



Pfizer's Next-Generation ALK/ROS1 Inhibitor, Lorlatinib, Granted Breakthrough Therapy Designation from FDA for ALK-Positive Metastatic Non-Small Cell Lung Cancer

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Pfizer Inc. today announced that its investigational next-generation ALK/ROS1 tyrosine kinase inhibitor, lorlatinib, was granted Breakthrough Therapy designation from the U.S. Food and Drug Administration (FDA) for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC), previously treated with one or more ALK inhibitors.

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.¹ The Breakthrough Therapy designation is distinct from the FDA's other mechanisms to expedite drug development and review.² ALK gene rearrangement is a genetic alteration that drives the development of lung cancer in some patients. ^{3,4} Due to additional mutations that the tumor may acquire during treatment, disease progression remains a challenge in patients with ALK-positive metastatic NSCLC.⁵

"This regulatory designation recognizes the potential for lorlatinib to provide an important treatment option for patients with ALK-positive NSCLC whose cancers have progressed despite treatment. Pfizer's rapid development of lorlatinib reflects a commitment to developing biomarker-driven therapies to meet the evolving needs of

patients,” said Mace Rothenberg, MD, chief development officer, Oncology, Pfizer Global Product Development. “We look forward to working with the FDA to accelerate the development of this therapy.”

The Breakthrough Therapy designation is supported by the efficacy and safety data of an ongoing Phase 1/2 clinical trial of lorlatinib, which includes patients with ALK-positive NSCLC who were previously treated with one or more ALK inhibitors.

Additionally, the Phase 3 CROWN study (NCT03052608) recently began enrolling patients. 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. Please visit clinicaltrials.gov for more information on this study.

About Non-Small Cell Lung Cancer

Worldwide, lung cancer is the leading cause of cancer death in both men and women.⁶ NSCLC accounts for about 85 percent of lung cancer cases and remains difficult to treat, particularly in the metastatic setting.⁷ Approximately 57 percent of NSCLC patients are diagnosed late with metastatic, or advanced, disease where the five-year survival rate is only 5 percent.⁸ NSCLC can be further categorized into distinct subsets that are classified by a number of factors, including histology and the molecular makeup of the tumor. Epidemiology studies suggest that approximately 3 to 5 percent of NSCLC tumors are ALK-positive.⁹

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

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.

Pfizer Inc.: 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 @PfizerNews, LinkedIn, YouTube and like us on Facebook at [Facebook.com/Pfizer](https://www.facebook.com/Pfizer).

DISCLOSURE NOTICE: The information contained in this release is as of April 27, 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 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 April 26, 2017.

2 U.S. Food and Drug Administration Frequently Asked Questions: Breakthrough Therapies. Available at: <http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCA>. Accessed March 16, 2015.

3 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.

4 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

5 Gainor et al. Molecular Mechanisms of Resistance to First- and Second-Generation ALK Inhibitors in ALK-Rearranged Lung Cancer. *Cancer Discovery*. 2016; 6(10): 1118-33.

6 The International Agency for Research on Cancer, the World Health Organization, GLOBOCAN 2012, Available at: http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx. Accessed October 15, 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 National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Seer Stat Fact Sheets: Lung and Bronchus Cancer.

<http://seer.cancer.gov/statfacts/html/lungb.html>. Accessed October 15, 2015.

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

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