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Pfizer’s Crizotinib Receives Positive Opinion For Conditional Marketing Authorization From The Committee For Medicinal Products For Human Use For The Treatment Of Adults With Previously Treated ALK-Positive Advanced Non-Small Cell Lung Cancer In The EU

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(BUSINESS WIRE)--Pfizer announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending that crizotinib be granted conditional marketing authorization in the European Union (EU), for the treatment of adults with previously treated anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC).

Similar to accelerated approvals in the United States, conditional marketing authorizations in the EU are granted to medicinal products with a positive benefit/risk assessment that address unmet medical needs and whose availability would result in a significant public health benefit. A conditional marketing authorization is renewable annually. If crizotinib is granted conditional marketing authorization, Pfizer will be required to submit data to the EMA from the recently completed PROFILE 1007 study, which the company announced in June met its primary endpoint in previously treated ALK-positive advanced NSCLC patients. Following review of the 1007 results by CHMP, the European Commission would then consider converting the conditional marketing authorization to a normal marketing authorization.

“The CHMP’s positive opinion brings us a step closer to potentially offering a new personalized treatment to patients with advanced NSCLC across Europe,” said Mace Rothenberg, MD, senior vice president of the clinical development and medical affairs for Pfizer’s Oncology Business Unit. “This achievement is made possible by our commitment to using knowledge of the underlying genetic drivers of diseases to identify patients most likely to benefit from treatment and to focus our clinical development program on those patients.”

The CHMP’s positive opinion will be reviewed by the European Commission, which has the authority to approve medicines for the European Union. Pfizer anticipates a decision from the Commission in the coming months.

Crizotinib is an oral, first-in-class, anaplastic lymphoma kinase (ALK) inhibitor. By inhibiting the ALK fusion protein, crizotinib blocks signaling in a number of cell pathways that are believed to be critical for the growth and survival of tumor cells, which may lead to growth inhibition or regression of tumors.[1,2]

About Crizotinib

Crizotinib is an investigational agent and has not been approved in the European Union. Crizotinib was first approved as XALKORI® in the U.S. in August 2011 for the treatment of locally advanced or metastatic NSCLC that is ALK-positive as detected by a Food and Drug Administration (FDA)-approved test. This indication is based on response rate. There are no data available demonstrating improvements in patient-reported outcomes or survival with XALKORI. XALKORI also has received approval in a number of other countries, including Switzerland, Canada, South Korea and Japan. Additional applications are under regulatory review in several countries worldwide.

Important XALKORI® (crizotinib) U.S. Safety Information[3]

Drug-induced hepatotoxicity with fatal outcome has occurred. Transaminase elevations generally occurred within the first 2 months of treatment. Monitor with liver function tests including Alanine Aminotransferase Test (ALT) and total bilirubin once a month and as clinically indicated, with more frequent repeat testing for increased liver transaminases, alkaline phosphatase, or total bilirubin in patients who develop transaminase elevations. Temporarily suspend, dose reduce, or permanently discontinue XALKORI as indicated.

XALKORI has been associated with severe, life-threatening, or fatal treatment-related pneumonitis in clinical trials with a frequency of 4 in 255 (1.6%) patients. All of these cases occurred within 2 months after the initiation of treatment. Monitor patients for pulmonary symptoms indicative of pneumonitis. Exclude other causes and permanently discontinue XALKORI in patients with treatment-related pneumonitis. QTc prolongation has been observed. Avoid use of XALKORI in patients with congenital long QT syndrome. Consider periodic monitoring with electrocardiograms (ECGs) and electrolytes in patients with congestive heart failure, bradyarrhythmias, electrolyte abnormalities, or who are taking medications that are known to prolong the QT interval. Permanently discontinue XALKORI for grade 4 QTc prolongation. XALKORI should be withheld for grade 3 QTc prolongation until recovery to ? grade 1. Permanently discontinue XALKORI if grade 3 QTc prolongation recurs.

Detection of ALK-positive NSCLC using an FDA-approved test, indicated for this use, is necessary for selection of patients for treatment with XALKORI.

XALKORI can cause fetal harm when administered to a pregnant woman based on its mechanism of action. Women of childbearing potential should be advised to avoid becoming pregnant while receiving XALKORI. If the patient or their partner becomes pregnant while taking this drug, apprise the patient of the potential hazard to the fetus.

Among the 397 patients for whom information on deaths and serious adverse reactions is available, deaths within 28 days of the last dose of study drug occurred in 45 patients. Ten (2.5%) patients died within 28 days of their first dose of study drug. Causes of death included disease progression (32 patients), respiratory events (9), and other (4).

Safety of XALKORI was evaluated in 255 patients with locally advanced or metastatic ALK-positive NSCLC in 2 single-arm clinical trials (Studies A and B). The most common adverse reactions (?25%) across both studies were vision disorder, nausea, diarrhea, vomiting, edema, and constipation. Grade 3-4 adverse reactions in ?4% of patients in both studies included ALT increased and neutropenia.

Vision disorders including visual impairment, photopsia, vision blurred, vitreous floaters, photophobia, and diplopia were reported in 159 (62%) patients in clinical trials. Consider ophthalmological evaluation, particularly if patients experience photopsia or experience new or increased vitreous floaters. Severe or worsening vitreous floaters and/or photopsia could also be signs of a retinal hole or pending retinal detachment. Advise patients to exercise caution when driving or operating machinery due to the risk of developing a vision disorder.

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 of biologics and small molecules, 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. 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 July 20, 2012. 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 that involves substantial risks and uncertainties about an oncology product candidate, crizotinib, including its potential benefits, that is under review by regulatory authorities in the EU and various other jurisdictions. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development; whether and when the European Commission and regulatory authorities in various other jurisdictions will approve drug applications that have been or may be filed for crizotinib as well as their decisions regarding labeling and other matters that could affect its availability or commercial potential; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2011 and in its reports on Form 10-Q and Form 8-K.

[1] 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.

[2] Zou HY, Li Q, Lee JH, et al. An orally available small-molecule inhibitor of c-MET, PF-2341066, exhibits cytoreductive antitumor efficacy through antiproliferative and antiangiogenic mechanisms. *Cancer Res.* 2007;67:4408-4417.

[3] XALKORI [Package Insert]. New York, NY: Pfizer, Inc. 2011.

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