



# Pfizer And Merck To Collaborate On Study Evaluating Novel Anti-Cancer Combination Regimen

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Agreement to Combine Merck's Investigational Anti-PD-1 Antibody Pembrolizumab and Pfizer's Crizotinib (XALKORI®) in Clinical Trial

Pfizer Inc. (NYSE:PFE) and Merck & Co. Inc. (NYSE: MRK), known as MSD outside the United States and Canada, through a subsidiary, announced today that they have entered into an agreement to explore the therapeutic potential of the combination of Pfizer's crizotinib (XALKORI®) with Merck's investigational anti-PD-1 antibody pembrolizumab, in a Phase 1b clinical study evaluating the safety and tolerability of the combination in patients with ALK-positive advanced or metastatic non-small cell lung cancer (NSCLC). The financial terms of the agreement were not disclosed.

"This collaboration between Pfizer and Merck is just one example of the willingness of sponsors to work together in an effort to accelerate progress against some of the most difficult-to-treat cancers," said Dr. Mace Rothenberg, senior vice president of Clinical Development and Medical Affairs and chief medical officer for Pfizer Oncology.

"Understanding the effects of combining one drug, XALKORI, which inhibits an abnormally activated enzyme in patients with ALK-positive metastatic lung cancer, with the investigational drug, pembrolizumab, which harnesses the body's immune system to fight

cancer, is vital if we are to continue to advance the care of lung cancer patients.”

This multi-center, open-label clinical study is expected to begin in 2015. Pfizer will conduct the study.

“We are pleased to build upon our ongoing collaboration with Pfizer to evaluate potential combination regimens incorporating Merck’s investigational immunotherapy pembrolizumab,” said Dr. Eric Rubin, vice president, Oncology, Merck Research Laboratories. “Evidence from early studies of pembrolizumab monotherapy together with XALKORI’s proven targeted therapeutic approach provides the scientific rationale for evaluating this combination for the treatment of lung cancer.”

Both companies previously announced plans to evaluate the safety and efficacy of pembrolizumab in combination with Pfizer’s small molecule kinase inhibitor axitinib (INLYTA®) in patients with renal cell carcinoma. Separately, pembrolizumab plus Pfizer’s PF-05082566 (PF-2566), an investigational immuno-oncology agent that targets the human 4-1BB receptor, will be evaluated in multiple cancer types. These studies are expected to begin enrollment later this year.

### **About Pembrolizumab**

Pembrolizumab (MK-3475) is an investigational, humanized, monoclonal antibody against PD-1 designed to reactivate anti-tumor immunity. Pembrolizumab exerts dual ligand blockade of the PD-1 pathway by inhibiting the interaction of PD-1 on T cells with its ligands PD-L1 and PD-L2.

Pembrolizumab is currently being evaluated across more than 30 types of cancers, as monotherapy and in combination. It is anticipated that by the end of 2014, the pembrolizumab development program will grow to more than 24 clinical trials, enrolling an estimated 6,000 patients at nearly 300 clinical trial sites worldwide. For information about Merck’s oncology clinical studies, please visit <http://www.merck.com/clinical->

trials/index.html.

## **XALKORI® (crizotinib) Indication and Important Safety Information**

XALKORI is a kinase inhibitor indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

**Hepatotoxicity:** Across three main clinical trials fatal hepatotoxicity occurred in 0.2% of patients. Monitor with periodic liver testing. Temporarily suspend, dose reduce, or permanently discontinue XALKORI.

**Pneumonitis:** Across three main clinical trials interstitial lung disease (ILD)/pneumonitis occurred in 2% of patients. Permanently discontinue in patients with ILD/pneumonitis.

**QT Interval Prolongation:** Across three main clinical trials QT interval prolongation occurred in 2.7% of patients. Monitor with electrocardiograms and electrolytes in patients who have a history of or predisposition for QTc prolongation, or who are taking medications that prolong QT. Temporarily suspend, dose reduce, or permanently discontinue XALKORI.

**Bradycardia:** Xalkori can cause bradycardia. Across three main clinical trials 11% of patients experienced a heart rate of less than 50 beats per minute. Monitor heart rate and blood pressure regularly. Temporarily suspend, dose reduce, or permanently discontinue XALKORI.

**Embryofetal Toxicity:** XALKORI can cause fetal harm when administered to a pregnant woman. Women of childbearing potential should be advised to avoid becoming pregnant while receiving XALKORI.

**Adverse Reactions:** Across three main clinical trials the most common adverse reactions ( $\geq 25\%$ ) were vision disorders, nausea, diarrhea, vomiting, constipation, edema, elevated transaminases, and fatigue.

In a phase 3 study in patients with ALK-positive metastatic NSCLC randomized to XALKORI (n=172) or chemotherapy (n=171), serious adverse reactions were reported in 37.2% of patients treated with XALKORI. The most frequent serious adverse reactions reported in patients treated with XALKORI were pneumonia (4.1%), pulmonary embolism (3.5%), dyspnea (2.3%), and ILD (2.9%). Fatal adverse reactions in XALKORI-treated patients occurred in 9 (5%) patients, consisting of: acute respiratory distress syndrome, arrhythmia, dyspnea, ILD, pneumonia, pneumonitis, pulmonary embolism, respiratory failure, and sepsis. Grade 3 or 4 events occurring at a higher incidence with XALKORI than with chemotherapy and at greater than 2%, were syncope (3%), QT prolongation (3%), and pulmonary embolism (5%). Elevation of ALT of any grade occurred in 76% of patients and grade 3 or 4 in 17% of patients. Neutropenia of any grade occurred in 49% of patients and grade 3 or 4 in 12% of patients. Lymphopenia of any grade occurred in 51% of patients and grade 3 or 4 in 9% of patients. Renal cysts occurred in 4% and neuropathy occurred in 19% of patients treated with 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. Dose reduction may be needed for co-administered drugs that are predominantly metabolized by CYP3A.

**Nursing Mothers:** Given the potential for serious adverse reactions in nursing infants, consider whether to discontinue nursing or discontinue XALKORI.

**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: Administer XALKORI at a starting dose of 250 mg taken orally once daily in patients with severe renal impairment ( $CL_{cr} < 30$  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](http://www.XALKORI.com).

### **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 of biologics and small molecules, 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 breakthrough medicines, to deliver the right drug for each patient at the right time. For more information, please visit [www.Pfizer.com](http://www.Pfizer.com).

### **About Merck Oncology**

At Merck Oncology, our goal is to translate breakthrough science into biomedical innovations to help people with cancer worldwide. Harnessing immune mechanisms to fight cancer is the priority focus of our oncology research and development program. The Company is advancing a pipeline of immunotherapy candidates and combination regimens. Cancer is one of the world's most urgent unmet medical needs. Helping to empower people to fight cancer is our passion. For information about Merck's commitment to Oncology visit the Oncology Information Center at <http://www.mercknewsroom.com/oncology-infocenter>.

## **About Merck**

Today's Merck is a global healthcare leader working to help the world be well. Merck is known as MSD outside the United States and Canada. Through our prescription medicines, vaccines, biologic therapies, and consumer care and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to healthcare through far-reaching policies, programs and partnerships. For more information, visit [www.merck.com](http://www.merck.com) and connect with us on Twitter, Facebook and YouTube.

## **PFIZER DISCLOSURE NOTICE**

*The information contained in this release is as of August 26, 2014. 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 agreement between Pfizer and Merck to study the anti-cancer therapeutic potential of Pfizer's XALKORI in combination with Merck's investigational anti-PD-1 antibody pembrolizumab (MK-3475), as well as agreements entered into earlier this year between Pfizer and Merck to study the anti-cancer therapeutic potential of Pfizer's INLYTA (axitinib) and PF-2566 in combination with Merck's pembrolizumab, 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 study commencement and completion dates as well as the possibility of unfavorable study results; whether and when drug applications may be filed in any jurisdictions for any of the combination therapies; whether and when any such applications may be approved by regulatory authorities, as well as their decisions regarding labeling and other matters that could affect the availability or commercial potential of any of the combination therapies; 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, 2013 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the SEC and available at [www.sec.gov](http://www.sec.gov) and [www.pfizer.com](http://www.pfizer.com).*

## **Merck Forward-Looking Statement**

*This news release includes "forward-looking statements" within the meaning of the safe harbor provisions of the United States Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of Merck's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.*

*Risks and uncertainties include, but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and healthcare legislation in the United States and internationally; global trends toward healthcare cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; Merck's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of Merck's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.*

*Merck undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in Merck's 2013 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site ([www.sec.gov](http://www.sec.gov)).*

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