Pfizer Presents Full Results from Phase 2 Study of Next-Generation Investigational ALK-Inhibitor Lorlatinib in ALK-Positive and ROS1-Positive Advanced Non-Small Cell Lung Cancer

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Strong, durable responses seen against lung tumors and brain metastases across multiple lines of therapy

Pfizer Inc. (NYSE:PFE) today announced full results from the Phase 2 clinical trial of the investigational, next-generation tyrosine kinase inhibitor lorlatinib that exhibited clinically meaningful activity against lung tumors and brain metastases in a range of patients with ALK-positive and ROS1-positive advanced non-small cell lung cancer (NSCLC), including those who were heavily pretreated. Further, side effects were generally manageable and primarily mild to moderate in severity. The results [Abstract #OA 05.06] were presented by Professor Benjamin Solomon, lead investigator and medical oncologist at Peter MacCallum Cancer Centre, Melbourne, Australia, today during an oral session at the International Association for the Study of Lung Cancer (IASLC) 18th World Conference on Lung Cancer (WCLC) in Yokohama, Japan. Pfizer will also present data from several other lung cancer clinical programs.

“The findings presented today suggest that lorlatinib, if approved, may represent an effective treatment option for patients with ALK-positive advanced non-small cell lung cancer across multiple lines of therapy. These are comprehensive data in non-small cell lung cancer patients previously treated with second-generation ALK inhibitors who currently have few available treatment options,” said Professor Benjamin Solomon, lead

investigator and medical oncologist at Peter MacCallum Cancer Centre, Melbourne, Australia. “Controlling brain metastases is very important to these patients and an especially challenging aspect of treating this disease. We saw excellent intracranial responses in all patient groups, including those who were heavily pretreated.”

“Lorlatinib is an extraordinary example of what can be achieved through translational research and precision medicine development. Recall that Xalkori (crizotinib) was the first drug approved for patients with ALK-positive and ROS1-positive NSCLC. By understanding the mutations that occurred in patients that rendered their tumors resistant to Xalkori and other ALK inhibitors, medicinal chemists working at Pfizer were able to design a molecule with the potential to overcome that resistance and inhibit ALK despite these mutations. We are very encouraged by the results of this Phase 2 trial that provide the first clinical evidence of the activity of lorlatinib in this setting,” said Mace Rothenberg, MD, chief development officer, Oncology, Pfizer Global Product Development.

The Phase 2 study examined the antitumor activity and safety of lorlatinib in 275 patients with or without asymptomatic, untreated or treated brain metastases. Patients were enrolled in six cohorts based on biomarker (ALK-positive or ROS1-positive) and prior therapy. The primary endpoints were objective response rate (ORR) and intracranial ORR (IC-ORR) confirmed by independent central review (ICR). Results by clinically relevant groups showed:

ALK-positive treatment-naïve: ORR was 90% (27/30; 95% CI: 74, 98) and IC-ORR was 75% (6/8; 95% CI: 35, 97). ALK-positive previously treated with crizotinib with or without chemotherapy: ORR was 69% (41/59; 95% CI: 56, 81) and IC-ORR was 68%(25/37; 95% CI: 50, 82). ALK-positive previously treated with a non-crizotinib ALK inhibitor with or without chemotherapy: ORR was 33% (9/27; 95% CI: 16, 54) and IC-ORR was 42% (5/12; 95% CI: 15, 72). ALK-positive previously treated with two or three prior ALK inhibitors with or without chemotherapy: ORR was 39% (43/111; 95% CI: 30, 49) and IC-ORR 48% (40/83; 95% CI: 37, 59). ROS1-positive regardless of prior treatment: ORR was 36% (17/47; 95% CI: 23, 52) and IC-ORR was 56% (14/25; 95% CI: 35, 76).
Lorlatinib was generally tolerable. Most adverse events were mild to moderate and were managed by dose reductions or delay or with standard medical therapy. There were no treatment-related deaths and a low (3%) rate of discontinuation due to drug-related adverse events. The most common adverse events were: hypercholesterolemia (81%), hypertriglyceridemia (60%), edema (43%), peripheral neuropathy (30%), weight increase (18%), cognitive effects (18%), mood effects (15%), fatigue (13%), diarrhea (11%), arthralgia (10%), and increased AST (10%).

The Phase 2 data will form the basis of discussions with global regulatory authorities, including the U.S. Food and Drug Administration. On April 26, 2017, the FDA granted Breakthrough Therapy designation for lorlatinib for the treatment of patients with ALK-positive metastatic NSCLC previously treated with one or more ALK inhibitors.

Pfizer Oncology continues to build on its heritage in biomarker-driven therapies by investigating novel targeted therapies and immunotherapy combination approaches aimed at addressing significant unmet needs for patients. In addition to the lorlatinib results, Pfizer will present data at the conference from studies examining its current and investigational lung cancer medicines:

Plasma genomic profiling and outcomes of patients with MET exon-14 altered NSCLC treated with crizotinib on PROFILE 1001 (Late-breaker oral presentation: Abstract #OA 12.06) First-line dacomitinib versus gefitinib in advanced non-small cell lung cancer with EGFR mutation subgroups (Oral presentation: Abstract #OA 05.01) Next-generation sequencing shows mechanisms of intrinsic resistance in ALK-positive NSCLC patients treated with crizotinib (Poster presentation: Abstract #P1.01-016) Dacomitinib versus gefitinib for first-line treatment of advanced EGFR NSCLC in Japanese patients (ARCHER 1050) (Poster presentation: Abstract #P3.01-072) Symptom impact of first-line dacomitinib versus gefitinib in EGFR-positive NSCLC: Results from a randomized phase 3 study (Poster presentation: Abstract #P3.01-012)

About Non-Small Cell Lung Cancer

Lung cancer is the leading cause of cancer death worldwide.1 NSCLC accounts for about 85 percent of lung cancer cases and remains difficult to treat, particularly in the metastatic setting.2 Approximately 75 percent of NSCLC patients are diagnosed late with metastatic or advanced disease where the five-year survival rate is only five percent.2,3,4

About Lorlatinib

Lorlatinib is an investigational next-generation ALK/ROS1 tyrosine kinase inhibitor that has been shown to be highly active in preclinical lung cancer models harboring chromosomal rearrangements of both ALK and ROS1. Lorlatinib was specifically designed to inhibit tumor mutations that drive resistance to other ALK inhibitors and to penetrate the blood brain barrier.

The Phase 3 CROWN study (NCT03052608) of lorlatinib began enrolling patients earlier this year. CROWN is an ongoing, open label, randomized, two-arm study comparing lorlatinib to crizotinib in the first-line treatment of patients with metastatic ALK-positive

NSCLC.

Lorlatinib is an investigational agent and has not received regulatory approval for any indication anywhere in the world.

About Dacomitinib

Dacomitinib is an investigational, second-generation, oral, once-daily, irreversible epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor. It has not received regulatory approval anywhere in the world.

About XALKORI® (crizotinib)

XALKORI is a tyrosine 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) or ROS1-positive as detected by an FDA-approved test. XALKORI has received approval for patients with ALK-positive NSCLC in more than 90 countries, including 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.

About the World Conference on Lung Cancer

The World Conference on Lung Cancer (WCLC) is the world's largest meeting dedicated to lung cancer and other thoracic malignancies, attracting over 6,000 researchers, physicians and specialists from more than 100 countries. The goal is to disseminate the latest scientific achievements; increase awareness, collaboration and understanding of lung cancer; and to help participants implement the latest developments across the globe. Organized under the theme of "Synergy to Conquer Lung Cancer," the conference will cover a wide range of disciplines and unveil several research studies and clinical trial results. For more information, visit http://wclc2017.iaslc.org/.

DISCLOSURE NOTICE: The information contained in this release is as of October 16, 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 an investigational oncology therapy, lorlatinib, 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; whether and when any new drug applications may be filed in any jurisdictions for lorlatinib; whether and when any such applications may be approved by 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 lorlatinib; 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 and www.pfizer.com .

1 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 13, 2017. 2 Reade CA, Ganti AK. EGFR targeted therapy in non-small cell lung cancer: potential role of cetuximab. Biologics. 2009; 3: 215–224. 3 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 4 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 13, 2017.

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