U.S., EU and Japan Health Authorities Accept Regulatory Submissions for Review of Pfizer's Third-Generation ALK Inhibitor Lorlatinib

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U.S. New Drug Application Granted FDA Priority Review

Pfizer Inc. (NYSE:PFE) today announced that the U.S. Food and Drug Administration (FDA) accepted and granted Priority Review to the company's New Drug Application for lorlatinib. Lorlatinib is an investigational, anaplastic lymphoma kinase (ALK) tyrosine kinase inhibitor (TKI) for the treatment of patients with ALK-positive metastatic non-small cell lung cancer (NSCLC), previously treated with one or more ALK TKIs. The European Medicines Agency and the Japan Pharmaceutical and Medical Devices Agency have also accepted marketing applications for the use of lorlatinib.

"Treatment resistance resulting in disease progression is a major challenge faced by patients with ALK-positive metastatic NSCLC. Lorlatinib was developed by Pfizer scientists with the specific goal of overcoming resistance to first- and second-generation ALK-targeted therapies," said Mace Rothenberg, MD, chief development officer, Oncology, Pfizer Global Product Development. "The encouraging results observed in a variety of patients previously treated with ALK inhibitors provides the basis for these applications."

The FDA grants Priority Review to medicines that may offer significant advances in treatment or may provide a treatment where no adequate therapy exists. In April 2017, lorlatinib received Breakthrough Therapy Designation from the FDA for patients with ALK-positive metastatic NSCLC previously treated with one or more ALK inhibitors.

The submissions are based on Phase 2 data from a Phase 1/2 clinical trial (NCT01970865) of lorlatinib, evaluating patients treated in distinct cohorts based on prior therapy. Full results from the Phase 2 portion of the trial were presented at the International Association for the Study of Lung Cancer (IASLC) 18th World Conference on Lung Cancer (WCLC) in October 2017.1

The Prescription Drug User Fee Act (PDUFA) goal date for a decision by the FDA is in August 2018.

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 five percent.2,4,5

ALK gene rearrangement is a genetic alteration that drives the development of lung cancer in some patients.6,7 Epidemiology studies suggest that approximately three to five percent of NSCLC tumors are ALK-positive.8

About Lorlatinib

Lorlatinib is an investigational TKI 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 for treatment-naïve patients with metastatic ALK-positive NSCLC.

Lorlatinib is an investigational agent and has not received regulatory approval anywhere in the world. A multi-center, open-label expanded access protocol (NCT03178071) is now open in the United States for lorlatinib, making it available for eligible adults with ALK-positive or ROS1-positive advanced NSCLC at select sites. More information can be found by visiting www.clinicaltrials.gov.

About Pfizer in Lung Cancer

Pfizer Oncology is committed to addressing the unmet needs of patients with lung cancer, the leading cause of cancer-related death worldwide and a particularly difficult-to-treat disease. Pfizer strives to address the diverse and evolving needs of patients with NSCLC by developing efficacious and tolerable therapies, including biomarker-driven therapies and immuno-oncology (IO) agents and combinations. By combining leading scientific insights with a patient-centric approach, Pfizer is continually advancing its work to match the right patient with the right medicine at the right time. Through our growing research pipeline and collaboration efforts, we are committed to delivering renewed hope to patients living with NSCLC.

About Pfizer Oncology

Pfizer Oncology is committed to pursuing innovative treatments that have a meaningful impact on people living with cancer. Our growing pipeline of biologics, small molecules, and immunotherapies is focused on identifying and translating the best scientific breakthroughs into clinical application for patients across a diverse array of solid tumors and hematologic cancers. Today, we have 10 approved oncology medicines and 17 assets currently in clinical development. By maximizing our internal scientific resources and collaborating with other companies, government and academic institutions, as well as non-profit and professional organizations, we are bringing together the brightest and most enterprising minds to take on the toughest cancers. Together we can accelerate breakthrough treatments to patients around the world and work to redefine life with cancer.

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

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DISCLOSURE NOTICE: The information contained in this release is as of February 12, 2018. 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 product candidate, lorlatinib, and Pfizer Oncology, including their 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 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; the risk that clinical trial data are subject to differing interpretations, and, even when we view data as sufficient to support the safety and/or effectiveness of a product candidate, regulatory authorities may not share our views and may require additional data or may deny approval altogether; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when new drug applications may be filed in any other jurisdictions for lorlatinib; whether and when the applications for lorlatinib pending with the FDA, the European Medicines Agency and the Japan Pharmaceutical and Medical Devices Agency or 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, and, if approved, whether lorlatinib will be commercially successful; 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 Solomon B., et al. Phase 2 Study of Lorlatinib in Patients with Advanced ALK+ /ROS1+ Non-Small-Cell Lung Cancer. As presented at the International Association for the Study of Lung Cancer (IASLC) 18th World Conference on Lung Cancer. October 16, 2017. Abstract #OA 05.06.

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 February 2018.

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 February 2018.

6 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.

7 Guérin A, Sasane M, Zhang J et al. ALK rearrangement testing and treatment patterns for patients with ALK-positive non-small cell lung cancer. Cancer Epidemiol. 2015 Jun; 39(3): 307-12. doi: 10.1016.

8 Garber K. ALK, lung cancer, and personalized therapy: portent of the future? J Natl Cancer Inst. 2010;102:672-675.

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