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# Pfizer Presents Overall Survival Data of XALKORI in Patients with ALK-Positive Advanced Non-Small Cell Lung Cancer

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Longest Ever Follow-up Reported for Patients with Advanced ALK-positive NSCLC

Pfizer Inc. (NYSE:PFE) today announced final overall survival (OS) data from the PROFILE 1014 trial examining XALKORI® (crizotinib) in previously untreated patients with ALK-positive advanced non-small cell lung cancer(NSCLC). After a median follow-up of 46 months, the median OS for patients randomized to XALKORI was not reached (95% CI: 45.8 months, not reached) and was 47.5 months for patients randomized to chemotherapy (95% CI: 32.2 months, not reached). Results indicated a numerical improvement in OS for patients treated with first-line XALKORI compared with chemotherapy, though this difference did not quite achieve statistical significance (HR=0.760 [95% CI: 0.548, 1.053]; p=0.0978). These data [Abstract #LBA50] were presented today at the 2017 European Society for Medical Oncology (ESMO) Congress in Madrid, Spain.

The majority (84%) of patients initially randomized to chemotherapy received XALKORI after they progressed and this likely affected the overall survival results. A pre-specified, exploratory statistical analysis, adjusting for the effects of crossover, determined that median OS would have been longer for patients randomized to XALKORI than for patients randomized to chemotherapy, if patients had not been allowed to cross over [HR: 0.346 (95% CI: 0.081, 0.718)].

“PROFILE 1014 has provided important new data for patients with non-small cell lung cancer," said Professor Tony Mok, Chair of Department of Clinical Oncology, The Chinese University of Hong Kong. "This is the first set of prospective data from a randomized Phase 3 study to report long-term survival outcomes for patients with ALK-positive non-small cell lung cancer. The longest survival outcomes were in patients who received two or more tyrosine kinase inhibitors, which provides insight into optimal treatment sequencing.”

Overall survival was a secondary endpoint of PROFILE 1014 and the threshold for statistical significance was p? 0.0247.1 PROFILE 1014 was a global, randomized, open-label, two-arm Phase 3 study that evaluated the efficacy and safety of XALKORI in patients with previously untreated ALK-positive advanced NSCLC. Progression-free survival (PFS) was the primary endpoint, and these results were previously published in *The New England Journal of Medicine (NEJM)*. There was a statistically significant improvement in PFS in the patients treated with XALKORI than with chemotherapy ($p<0.001$). A total of 343 patients were randomized into the trial, with approximately half of the patients in the XALKORI arm and the other half of the patients in the platinum doublet chemotherapy arm.

“XALKORI was the first biomarker-driven therapy for ALK-positive NSCLC and as such, dramatically changed the treatment paradigm for these patients. It remains the only ALK inhibitor with mature survival data from a

randomized Phase 3 trial. We are extremely proud of the impact XALKORI continues to make on patients' lives," said Mace Rothenberg, MD, chief development officer, Oncology, Pfizer Global Product Development.

The most commonly reported adverse events with XALKORI were vision disorder (71%), diarrhea (61%), nausea (56%) and edema (49%), and with chemotherapy, nausea (59%), fatigue (38%), vomiting (36%) and decreased appetite (34%). Most adverse events in both treatment groups were grade 1 or 2 in severity. Grade 3 or 4 elevations of aminotransferase levels occurred in 14% of patients in the XALKORI group and 2% of patients in the chemotherapy group, and these elevations were managed primarily with dose interruptions or dose reductions. Grade 3 or 4 neutropenia occurred in 11% and 15% of patients in the XALKORI and chemotherapy groups, respectively, with no cases of febrile neutropenia reported with XALKORI and two cases with chemotherapy.

**About Non-Small Cell Lung Cancer**

Lung cancer is the leading cause of cancer death worldwide.2 NSCLC accounts for about 85 percent of lung cancer cases and remains difficult-to-treat, particularly in the metastatic setting.3 Approximately 75 percent of NSCLC patients are diagnosed late with metastatic, or advanced, disease where the five-year survival rate is only 5 percent.3,4,5

**About XALKORI® (crizotinib)**

XALKORI is a tyrosine kinase inhibitor indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK) or ROS1-positive as detected by an FDA-approved test. XALKORI has received approval for patients with ALK-positive NSCLC in more than 90 countries6including Australia, Canada, China, Japan, South Korea and the European Union.

**XALKORI® Important Safety Information**

**Hepatotoxicity**: Drug-induced hepatotoxicity with fatal outcome occurred in 0.1% of patients treated with XALKORI across clinical trials (n=1719). Transaminase elevations generally occurred within the first 2 months. Monitor liver function tests, including ALT, AST, 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=1719), 2.9% of XALKORI-treated patients had any grade ILD, 1.0% had Grade 3/4, and 0.5% had fatal ILD. ILD 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=1616), 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 ECGs. Avoid use in patients with congenital long QT syndrome. Monitor 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 12.7% of patients treated with XALKORI (n=1719). 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=1719). 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 63.1% of 1719 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.

**Embryo-Fetal 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.

**ROS1-positive Metastatic NSCLC**: Safety was evaluated in 50 patients with ROS1-positive metastatic NSCLC from a single-arm study, and was generally consistent with the safety profile of XALKORI evaluated in patients with ALK-positive metastatic NSCLC. Vision disorders occurred in 92% of patients in the ROS1 study; 90% of patients had Grade 1 vision disorders and 2% had Grade 2.

**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%), esophagitis (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 breastfeed 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**: Decreases in estimated glomerular filtration rate occurred in patients treated with XALKORI. 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 pursuing innovative treatments that have a meaningful impact on those living with cancer. As a leader in oncology speeding cures and accessible breakthrough medicines to patients, Pfizer Oncology is helping to redefine life with cancer. Our strong pipeline of biologics, small molecules and immunotherapies, 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 its breakthrough medicines. Because Pfizer Oncology knows that success in oncology is not measured solely by the medicines you manufacture, but rather by the meaningful partnerships you make to have a more positive impact on people’s lives.

**Working together for a healthier world®**

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, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, YouTube, and like us on Facebook at Facebook.com/Pfizer.

*DISCLOSURE NOTICE: The information contained in this release is as of September 11, 2017. 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 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 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; uncertainties regarding the commercial impact of the final overall survival data from the PROFILE 1014 trial; 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, 2016 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 U.S. Securities and Exchange Commission and available at www.sec.gov (link is external) and www.pfizer.com.*

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1 Solomon B., Mok T. et al. First-Line Crizotinib versus Chemotherapy in ALK-Positive Lung Cancer. *N Engl J Med.* 2014; 371:2167-2177. December 4, 2014DOI: 10.1056/NEJMoa1408440.

2 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 October 31, 2014.

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

4 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

5 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 October 31, 2014.

6 Pfizer data on file.

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