML who had been previously treated with imatinib only (n=266) was 33.8 percent (95% CI: 28.2, 39.9). With a minimum follow-up of 23 months, 53.4 percent of patients achieved a MCyR. Of patients who achieved MCyR, 52.8 percent had a MCyR lasting at least 18 months. The median duration of MCyR was not reached for these patients.[1]

The MCyR by 24 weeks for patients with chronic phase CML who had been treated with imatinib and at least one other TKI (n=108) was 26.9 percent (95% CI: 18.8, 36.2). With a minimum follow-up of 13 months, 32.4 percent of patients achieved a MCyR. Of patients who achieved MCyR, 51.4 percent had a MCyR lasting at least nine months. The median duration of MCyR was not reached for these patients.[1]

A low rate of transformation (4 percent, n=16) from the chronic phase to the advanced or blast phase was also observed in patients treated with BOSULIF.[1]

The most common all grade adverse reactions (ARs) observed in the chronic phase of Study 200 included diarrhea (84 percent), nausea (46 percent), abdominal pain (40 percent), thrombocytopenia (40 percent) and vomiting (37 percent). Grade 3/4 ARs included thrombocytopenia (26 percent), neutropenia (11 percent), diarrhea (9 percent), anemia (9 percent) and rash (8 percent).[1]

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

About Pfizer’s Patient Assistance Programs

Pfizer believes patients should have access to medications they need, and has established reimbursement support services and patient assistance programs for patients who qualify.

Pfizer is committed to helping patients prescribed BOSULIF gain access to the medication, and offers the Pfizer First Resource® Program to facilitate this process. The program can connect insured patients to reimbursement support services and information on how to obtain their medicines. For uninsured and underinsured patients, the program can provide eligible patients with free medicine. In addition to the Pfizer First Resource Program, we have also developed a co-pay assistance program for eligible privately-insured and cash-paying patients.

Patients can visit www.BOSULIF.com or call Pfizer First Resource® at 1-877-744-5675 to learn more.

BOSULIF (bosutinib) Indication and Important Safety Information

BOSULIF is indicated for the treatment of adult patients with chronic, accelerated, or blast phase Ph+ CML with resistance, or intolerance to prior therapy.

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

Gastrointestinal Toxicity: Diarrhea, nausea, vomiting and abdominal pain have been observed. Median time to onset for diarrhea was two days, median duration was one day and median number of episodes per patient was three. 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 have been observed. 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 ALT or AST. Liver enzyme elevation usually occurs early in treatment. Perform monthly hepatic enzyme tests for the first three 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 has been reported 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.

The most common adverse reactions observed in greater than 20 percent of the 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 percent of patients were thrombocytopenia, anemia and neutropenia.

Drug Interactions: Avoid concurrent use with strong or moderate CYP3A4 inhibitors or inducers.

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

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.

Gleevec® is a registered trademark of Novartis.

[1] BOSULIF® (bosutinib) Prescribing Information. New York, NY: Pfizer, Inc.; 2012.

[2] American Cancer Society. What is Chronic Myeloid Leukemia? http://www.cancer.org/Cancer/Leukemia-ChronicMyeloidCML/DetailedGuide/leukemia-chronic-myeloid-myelogenous-what-is-c-m-l. Accessed July 27, 2012.

[3] The Leukemia and Lymphoma Society. Chronic Myeloid Leukemia. http://www.lls.org/content/nationalcontent/resourcecenter/freeeducationmaterials/leukemia/pdf/cml.pdf. Accessed July 27, 2012.

[4] O'Hare T. Toward a Cure for Chronic Myeloid Leukemia. *Clinical Cancer Research.* 2008; 14: 7971-7974.

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

[6] 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.

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