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Pfizer Receives U.S. FDA Breakthrough Therapy Designation For XALKORI® (crizotinib) For The Treatment Of Patients With ROS1-Positive Non-Small Cell Lung Cancer

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Pfizer Inc. announced today that XALKORI® (crizotinib) received Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA) for the potential treatment of patients with ROS1-positive non-small cell lung cancer (NSCLC). Occurring in approximately one percent of NSCLC cases1, ROS1-positive NSCLC represents a particular molecular subgroup of NSCLC.2 XALKORI currently is approved in the U.S. for the treatment of patients with metastatic NSCLC whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

Enacted as part of the 2012 FDA Safety and Innovation Act (FDASIA), Breakthrough Therapy designation is intended to expedite the development and review of a potential new medicine if it is "intended to treat a serious or life-threatening disease and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies."3The Breakthrough Therapy designation is distinct from the FDA's other mechanisms to expedite drug development and review.4

"We are excited that the FDA has granted Breakthrough Therapy designation for XALKORI as a potential treatment for patients with ROS1-positive NSCLC," said Dr. Mace Rothenberg, senior vice president of Clinical Development and Medical Affairs and chief medical officer for Pfizer Oncology. "XALKORI pioneered precision medicine for ALK-positive metastatic NSCLC, and ROS1 represents a second molecular subgroup of NSCLC in which XALKORI has demonstrated a level of anti-tumor activity that can potentially make a real difference for patients."

Pfizer will work closely with the FDA on the development of XALKORI for ROS1-positive NSCLC and provide the information needed to support a potential regulatory submission.

The Breakthrough Therapy designation was based on a data analysis from an expansion cohort of a global Phase 1 study (Study 1001), which evaluated XALKORI in 50 patients with ROS1-positive advanced NSCLC. These data published in the November 20, 2014 issue of the *New England Journal of Medicine* demonstrated that XALKORI exhibited marked anti-tumor activity in patients with ROS1-positive advanced NSCLC.5 The safety profile of XALKORI in ROS1-rearranged advanced NSCLC was similar to that observed in patients with ALK-positive advanced NSCLC.5

About Non-Small Cell Lung Cancer

Lung cancer is the leading cause of cancer death worldwide.6 NSCLC accounts for about 85 percent of lung cancer cases and remains difficult to treat, particularly in the metastatic setting.7 Approximately 75 percent of NSCLC patients are diagnosed late with metastatic, or advanced, disease where the five-year survival rate is only 5 percent.7,8,9

About XALKORI® (crizotinib)

XALKORI is a kinase inhibitor indicated in the U.S. 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. XALKORI has received approval in more than 80 countries10 including Australia, Canada, China, Japan, South Korea and the European Union.

XALKORI® Important Safety Information

Hepatotoxicity: Across three main clinical trials fatal hepatotoxicity occurred in 0.2% of patients. Monitor with periodic liver testing. Temporarily suspend, dose reduce, or permanently discontinue XALKORI.

Pneumonitis: Across three main clinical trials interstitial lung disease (ILD)/pneumonitis occurred in 2% of patients. Permanently discontinue in patients with ILD/pneumonitis.

QT Interval Prolongation: Across three main clinical trials QT interval prolongation occurred in 2.7% of patients. Monitor with electrocardiograms and electrolytes in patients who have a history of or predisposition for QTc prolongation, or who are taking medications that prolong QT. Temporarily suspend, dose reduce, or permanently discontinue XALKORI.

Bradycardia: XALKORI can cause bradycardia. Across three main clinical trials 11% of patients experienced a heart rate of less than 50 beats per minute. Monitor heart rate and blood pressure regularly. Temporarily suspend, dose reduce, or permanently discontinue XALKORI.

Embryofetal Toxicity: XALKORI can cause fetal harm when administered to a pregnant woman. Women of childbearing potential should be advised to avoid becoming pregnant while receiving XALKORI.

Adverse Reactions: Across three main clinical trials the most common adverse reactions (?25%) were vision disorders, nausea, diarrhea, vomiting, constipation, edema, elevated transaminases, and fatigue.

In a phase 3 study in patients with previously treated ALK-positive metastatic NSCLC randomized to XALKORI (n=172) or chemotherapy (n=171), serious adverse reactions were reported in 37.2% of patients treated with XALKORI. The most frequent serious adverse reactions reported in patients treated with XALKORI were pneumonia (4.1%), pulmonary embolism (3.5%), dyspnea (2.3%), and ILD (2.9%). Fatal adverse reactions in XALKORI-treated patients occurred in 9 (5%) patients, consisting of: acute respiratory distress syndrome, arrhythmia, dyspnea, ILD, pneumonia, pneumonitis, pulmonary embolism, respiratory failure, and sepsis. Grade 3 or 4 events occurring at a higher incidence with XALKORI than with chemotherapy and at greater than 2%, were syncope (3%), QT prolongation (3%), and pulmonary embolism (5%). Elevation of ALT of any grade occurred in 76% of patients and grade 3 or 4 in 17% of patients. Neutropenia of any grade occurred in 49% of patients and grade 3 or 4 in 12% of patients. Lymphopenia of any grade occurred in 51% of patients and grade 3 or 4 in 9% of patients. Renal cysts occurred in 4% and neuropathy occurred in 19% of patients treated with 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. Dose reduction may be needed for co-administered drugs that are predominantly metabolized by CYP3A.

Nursing Mothers: Given the potential for serious adverse reactions in nursing infants, consider whether to discontinue nursing or discontinue XALKORI.

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, please 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 visit www.Pfizer.com.

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At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, Pfizer has worked to make a difference for all who rely on us. To learn more, please visit us at www.pfizer.com.

DISCLOSURE NOTICE: *The information contained in this release is as of April 21, 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 a potential new indication for XALKORI for the treatment of patients with ROS1-positive non-small cell lung cancer (the "Potential Indication"), 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, the uncertainties inherent in research and development, including, without limitation, the ability to meet 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 any applications may be filed with the FDA or other regulatory authorities for XALKORI for the Potential Indication; whether and when

regulatory authorities may approve any such applications, 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 for the Potential Indication; 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 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.

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1 Gainor JF, Shaw AT. Novel targets in non-small cell lung cancer: ROS1 and RET fusions. Oncologist 2013;18:865-75.
2 Bergethon K, Shaw AT, Ignatius Ou SH, et al. ROS1 Rearrangements Define a Unique Molecular Class of Lung Cancers. J Clin Oncol 2012;30:863-70.
3 U.S. Food and Drug Administration Safety and Innovation Act. Available at: http://www.gpo.gov/fdsys/pkg/PLAW-112publ144/pdf/PLAW-112publ144.pdf. Accessed March 16, 2015.
4 U.S. Food and Drug Administration Frequently Asked Questions: Breakthrough Therapies. Available at: http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendme
. Accessed March 16, 2015.
5 Shaw AT, Ou SI, Bang Y, et al. Crizotinib in ROS1-Rearranged Non–Small-Cell Lung Cancer. N Engl J Med 2014; 371:1963-1971.
6 The International Agency for Research on Cancer, the World Health Organization, GLOBOCAN 2008, Available at:http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx (select "Lung" from the drop-down menu). Accessed March 16, 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 Yang P, Allen MS, Aubry MC, et al. Clinical features of 5,628 primary lung cancer patients: experience at Mayo Clinic from 1997 to 2003. Chest. 2005;128(1):452–462.
9 American Cancer Society. Detailed Guide: Lung Cancer (Non-Small Cell). Available at: http://www.cancer.org/cancer/lungcancer-non-smallcell/detailedguide/non-small-cell-lung-cancer-survival-rates. Accessed March 16, 2015.
10 Pfizer data on file.

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