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Pfizer Announces Detailed Results For Phase 3 OPT Retreatment Study Of Tofacitinib In Adults With Moderate-To-Severe Chronic Plaque Psoriasis

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Findings Presented During 11th European Academy of Dermatology and Venereology Spring Symposium in Belgrade, Serbia

Pfizer Inc. (NYSE:PFE) announced today detailed results from the **O**ral treatment **P**soriasis **T**rial (OPT) Retreatment study (A3921111), a Phase 3 study investigating tofacitinib for the treatment of adult patients with moderate-to-severe chronic plaque psoriasis. This three-period study showed that tofacitinib, as a 5 mg or 10 mg pill taken twice daily, met its two primary efficacy endpoints. The safety profile of tofacitinib in OPT Retreatment was consistent with previous studies and there were no new safety findings in this trial.

The first primary endpoint of OPT Retreatment evaluated the maintenance of clinical response in patients who remained on tofacitinib after an initial treatment phase compared to patients who were switched to placebo (withdrawal phase). The second primary endpoint examined patients who lost half of their original clinical response during the withdrawal phase, and measured the proportion of these patients who regained their original clinical response after restarting treatment with tofacitinib. Throughout the study, the efficacy response was measured by the proportion of subjects achieving a Physician's Global Assessment (PGA) response of "clear" or "almost clear" skin and the proportion of subjects achieving at least a 75% reduction in the Psoriasis Area and Severity Index (PASI75), two commonly used measures of efficacy in psoriasis.

"Psoriasis is a chronic disease that affects approximately two-to-three percent of people worldwide, and there are times when patients with psoriasis may need to stop and restart therapy for medical or non-medical reasons, such as elective surgery or receipt of live immunizations," said lead investigator Robert Bissonnette, M.D., Innovaderm Research, Montreal, QC, Canada. "The OPT Retreatment data showed that patients who stayed on therapy with tofacitinib maintained their rates of response and for those who stopped therapy, a proportion of patients were able to regain their original clinical response when retreated with tofacitinib."

Tofacitinib, an oral Janus kinase (JAK) inhibitor, is part of a new class of medicines in development for the treatment of moderate-to-severe plaque psoriasis. Top-line results from OPT Retreatment were previously announced in October 2013, and the detailed results of this study were shown today in an oral presentation during the 11th European Academy of Dermatology and Venereology (EADV) Spring Symposium in Belgrade, Serbia.

OPT Retreatment was a Phase 3 randomized, double-blind, three-period, parallel group, placebo-controlled 56-week study. This study evaluated the efficacy and safety of the withdrawal and retreatment with tofacitinib 5 mg and 10 mg twice daily compared to placebo in 674 adult patients with moderate-to-severe chronic plaque

psoriasis. During the first period (24 weeks), which was a secondary endpoint of this study, patients were treated with either tofacitinib at a dose of 5 mg or 10 mg twice daily in a blinded manner. During this initial 24 weeks of treatment:

- 44% and 68% of patients who received tofacitinib 5 mg and 10 mg twice daily achieved at least a 75% reduction in the Psoriasis Area and Severity Index (PASI75), respectively, and
- 42% and 63% of patients who received tofacitinib 5 mg and 10 mg twice daily achieved a PGA response of “clear” or “almost clear” skin, respectively.

The patients who achieved a PASI75 and PGA response were then randomized to either continue tofacitinib or switch to placebo for 16 weeks or until they lost half of their original PASI response to treatment, whichever occurred first. During this withdrawal period:

- A statistically significantly greater proportion of patients who remained on both doses of tofacitinib maintained PASI75 and PGA responses relative to patients who were switched to placebo, and
- No patients experienced psoriasis rebound (rapidly spreading psoriasis after treatment withdrawal).

In the retreatment period, all patients resumed their original tofacitinib dose until week 56. After 16 weeks of restarting therapy with tofacitinib, the efficacy response was evaluated in the proportion of patients who lost half of their original PASI or PGA response during the withdrawal phase and showed that:

- 36.8% and 61.0% of patients who received tofacitinib 5 mg and 10 mg twice daily, respectively, achieved a PASI75; and
- 44.8% and 57.1% of patients who received tofacitinib 5 mg and 10 mg twice daily, respectively, achieved a PGA of “clear” or “almost clear” skin.

The most common adverse events for all study periods were nasopharyngitis and upper respiratory tract infection. There was one cardiac-related death that occurred during the OPT Retreatment study at the 5 mg dose. However, in the opinion of the investigator, there was not a reasonable possibility that this death was related to tofacitinib.

OPT Retreatment is one of five studies from the Phase 3 OPT Clinical Trial Program, one of the largest global clinical trial programs in moderate-to-severe chronic plaque psoriasis to date. The results from this study will be included in the planned tofacitinib psoriasis submission package to regulatory authorities in various markets. Pfizer currently intends to submit a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) for the approval of tofacitinib for the treatment of adults with moderate-to-severe chronic plaque psoriasis by early 2015.

About the OPT Clinical Trial Program

The Phase 3 OPT clinical trial program consists of five studies (including one long-term extension study) evaluating oral tofacitinib 5 mg and 10 mg twice daily in adults with moderate-to-severe chronic plaque psoriasis. It is a global, comprehensive clinical development program that includes over 3,600 patients in 36 countries, and is one of the largest global clinical trial programs in moderate-to-severe chronic plaque psoriasis to date. In addition to the OPT Retreatment study, the OPT Program includes the following Phase 3 studies of tofacitinib in adults with moderate-to-severe plaque psoriasis:

- **OPT Pivotal #1 (A3921078) and OPT Pivotal #2 (A3921079):** OPT Pivotal #1 and OPT Pivotal #2 are 52-week, randomized, double-blind, placebo-controlled, parallel-group studies evaluating the safety and efficacy of tofacitinib 5 mg and 10 mg twice daily in patients who are candidates for systemic therapy or

phototherapy. There were over 900 patients randomized into the each of the studies. As previously announced in April 2014, the OPT Pivotal #1 and OPT Pivotal #2 studies showed that tofacitinib, as a 5 mg or a 10 mg dose taken as a pill twice daily, met the primary efficacy endpoints of statistically significant superiority over placebo at Week 16 in the proportion of subjects achieving a PGA response of "clear" or "almost clear" skin, and the proportion of subjects achieving at least a 75% reduction in Psoriasis Area and Severity Index (PASI75).

- **OPT Compare** (**A3921080**): A 12-week, Phase 3 study comparing the efficacy and safety of tofacitinib 5 mg and 10 mg twice daily to high-dose ENBREL® (etanercept) 50 mg twice weekly as well as to placebo. There were 1,106 patients enrolled in this study.
- **OPT Extend (A3921061):** A long-term extension study evaluating the safety and tolerability of tofacitinib. Patients who participated in the Phase 2 trial or any of the other Phase 3 studies had the option, if eligible, to enroll in this study.

About Plaque Psoriasis

Psoriasis is a chronic, immune-mediated disease, affecting primarily the skin but also other organs, such as nails and joints. It affects approximately two-to-three percent of people worldwide and 7.4 million people in the United States.[1,2,3,4,5,6,7] Due to inconsistent response to treatment, adverse effects, and the limited persistence of therapeutic effects of some therapies, a need for additional therapies for patients with moderate-to-severe chronic plaque psoriasis remains.[8,9,10] According to recent published surveys, approximately 50 percent of patients with psoriasis are dissatisfied with their treatment and under-treatment represents a significant problem. Even though guidelines typically state that moderate-to-severe patients are candidates for systemic therapy – e.g., medicines given by mouth or an injection - many adult plaque psoriasis patients appear to be undertreated. Approximately 30 percent of treated moderate patients and 22 percent of treated severe patients receive only topical therapies like ointments and creams in the U.S.[11]

XELJANZ® (tofacitinib citrate) 5 mg Tablets RA U.S. Label Information

Tofacitinib is currently approved in more than 20 countries around the world for the treatment of moderate-to-severe rheumatoid arthritis. In the U.S., the brand name for tofacitinib is XELJANZ® (ZEL' JANS'), and it is approved at the 5 mg dose for the treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate.

XELJANZ is a prescription medicine called a Janus kinase (JAK) inhibitor. XELJANZ is used to treat adults with moderately to severely active rheumatoid arthritis in which methotrexate did not work well.

- It is not known if XELJANZ is safe and effective in people with Hepatitis B or C.
- XELJANZ is not for people with severe liver problems.
- It is not known if XELJANZ is safe and effective in children.

Important Safety Information

- **XELJANZ can lower the ability of the immune system to fight infections. Some people have serious infections while taking XELJANZ, including tuberculosis (TB), and infections caused by bacteria, fungi, or viruses that can spread throughout the body. Some people have died from these infections. Healthcare providers should test patients for TB before starting XELJANZ, and monitor them closely for signs and symptoms of TB and other infections during treatment. People should not start taking XELJANZ if they have any kind of infection unless their healthcare provider tells them it is okay.**

- **XELJANZ may increase the risk of certain cancers by changing the way the immune system works. Malignancies were observed in clinical studies of XELJANZ.**
- The risks and benefits of treatment should be considered prior to initiating XELJANZ in patients with chronic or recurrent infection; who have been exposed to tuberculosis; with a history of a serious or an opportunistic infection; who have resided or traveled in areas of endemic tuberculosis or endemic mycoses; or with underlying conditions that may predispose them to infection.
- Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster), was observed in clinical studies with XELJANZ.
- Use of live vaccines should be avoided concurrently with XELJANZ. Update immunizations in agreement with current immunization guidelines prior to initiating XELJANZ therapy.
- Some people who have taken XELJANZ with certain other medicines to prevent kidney transplant rejection have had a problem with certain white blood cells growing out of control (Epstein Barr virus-associated post-transplant lymphoproliferative disorder).
- Some people taking XELJANZ get tears in their stomach or intestines. This happens most often in people who also take nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, or methotrexate. Patients should tell their healthcare provider right away if they have fever and stomach-area pain that does not go away, or a change in bowel habits. XELJANZ should be used with caution in patients who may be at increased risk for gastrointestinal perforation (e.g., patients with a history of diverticulitis).
- XELJANZ can cause changes in certain lab test results including low blood cell counts, increases in certain liver tests, and increases in cholesterol levels. Healthcare providers should do blood tests before starting patients on XELJANZ and while they are taking XELJANZ, to check for these side effects. Normal cholesterol levels are important to good heart health. Healthcare providers may stop XELJANZ treatment because of changes in blood cell counts or liver test results.
- Use of XELJANZ in patients with severe hepatic impairment is not recommended.
- Patients should tell their healthcare providers if they plan to become pregnant or are pregnant.

It is not known if XELJANZ will harm an unborn baby. To monitor the outcomes of pregnant women exposed to XELJANZ, a registry has been established. Physicians are encouraged to register patients and pregnant women are encouraged to register themselves by calling 1-877-311-8972.

- Patients should tell their healthcare providers if they plan to breastfeed or are breastfeeding. Patients and their healthcare provider should decide if they will take XELJANZ or breastfeed. They should not do both.
- In carriers of the hepatitis B or C virus (viruses that affect the liver), the virus may become active while using XELJANZ. Healthcare providers may do blood tests before and during treatment with XELJANZ.
- Common side effects include upper respiratory tract infections (common cold, sinus infections), headache, diarrhea, and nasal congestion, sore throat, and runny nose (nasopharyngitis).

Please click the direct link to the full prescribing information for XELJANZ, including boxed warning and Medication Guide:http://labeling.pfizer.com/ShowLabeling.aspx?id=959.

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, Pfizer has worked to make a difference for all who rely on us. To learn more, please visit us at www.pfizer.com.

DISCLOSURE NOTICE: The information contained in this release is as of May 23, 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 tofacitinib, including its potential benefits and the anticipated submission of applications with regulatory authorities, that involves substantial risks and uncertainties. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development, including, without limitation, the ability to meet anticipated clinical trial completion dates as well as the possibility of unfavorable clinical trial results; whether an sNDA will be submitted in the U.S. by early 2015, and whether and when any applications may be submitted with regulatory authorities in various other jurisdictions, for tofacitinib for the treatment of moderate-to-severe chronic plaque psoriasis; whether and when the FDA and regulatory authorities in other jurisdictions may approve any such applications, as well as their decisions regarding labeling and other matters that could affect its availability or commercial potential; 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 and Form 8-K.

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