Pfizer Announces Phase 3 Results of Investigational Compound Bosutinib in Patients With Newly Diagnosed Chronic Myeloid Leukemia

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Bosutinib Demonstrates Improvement Over Imatinib in Major Molecular Response Rate at One Year Despite Missing Primary Endpoint of Complete Cytogenetic Response Rate at One Year

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(BUSINESS WIRE)--Pfizer Inc. (NYSE: PFE) announced today that a significantly higher proportion of patients with newly diagnosed chronic myeloid leukemia who were treated with bosutinib (39 percent) experienced a major molecular response (MMR), a secondary endpoint, compared with patients treated with imatinib (26 percent) in the intent-to-treat (ITT) population (p=0.002). However, the study did not meet its primary endpoint of superior complete cytogenetic response (CCyR) rate at one year versus imatinib (70 percent vs. 68 percent, respectively, [p=0.601]), in the ITT population. These results are from a Phase 3 study of the investigational compound bosutinib as a first-line treatment in patients with Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML), called the Bosutinib Efficacy and safety in chronic myeloid LeukemiA [BELA] study. These

data were presented at an oral presentation at the 52nd Annual Meeting of the American Society of Hematology (ASH) (Abstract #208).(1)

Preliminary data show that fewer patients who took bosutinib progressed to an advanced phase of the disease (n=4, 1.6 percent) compared to patients treated with imatinib (n= 10, 4.0 percent), and there were fewer deaths in the bosutinib arm (n=4, 1.2 percent) than in the imatinib arm (n= 10, 3.2 percent). Patients responding to bosutinib achieved CCyR faster than those responding to imatinib (13 weeks vs. 25 weeks, $p<0.001$).(1)

A pre-specified exploratory analysis also showed that bosutinib produced a higher rate of CCyR at one year compared to imatinib when CCyR was assessed only in the evaluable patient population, 78 percent with bosutinib (n=219) compared to 69 percent with imatinib (n=241). The evaluable population was different from the ITT population in that it included only those patients who received follow-up assessments for efficacy.(1)

The most frequently reported all-grade drug-related adverse events with bosutinib were diarrhea (66 percent), nausea (27 percent), vomiting (25 percent), and rash (18 percent). The most frequent grade 3/4 adverse events with bosutinib included diarrhea (8 percent) and rash (2 percent), although no patients on the bosutinib arm discontinued therapy due to diarrhea. Gastrointestinal events associated with bosutinib had an early onset and usually subsided within the first four weeks of treatment. Most frequent grade 3/4 laboratory abnormalities with bosutinib included elevated ALT (21 percent), elevated AST (10 percent), and thrombocytopenia (7 percent).(1)

More patients on bosutinib experienced serious adverse events (25.4 percent vs. 13.5 percent) and adverse events leading to discontinuation (19.4 percent vs. 5.6 percent) than on imatinib. Adverse events leading to discontinuation were most frequently due to liver enzyme elevations in the bosutinib arm and neutropenia in the imatinib arm. There were no deaths in the study due to treatment-related adverse events. The majority of patients on both treatment arms continued on study treatment after a median follow-up of 14 months.(1)

"We are encouraged by these data, as they demonstrate early and meaningful response to bosutinib in patients with newly diagnosed CML. Given the length of time these patients are treated for CML, we need more therapeutic options to choose from since each patient is different and has different needs," said Dr. Carlo Gambacorti-Passerini, professor of internal medicine and director, clinical research unit, University of Milano Bicocca, San Gerardo Hospital, Monza, Italy, and a lead investigator of the BELA study. "Based on my experience with bosutinib, I feel it would be an important option for

patients with CML."

BELA Study Design and Other Key Studies at ASH

The BELA study is a global, open label, multicenter trial of 502 adult patients randomized to receive either bosutinib (n=250) or imatinib (n=252). The primary objective of the study was to compare the CCyR rate at one year between the bosutinib and imatinib arms in the ITT population. MMR rate at one year was a key secondary endpoint.(1) Although closed to enrollment, the study remains ongoing, and patients will continue to be followed for safety and efficacy outcomes.

Bosutinib is also being studied as a single agent in patients with previously treated chronic phase CML in an ongoing clinical trial with over 500 patients, known as Study 200. Interim results from a patient cohort of this study that have failed prior imatinib therapy and were resistant or intolerant to dasatinib or resistant to nilotinib are also being presented at the ASH annual meeting during an oral data presentation (Abstract #892, December 7).(2)

"Based on the totality of evidence from the bosutinib clinical development program, we are actively engaged in discussions with regulatory authorities which we hope will enable Pfizer to offer a new treatment option for patients with CML," said Dr. Mace Rothenberg, senior vice president of clinical development and medical affairs for Pfizer's Oncology Business Unit.

About Bosutinib

Bosutinib is an investigational oral dual Src and Abl kinase inhibitor.(1) It is believed that by dual inhibition of the Src and Abl tyrosine kinases, bosutinib may inhibit signaling in CML cells that allows the cells to grow, survive and reproduce.(3)

About Chronic Myeloid Leukemia

Chronic myeloid leukemia (CML), one of the four main types of leukemia,(4) accounts for 15 percent of all leukemias worldwide.(5) A hallmark of CML is an abnormal chromosome known as the Philadelphia Chromosome, a DNA mutation that initiates a series of events leading to the development of Bcr-Abl, a tyrosine kinase that causes CML cells to grow and reproduce rapidly.(6)

Response to treatment in CML can be assessed via cytogenetic or molecular markers. A complete cytogenetic response (CCyR) indicates no cells with the Philadelphia

chromosome can be found in the blood or bone marrow. A major molecular response (MMR) as measured by a polymerase chain reaction (PCR) test, means that the amount of Bcr-Abl in the blood is very low. A PCR test checks for the Bcr-Abl oncogene in leukemia cells in a blood or bone marrow sample and is sensitive enough to detect this oncogene even when doctors cannot identify the Philadelphia chromosome in bone marrow cells with cytogenetic testing.(6)

Pfizer's Commitment to Hematology

Pfizer Oncology is committed to developing therapies to treat a variety of hematologic malignancies in both adult and pediatric patient populations. Collectively, hematologic cancers represent the fifth most commonly occurring cancers and the second leading cause of cancer death. While there have been significant advancements in the treatment of hematologic cancers, there continues to be a need for new therapeutic approaches, both for newly diagnosed patients and relapsed patients. In order to deliver new options that target specific hematologic abnormalities and mutations, it is important to understand the molecular subtypes and genetic variations associated with hematologic cancers. Pfizer Oncology has biologics and small molecules in clinical development across a number of hematologic malignancies.

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. Our strong pipeline, one of the most robust in the industry, is studied with precise focus on identifying and translating the best scientific breakthroughs into clinical application for patients across a wide range of cancers. Pfizer Oncology has biologics and small molecules in clinical development and more than 100 clinical trials underway. By working collaboratively with academic institutions, individual researchers, cooperative research groups, governments, and licensing partners, Pfizer Oncology strives to cure or control cancer with breakthrough medicines, to deliver the right drug for each patient at the right time. For more information please visit www.Pfizer.com.

DISCLOSURE NOTICE: The information contained in this release is as of December 6, 2010. 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 certain potential indications for bosutinib, an oncology product candidate, including their potential benefits and potential

regulatory submissions for such indications, that involves substantial risks and uncertainties. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development, including with regard to the final results of Study 200; 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 the availability or commercial potential of such indications; and competitive developments.

A further list and 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.

(1) ASH Accepted Abstract #208. An Ongoing Phase 3 Study of Bosutinib (SKI-606) Versus Imatinib In Patients with Newly Diagnosed Chronic Phase Chronic Myeloid Leukemia. Oral Presentation. Carlo Gambacorti- Presenter. 52nd American Society of Hematology Annual Meeting. Orlando, FL. December 4-7, 2010.

(2) ASH Accepted Abstract #892. Bosutinib as Third-Line Treatment for Chronic Phase Chronic Myeloid Leukemia Following Failure of Second-Line Therapy with Dasatinib or Nilotinib. Oral Presentation. H. J. Khoury - Presenter. 52nd American Society of Hematology Annual Meeting. Orlando, FL. December 4-7, 2010.

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

(4) National Cancer Institute. What you need to know about leukemia – Types of Leukemia. Available here: http://www.cancer.gov/cancertopics/wyntk/leukemia/page3. Accessed November 16, 2010.

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

(6) American Cancer Society. Detailed Guide: Leukemia – Chronic Myeloid (Myelogenous). Available at: files\pressrelease_assets\pdf\003112-pdf.pdf. Accessed November 16, 2010.

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