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Pfizer Receives European Approval to Expand Use of XALKORI® (crizotinib) to First-Line Treatment of Adults with ALK-Positive Advanced Non-Small Cell Lung Cancer

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Pfizer Inc. (NYSE:PFE) today announced that the European Commission has approved a label update to expand use of XALKORI® (crizotinib) to first-line treatment of adults with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC). The Summary of Product Characteristics also has been updated to include efficacy data from PROFILE 1014, which demonstrated that XALKORI significantly prolonged progression-free survival (PFS) in previously untreated patients with ALK-positive advanced nonsquamous NSCLC when compared to standard platinum-based chemotherapy regimens.1

“The European Commission’s decision to approve XALKORI in the first-line setting reinforces XALKORI’s role as a standard of care for patients with ALK-positive advanced NSCLC,” said Andreas Penk, MD, regional president Oncology Europe, Africa and the Middle East, Head Greater China and Asia-Pacific Oncology Regions. “This milestone further underscores the importance of early and routine biomarker testing in patients with advanced NSCLC so that these patients can be identified and treated appropriately.”

The European Commission’s approval of XALKORI follows the positive opinion issued by the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency, and is supported by the results from PROFILE 1014, a Phase 3 global, randomized, open-label, two-arm study evaluating the efficacy and safety of XALKORI in patients previously untreated for ALK-positive advanced nonsquamous NSCLC.1

XALKORI was the first ALK inhibitor approved by regulatory authorities in the United States (U.S.), EU, China and Japan, and it is now approved in more than 85 countries. XALKORI is widely recognized as a standard of care for patients with ALK-positive advanced NSCLC. To date, more than 20,000 patients have been treated with XALKORI worldwide.2

XALKORI is an oral, ALK inhibitor.3 By inhibiting the ALK fusion protein, XALKORI 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.4,5

About Non-Small Cell Lung Cancer

Worldwide, lung cancer is the leading cause of cancer death in both men and women.6 NSCLC accounts for about 85 percent of lung cancer cases and remains difficult to treat, particularly in the metastatic setting.7 Approximately 57 percent of NSCLC patients are diagnosed late with metastatic, or advanced, disease where the five-year survival rate is only 5 percent.8

XALKORI® (crizotinib) Indication and Important Safety Information (as per U.S. Prescribing Information)

XALKORI is a kinase inhibitor indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

Hepatotoxicity: Drug-induced hepatotoxicity with fatal outcome occurred in 0.1% of patients treated with XALKORI across clinical trials (n=1669). Transaminase elevations generally occurred within the first 2 months. Monitor with liver function tests including ALT and total bilirubin every 2 weeks during the first 2 months of treatment, then 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. Permanently discontinue for ALT/AST elevation >3 times ULN with concurrent total bilirubin elevation >1.5 times ULN (in the absence of cholestasis or hemolysis); otherwise, temporarily suspend and dose-reduce XALKORI as indicated.

Interstitial Lung Disease (Pneumonitis): Severe, life-threatening, or fatal interstitial lung disease (ILD)/pneumonitis can occur. Across clinical trials (n=1669), 2.9% of XALKORI-treated patients had any grade ILD, 1.1% had Grade 3/4, and 0.5% had fatal ILD. These cases generally occurred within 3 months after initiation of treatment. Monitor for pulmonary symptoms indicative of ILD/pneumonitis. Exclude other potential causes and permanently discontinue XALKORI in patients with drug-related ILD/pneumonitis.

QT Interval Prolongation: QTc prolongation can occur. Across clinical trials (n=1560), 2.1% of patients had QTcF (corrected QT by the Fridericia method) ?500 ms and 5.0% had an increase from baseline QTcF ?60 ms by automated machine-read evaluation of ECG. Avoid use in patients with congenital long QT syndrome. Consider periodic monitoring with ECGs and electrolytes in patients with congestive heart failure, bradyarrhythmias, electrolyte abnormalities, or who are taking medications that prolong the QT interval. Permanently discontinue XALKORI in patients who develop QTc >500 ms or ?60 ms change from baseline with Torsade de pointes, polymorphic ventricular tachycardia, or signs/symptoms of serious arrhythmia. Withhold XALKORI in patients who develop QTc >500 ms on at least 2 separate ECGs until recovery to a QTc ?480 ms, then resume at a reduced dose.

Bradycardia: Symptomatic bradycardia can occur. Across clinical trials, bradycardia occurred in 12.3% of patients treated with XALKORI (N=1669). Avoid use in combination with other agents known to cause bradycardia. Monitor heart rate and blood pressure regularly. In cases of symptomatic bradycardia that is not life-threatening, hold XALKORI until recovery to asymptomatic bradycardia or to a heart rate of ?60 bpm, re-evaluate the use of concomitant medications, and adjust the dose of XALKORI. Permanently discontinue for life-threatening bradycardia due to XALKORI; however, if associated with concomitant medications known to cause bradycardia or hypotension, hold XALKORI until recovery to asymptomatic bradycardia or to a heart rate of ?60 bpm. If concomitant medications can be adjusted or discontinued, restart XALKORI at 250 mg once daily with frequent monitoring.

Severe Visual Loss: Across clinical trials, the incidence of Grade 4 visual field defect with vision loss was 0.2% (N=1669). Discontinue XALKORI in patients with new onset of severe visual loss (best corrected vision less than 20/200 in one or both eyes). Perform an ophthalmological evaluation. There is insufficient information to characterize the risks of resumption of XALKORI in patients with a severe visual loss; a decision to resume should consider the potential benefits to the patient.

Vision Disorders: Most commonly visual impairment, photopsia, blurred vision or vitreous floaters, occurred in 62% of 1669 patients. The majority (95%) of these patients had Grade 1 visual adverse reactions. 0.8% of patients had Grade 3 and 0.2% had Grade 4 visual impairment. The majority of patients on the XALKORI arms

in Studies 1 and 2 (>50%) reported visual disturbances which occurred at a frequency of 4-7 days each week, lasted up to 1 minute, and had mild or no impact on daily activities.

Embryofetal Toxicity: XALKORI can cause fetal harm when administered to a pregnant woman. Advise of the potential risk to the fetus. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment and for at least 45 days (females) or 90 days (males) respectively, following the final dose of XALKORI.

Adverse Reactions: Safety was evaluated in a phase 3 study in previously untreated patients with ALK-positive metastatic NSCLC randomized to XALKORI (n=171) or chemotherapy (n=169). Serious adverse events were reported in 34% of patients treated with XALKORI, the most frequent were dyspnea (4.1%) and pulmonary embolism (2.9%). Fatal adverse events in XALKORI-treated patients occurred in 2.3% of patients, consisting of septic shock, acute respiratory failure, and diabetic ketoacidosis. Common adverse reactions (all grades) occurring in ?25% and more commonly (?5%) in patients treated with XALKORI vs chemotherapy were vision disorder (71% vs 10%), diarrhea (61% vs 13%), edema (49% vs 12%), vomiting (46% vs 36%), constipation (43% vs 30%), upper respiratory infection (32% vs 12%), dysgeusia (26% vs 5%), and abdominal pain (26% vs 12%). Grade 3/4 reactions occurring at a ?2% higher incidence with XALKORI vs chemotherapy were QT prolongation (2% vs 0%), and constipation (2% vs 0%). In patients treated with XALKORI vs chemotherapy, the following occurred: elevation of ALT (any grade [79% vs 33%] or Grade 3/4 [15% vs 2%]); elevation of AST (any grade [66% vs 28%] or Grade 3/4 [8% vs 1%]); neutropenia (any grade [52% vs 59%] or Grade 3/4 [11% vs 16%]); lymphopenia (any grade [48% vs 53%] or Grade 3/4 [7% vs 13%]); hypophosphatemia (any grade [32% vs 21%] or Grade 3/4 [10% vs 6%]). In patients treated with XALKORI vs chemotherapy, renal cysts occurred (5% vs 1%). Nausea (56%) decreased appetite (30%), fatigue (29%), and neuropathy (21%) also occurred in patients taking XALKORI.

Drug Interactions: Exercise caution with concomitant use of moderate CYP3A inhibitors. Avoid grapefruit or grapefruit juice which may increase plasma concentrations of crizotinib. Avoid concomitant use of strong CYP3A inducers and inhibitors. Avoid concomitant use of CYP3A substrates with narrow therapeutic range in patients taking XALKORI. If concomitant use of CYP3A substrates with narrow therapeutic range is required in patients taking XALKORI, dose reductions of the CYP3A substrates may be required due to adverse reactions.

Lactation: Because of the potential for adverse reactions in breastfed infants, advise females not to breast feed during treatment with XALKORI and for 45 days after the final dose.

Hepatic Impairment: XALKORI has not been studied in patients with hepatic impairment. As crizotinib is extensively metabolized in the liver, hepatic impairment is likely to increase plasma crizotinib concentrations. Use caution in patients with hepatic impairment.

Renal Impairment: Administer XALKORI at a starting dose of 250 mg taken orally once daily in patients with severe renal impairment (CLcr <30 mL/min) not requiring dialysis. No starting dose adjustment is needed for patients with mild and moderate renal impairment.

For more information and full prescribing information visit www.XALKORI.com.

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 visitwww.pfizer.com.

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DISCLOSURE NOTICE: The information contained in this release is as of November 25, 2015. 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 XALKORI, including its potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of XALKORI; the uncertainties inherent in research and development, including the ability to meet anticipated clinical trial commencement and completion dates and regulatory submission dates, as well as the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; whether and when drug applications or supplemental drug applications may be filed with other jurisdictions for XALKORI for the first-line treatment of adults with ALK-positive advanced NSCLC; whether and when any other applications may be approved by other regulatory authorities, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of XALKORI; 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, 2014 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the SEC and available at www.sec.gov and www.pfizer.com.

1 Solomon B, Mok T, Dong-Wan K, et al. First-Line Crizotinib versus Chemotherapy in ALK-Positive Lung Cancer. N Engl J Med 2014; 371:2167-2177. DOI: 10.1056/NEJMoa1408440.

2 Pfizer data on file.

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4 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.

5 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.

6 The International Agency for Research on Cancer, the World Health Organization, GLOBOCAN 2012, Available at:http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx. Accessed October 15, 2015.

7 Reade CA, Ganti AK. EGFR targeted therapy in non-small cell lung cancer: potential role of cetuximab. Biologics. 2009; 3: 215 224.

8 National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Seer Stat Fact Sheets: Lung and Bronchus Cancer. http://seer.cancer.gov/statfacts/html/lungb.html. Accessed October 15, 2015.

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