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U.S. Food And Drug Administration Approves Pfizer's XALKORI® (crizotinib) As First And Only Therapy Specifically For Patients With Locally Advanced Or Metastatic ALK-Positive Non-Small Cell Lung Cancer

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XALKORI Underscores Importance of Molecular Testing in NSCLC and Marks New Milestone in Personalized Medicine Significant Tumor Response Observed in Prospectively Identified Patient Population First New Drug Approved for Lung Cancer in the U.S. in More Than Six Years

"We strongly encourage lung cancer patients to talk to their oncologists about molecular tumor testing. By having a full understanding of the molecular biology of their tumor, patients and physicians can make well-informed treatment decisions."

(BUSINESS WIRE)--Pfizer Inc. announced today that the U.S. Food and Drug Administration (FDA) has approved XALKORI® (crizotinib) capsules, the first-ever therapy targeting anaplastic lymphoma kinase (ALK), for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) that is ALK-positive as detected by an FDA-approved test. The effectiveness of XALKORI is based on objective response rates (ORR) and, as XALKORI received accelerated approval from the FDA, Pfizer is conducting post-marketing clinical trials to further evaluate its clinical benefit.

"Overall, lung cancer is responsible for more deaths each year worldwide than any other type of cancer. XALKORI is an advance in the treatment of this devastating illness, providing a new therapeutic option for a subset of patients with the disease," said Ian Read, president and chief executive officer of Pfizer. "The acceleration, collaboration and critical focus of the XALKORI clinical development program reflect Pfizer's Precision Medicine approach to advancing our pipeline and strengthening our innovative core to deliver medicines that matter most."

Aligned with the FDA's latest guidance on targeted therapies and companion diagnostics, the Company worked closely with the FDA and partnered with Abbott Molecular's business in Pfizer's clinical studies to ensure the simultaneous review and approval of XALKORI along with a diagnostic test, Abbott Molecular's Vysis ALK Break Apart FISH Probe Kit, to identify presence of the ALK fusion gene. The simultaneous approval of XALKORI in parallel with Abbott Molecular's ALK FISH Test marks the first time a Pfizer oncology drug or any lung cancer medication was developed and approved in parallel with a diagnostic test.

XALKORI is available immediately through a number of specialty pharmacies. Patients prescribed XALKORI can call 1-877-744-5675 for assistance accessing the medication. For more information about the FDA-approved ALK test, call (855) TEST-ALK (837-8255).

“By truly understanding the underlying genetic drivers of NSCLC, such as ALK, we can select patients who are more likely to respond to treatment. XALKORI provides a model for how to approach future drug development and cancer care,” said Dr. Paul Bunn, professor of medicine and the James Dudley chair in cancer research at the University of Colorado, Denver. “XALKORI, the first new drug approved for lung cancer by the FDA in more than six years, represents a paradigm shift in NSCLC treatment, where we’re moving away from a one-size-fits-all approach to biomarker-based treatment decisions.”

In the clinical trials for XALKORI, the study design required patients’ tumors to prospectively test positive for the ALK fusion gene biomarker, increasing the likelihood of response to the treatment. This method, a first for a lung cancer therapy not yet on the market, allowed researchers to observe a strong efficacy signal in a selected patient population.[1] Preliminary epidemiology suggests that approximately 3-5 percent of NSCLC tumors are ALK-positive, translating to approximately 6,500 to 11,000 NSCLC patients in the U.S. each year.[2,3,4,5,6,7,8,9,10]

“XALKORI represents a new chapter in personalized therapy for lung cancer, enabling physicians to provide the right treatment for the right patient,” said Dr. Mace Rothenberg, senior vice president of clinical development and medical affairs for Pfizer’s Oncology Business Unit. “The development of XALKORI – from publication of the discovery of the ALK fusion gene in NSCLC to FDA approval in just four years - is a remarkable feat in the oncology world and reinforces the importance of collaboration among academic research, pharmaceutical, diagnostic and regulatory organizations.”

Using a targeted approach in the XALKORI registration trials, ORR of 50 and 61 percent were observed in patients with advanced ALK-positive NSCLC.[1]

“Today’s approval of XALKORI underscores the important role of molecular biomarkers in cancer treatment,” said Dr. Joan Schiller, president of National Lung Cancer Partnership and chief of Hematology/Oncology, University of Texas Southwestern Medical Center. “We strongly encourage lung cancer patients to talk to their oncologists about molecular tumor testing. By having a full understanding of the molecular biology of their tumor, patients and physicians can make well-informed treatment decisions.”

New Drug Applications for crizotinib have also been filed by Pfizer with the Japanese Ministry of Health, Labour and Welfare, the Korean Ministry of Health, the European Medicines Agency and the Swiss Agency for Therapeutic Products.

XALKORI Clinical Data

The FDA approval of XALKORI is based on data from 255 patients with locally advanced or metastatic ALK-positive NSCLC across 2 multi-center, single-arm studies, including a Phase 2 study (PROFILE 1005) and a Part 2 expansion cohort of a Phase 1 study (Study 1001).[1] The primary efficacy endpoint in both studies was Objective Response Rate (ORR) according to Response Evaluation Criteria in Solid Tumors (RECIST). Response was evaluated by the investigator. Duration of Response (DR) was also evaluated.[1]

In PROFILE 1005 (n=136), based on investigator assessments, the ORR was 50 percent, including one complete response and 67 partial responses.[1] The median duration of treatment was 22 weeks. Seventy-nine percent of objective tumor responses were achieved during the first 8 weeks of treatment. The median response duration was 41.9 weeks.[1]

In Study 1001 (n=119), based on investigator assessments, the ORR was 61 percent, including two complete responses and 69 partial responses.[1] The median duration of treatment was 32 weeks. Fifty-five percent of objective tumor responses were achieved during the first 8 weeks of treatment. The median response duration was 48.1 weeks.[1]

The most common adverse reactions (?25 percent) across both studies were vision disorder, nausea, diarrhea, vomiting, edema and constipation.[1] Grade 3 or 4 adverse reactions in at least 4 percent of patients in both studies included ALT increased and neutropenia.[1]

ABOUT XALKORI(®) (crizotinib) Phase 3 Clinical Trials

As part of its post-marketing requirements, Pfizer continues to evaluate XALKORI in confirmatory, randomized, open-label Phase 3 trials. PROFILE 1007 compares the efficacy and safety of XALKORI with standard of care chemotherapy (pemetrexed or docetaxel) in patients with previously treated advanced ALK-positive NSCLC.[11] Profile 1014 compares the efficacy and safety of XALKORI to pemetrexed/cisplatin or pemetrexed/carboplatin in previously untreated patients with advanced ALK-positive non-squamous NSCLC.[12]

About Non-Small Cell Lung Cancer

Worldwide, lung cancer is the leading cause of cancer death in both men and women.[10] NSCLC accounts for about 85 percent of lung cancer cases and remains difficult to treat, particularly in the metastatic setting.[13,14] Approximately 75 percent of NSCLC patients are diagnosed late with metastatic, or advanced, disease, where the five-year survival rate is only 6 percent.[15,16]

About Pfizer's Patient Assistance Programs

Pfizer is committed to helping eligible patients prescribed XALKORI gain access to the medication, and offers the Pfizer First Resource® Program to facilitate this process. The program will connect eligible insured patients to specialty pharmacies for reimbursement support services and to obtain their medicines. For uninsured and underinsured patients, the program will provide eligible patients with free medicine. We have also developed a co-pay assistance program for eligible privately-insured patients. Patients who need assistance should call First Resource to determine whether they qualify (1-877-744-5675), or visit www.XALKORI.com to learn more.

About XALKORI(®) (crizotinib)

XALKORI is a kinase inhibitor indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test. This indication is based on response rate. There are no data available demonstrating improvement in patient reported outcomes or survival with XALKORI.[1] 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 stabilization or regression of tumors.[17,18] Alterations in the ALK gene are believed to be a key driver of tumor development in cancers like NSCLC.[19] Although ALK is known to occur more frequently in patients with non-squamous cell carcinoma and histories of light or non-smoking, it has also been identified in smokers and in patients with squamous cell carcinoma histologies.[20] Alterations in the ALK gene can occur independent of age, gender, ethnicity and smoking history.[2]

XALKORI has also demonstrated inhibition of the c-MET receptor tyrosine kinase and is under investigation.[19]

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

Important XALKORI(®) (crizotinib) Safety Information[1]

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. Other causes of pneumonitis should be excluded. XALKORI should be permanently discontinued in patients with treatment-related pneumonitis.

Grade 3 or 4 ALT elevation was observed in 7% of patients in Study A and 4% of patients in Study B. Three patients from Study A (2%) and 1 patient from Study B (<1%) required permanent discontinuation from treatment. Liver function tests, including ALT and total bilirubin, should be monitored once a month and as clinically indicated, with more frequent repeat testing for grade 2-4 transaminase elevations. Temporarily suspend, dose reduce, or permanently discontinue XALKORI as indicated.

QT prolongation has been observed. XALKORI should be avoided in patients with congenital long QT syndrome. In patients with congestive heart failure, bradyarrhythmias, electrolyte abnormalities, or who are taking medications that are known to prolong the QT interval, periodic monitoring with electrocardiograms and electrolytes should be considered. 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, the patient should be apprised of the potential hazard to the fetus.

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 (perceived flashes of light), vision blurred, vitreous floaters, photophobia (sensitivity to bright light), and diplopia (seeing double) were experienced in 159 (62%) patients in clinical trials.

Ophthalmological evaluation should be considered, 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. Caution should be exercised when driving or operating machinery by patients who experience 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, 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. Pfizer Oncology has biologics and small molecules in clinical development and more than 100 clinical trials underway. 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 improve health and well-being at every stage of life. We strive to set the standard for quality, safety and value in the discovery, development and manufacturing of medicines for people and animals. Our diversified global health care portfolio includes human and animal biologic and small molecule medicines and vaccines, as well as nutritional products and many of the world's best-known consumer 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 the world's leading biopharmaceutical company, we also 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 about our commitments, please visit us at www.pfizer.com.

DISCLOSURE NOTICE: The information contained in this release is as of August 26, 2011. 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 (crizotinib), including its potential benefits, that involves substantial risks and uncertainties. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development, including further investigation as a c-MET receptor tyrosine kinase; decisions by regulatory authorities in the E.U., Japan, Korea and other jurisdictions regarding whether and when to 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, 2010 and in its reports on Form 10-Q and Form 8-K.

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