

COMPOUND DESCRIPTION	Bosutinib is an investigational orally available dual Src and Abl kinase inhibitor with minimal inhibitory activity against c-kit and PDGFR. ¹
ABOUT SRC-ABL KINASES	<p>The Philadelphia Chromosome, a hallmark abnormal chromosome of chronic myeloid leukemia (CML), initiates a series of events leading to the development of Bcr-Abl, a tyrosine kinase that causes CML cells to reproduce rapidly.² In some cases, CML develops resistance to therapies that focus strictly on the inhibition of the Bcr-Abl tyrosine kinase.³ Newer therapies target the inhibition of both Src and Abl tyrosine kinases to help overcome this resistance,⁴ as overexpression of the Src family of tyrosine kinases have been implicated in imatinib resistance and CML progression.²</p> <p>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.²</p>
CLINICAL STUDIES	<p>Bosutinib is being studied as both a single-agent and in combination across several tumor types. Following is a list of some of the ongoing bosutinib clinical trials:</p> <p><u>Chronic Myeloid Leukemia:</u></p> <p>Phase 3</p> <ul style="list-style-type: none"> • Randomized, open-label study of bosutinib versus imatinib in subjects with newly diagnosed chronic phase Philadelphia chromosome positive CML⁵ <p>Phase 1/2</p> <ul style="list-style-type: none"> • Bosutinib monotherapy in CML in patients resistant or intolerant to imatinib +/- other tyrosine kinase inhibitors⁶ <p><u>Breast Cancer:</u></p> <p>Phase 1/2</p> <ul style="list-style-type: none"> • Open-label study of bosutinib administered in combination with capecitabine in subjects with solid tumor and ErbB2 negative locally advanced or metastatic breast cancer⁷

For more information, please visit www.pfizerclinicaltrials.com or www.clinicaltrials.gov or call toll-free 1-877-369-9753 (in the United States and Canada) or +1-646-277-4066 (outside of the United States and Canada).

¹ Gambacorti-Passerini C et al. Bosutinib (SKI-606) Demonstrates Clinical Activity and is Well Tolerated in Patients with AP and BP CML and Ph+ ALL. Poster Presented at the American Society of Hematology Meeting, December 6-9, 2008, San Francisco, CA. Wyeth.

² 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.

³ Redaelli S. Activity of Bosutinib, Dasatinib, and Nilotinib Against 18 Imatinib-Resistant BCR/ABL Mutants. *Journal of Clinical Oncology*. 2008; 27: 1-3.

⁴ CenterWatch. Drug Information: Sprycel. CenterWatch. Available at: <http://www.centerwatch.com/drug-information/fda-approvals/drug-details.aspx?DrugID=903>. Accessed January 15, 2010.

⁵ ClinicalTrials.gov. Compare Bosutinib To Imatinib in Subjects with Newly Diagnosed Chronic Phase Philadelphia Chromosome Positive CML. 2010. Available at:

<http://www.clinicaltrials.gov/ct2/show/NCT00574873?term=bosutinib&rank=8>. Accessed January 15, 2010.

⁶ ClinicalTrials.gov. Study Evaluating SKI-606 in Philadelphia Chromosome Positive Leukemias. 2010. Available at: <http://www.clinicaltrials.gov/ct2/show/NCT00261846?term=bosutinib&phase=1&rank=7>. Accessed January 15, 2010.

⁷ ClinicalTrials.gov. Study of Bosutinib With Capecitabine in Solid Tumors and Locally Advanced or Metastatic Breast Cancer. 2010. Available at: <http://www.clinicaltrials.gov/ct2/show/NCT00959946?term=bosutinib&rank=5>. Accessed February 5, 2010.