BELA STUDY (BELA Bosutinib Efficacy and safety in chronic myeloid Leukemia): Bosutinib Compared to Imatinib in Subjects With Newly Diagnosed Chronic Phase Philadelphia Chromosome Positive Chronic Myeloid Leukemia (CML)

**INTRODUCTION**
- Chronic myeloid leukemia (CML), one of the four main types of leukemia, is a slow-growing blood cancer that starts in the blood-forming cells of bone marrow, the soft inner part of some bones.\(^1\) Once these cells are affected by leukemia, they do not go through their normal process of maturing.\(^2\)
- An abnormal chromosome, the Philadelphia chromosome, is a hallmark of CML. The Philadelphia chromosome initiates a series of events leading to the development of Bcr-Abl, a tyrosine kinase that causes CML cells to reproduce rapidly.\(^3\)
- Therapies such as imatinib,\(^4\) dasatinib\(^5\) and nilotinib\(^6\) target the inhibition of the Abl tyrosine kinase.
- The Src family of nonreceptor tyrosine kinases, which are located further downstream, have been identified as potential mediators of Bcr-Abl-induced leukemogenesis. Overexpression of the Src family of tyrosine kinases have been implicated in imatinib resistance and CML progression.\(^3\)
- Bosutinib is an investigational orally available dual Src and Abl kinase inhibitor with minimal inhibitory activity against c-kit and PDGFR.\(^7\)

**RATIONALE**
- Based on the results of an ongoing Phase 1/2 study in imatinib–resistant CML patients,\(^7\) Pfizer initiated the Phase 3 BELA study in subjects with newly diagnosed chronic phase Philadelphia chromosome positive (Ph+) CML.\(^8\)

**OBJECTIVES**
- **Primary:**\(^8\)
  - Complete cytogenetic response rate at one year of treatment
- **Select Secondary:**\(^8\)
  - Major molecular response rate at one year
  - Duration of complete cytogenetic response
  - Complete hematologic response and major molecular response
  - Time to transformation to accelerated and blast phases
  - Pharmacokinetics
  - Comparative safety

**STUDY DESIGN**
- Phase 3, open-label, randomized, active comparator (head-to-head) study\(^9\)
  - Arm A: Patients will receive bosutinib by mouth daily (500 mg)
  - Arm B: Patients will receive imatinib by mouth daily (400 mg)

**SELECTED ELIGIBILITY CRITERIA**
- **Selected Inclusion Criteria:**\(^9\)
  - Cytogenetic diagnosis of chronic phase Ph+ CML diagnosed less than six months
  - Ability to take oral tablets
  - Age greater than or equal to 18 years
- **Selected Exclusion Criteria:**\(^8\)
  - Philadelphia negative CML
  - Prior anti-leukemia treatment
  - Prior stem cell transplant

**NUMBER OF PATIENTS**
- The trial enrolled 502 patients from research sites in the United States and ex-U.S.
- This study is currently ongoing, but is closed to enrollment.

**RESULTS**
- Initial results of the ongoing Phase 3 BELA study in patients with newly diagnosed chronic phase Ph+ CML, were previously presented at the American Society of Hematology 2010 annual meeting.


