PROFILE 1007: A Phase 3 Trial of Crizotinib (PF-02341066) Versus Standard Of Care In Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) With a Specific Alteration of the Anaplastic Lymphoma Kinase (ALK) Gene

Crizotinib (PF-02341066) is an investigational agent and has not been approved by regulatory agencies.

INTRODUCTION	• Crizotinib (PF-02341066) is a first-in-class oral compound that inhibits the anaplastic lymphoma kinase, or ALK, and is representative of Pfizer's personalized medicine approach to cancer treatment.[1] • Scientific advances have led to the identification of ALK as a new therapeutic target in cancer.[2] Originally discovered in anaplastic large cell lymphomas, alterations in the *ALK* gene have since been identified as an important factor in cancers such as NSCLC, neuroblastomas and rare sarcomas. [3] • These alterations lead to activation of the ALK fusion gene, believed to be a tumor-exclusive target that is a key driver of oncogenesis, or tumor development. When ALK is inhibited, important growth and survival pathways in tumor cells are blocked, which may lead to stabilization or regression of tumors.[3]
RATIONALE	• Based on the activity of crizotinib (PF-02341066) as demonstrated in a Phase 1 expanded cohort study,[1] Pfizer has initiated PROFILE 1007 to evaluate crizotinib (PF-02341066) compared to the standard of care chemotherapy in patients with previously treated *ALK*-positive advanced NSCLC, a disease with a significant unmet medical need.[4] o There is currently a five-year survival rate of less than 10 percent for NSCLC patients in the advanced setting.[5] o Approximately 3-5 percent of NSCLC tumors are *ALK*-positive.[3]
OBJECTIVES	• Primary: o Determine whether crizotinib (PF-02341066) prolongs progression-free survival (PFS) versus standard of care chemotherapy in NSCLC patients with an alteration in the *ALK* gene, who have failed one prior treatment with a platinum-based chemotherapy.[4] • Secondary:[4] o Objective response rate o Overall survival o Duration of response o Disease control rate o Safety and tolerability o Patient reported outcomes of lung cancer and health-related quality of life
STUDY DESIGN	• Phase 3, open-label, randomized, two-arm study:[4] o Arm A: Patients will receive oral crizotinib (PF-02341066) 250 mg twice daily on a continuous schedule o Arm B: Patients will receive either pemetrexed 500 mg/m2 by intravenous infusion on Day 1 of each 21-day cycle over 10 minutes or docetaxel 75 mg/m2by intravenous infusion on Day 1 of each 21-day cycle over one hour
SELECTED ELIGIBILITY CRITERIA	• Selected Inclusion Criteria o Histologically/cytologically confirmed diagnosis of NSCLC that is locally advanced or metastatic[4,6] o Positive for the *ALK* fusion gene (test performed by a central lab)[4]

	○ Disease progression after only one prior chemotherapy regimen that was platinum-based[4] ▪ Prior treatment with an EGFR tyrosine kinase inhibitor is acceptable; however, patients must have also received only 1 prior chemotherapy regimen that was platinum-based[6] ○ Measurable tumor(s)[4] ○ ECOG performance status score of 0 to 2[6] • Selected Exclusion Criteria ○ Prior *ALK*-directed therapy, including crizotinib (PF-02341066)[4] ○ Current treatment in another clinical trial[4]
NUMBER OF PATIENTS	• An estimated 318 patients will be enrolled from research sites in the United States and ex-U.S.[4]
PATIENT ENROLLMENT INFORMATION	For more information, contact the Pfizer Oncology Clinical Trial Information Services. • Contact options ○ Phone (US/Canada): 1-877-369-9753 ○ Phone (International): 1-646-277-4066 ○ E-mail: PfizerHPTrials@emergingmed.com ○ Website: www.pfizercancertrials.com

[1] Bang Y et al. Clinical Activity of the Oral ALK Inhibitor, Crizotinib (PF-02341066), in Patients with *ALK*-positive Non-Small Cell Lung Cancer. Accepted Plenary Presentation at the American Society of Clinical Oncology Annual Meeting, June 4-8, 2010. Chicago, IL.

[2] Horn L and Pao W. EML4-ALK:Honing in on a new target in non-small cell lung cancer. J Clin Oncol. Published online August 10, 2009.

[3] Chiarle R, Voena C, Ambrogio C et al. The anaplastic lymphoma kinase in the pathogenesis of cancer. Nat Rev Cancer. 2008;8(1): 11-23

[4] ClinicalTrials.gov. An Investigational Drug, PF-02341066 Is Being Studied Versus Standard Of Care in Patients With Advanced Non-Small Cell Lung Cancer With A Specific Gene Profile Involving The Anaplastic Lymphoma Kinase (ALK) Gene. 2010. Available at: http://clinicaltrials.gov/ct2/show/NCT00932893. Accessed April 2, 2010.

[5] American Cancer Society. Detailed Guide: Lung Cancer (Non-Small Cell). Available at: http://www.cancer.org/acs/groups/cid/documents/webcontent/003115-pdf.pdf. Accessed September 20, 2010.

[6] Data on file. Pfizer Inc. 2010.