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Pfizer Announces Positive Top-Line Results from the First Phase 3 Trial of Investigational Tofacitinib in Adults with Psoriatic Arthritis

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NEW YORK, N.Y., April 5 – Pfizer Inc. announced today top-line results from its first Phase 3 study investigating tofacitinib for the treatment of psoriatic arthritis, Oral Psoriatic Arthritis triaL (OPAL) Broaden. This study evaluated the efficacy and safety of tofacitinib 5 mg and 10 mg twice daily (BID) in adult patients with active psoriatic arthritis (PsA) who had an inadequate response to at least one conventional synthetic disease-modifying antirheumatic drug (csDMARD) and who were tumor necrosis factor inhibitor (TNFi)-naïve. OPAL Broaden met its primary efficacy endpoints demonstrating that both tofacitinib 5 mg BID and 10 mg BID were superior to treatment with placebo at 3 months as measured by American College of Rheumatology 20 (ACR20) response and Health Assessment Questionnaire Disability Index (HAQ-DI) score.

“As a chronic inflammatory disease, psoriatic arthritis can have a significant impact on a person’s daily life. Despite available therapies, including biologic and oral treatments, there remains an unmet need for additional options,” said Michael Corbo, Category Development Lead, Inflammation & Immunology, Pfizer Global Innovative Pharmaceuticals Business. “The results seen in the OPAL Broaden study are encouraging as they suggest that tofacitinib may have the potential to offer an additional effective oral option for patients living with psoriatic arthritis. We look forward to sharing detailed results at a future scientific meeting.”

OPAL Broaden is a Phase 3 placebo-controlled study that investigated the efficacy and safety of tofacitinib 5 mg and 10 mg BID in treating the signs and symptoms of PsA, and improvement in physical function in patients with active PsA who had an inadequate response to at least one csDMARD due to lack of efficacy or adverse event, and who were TNFi-naive. Patients enrolled in the study were required to be on one csDMARD as background therapy and continue that dose for the duration of the study. The study also included adalimumab 40 mg subcutaneously administered every 2 weeks (q2 wk) as an active control arm. However, this study was not powered for non-inferiority or superiority comparisons between tofacitinib and adalimumab. A total of 422 patients were randomized in a 2:2:2:1:1 ratio to the following treatment arms: tofacitinib 5 mg BID, tofacitinib 10 mg BID, adalimumab 40 mg q2 wk, placebo to tofacitinib 5 mg BID and placebo to tofacitinib 10 mg BID treatment sequences.

Overall safety findings in this study were consistent with those observed in the broader rheumatology clinical development program for tofacitinib. All treatment groups had similar rates of treatment-emergent adverse events, serious adverse events, and discontinuations due to adverse events over the 12-month duration of the study. Serious adverse events observed were similar to those seen in other clinical development programs for tofacitinib.

About the OPAL Global Clinical Development Program

The OPAL global clinical development program includes two Phase 3 studies, OPAL Broaden and OPAL Beyond, as well as a long-term extension trial, OPAL Balance. Results for OPAL Beyond are anticipated in the first half of 2016. We expect that these three studies will form the potential submission package for possible future regulatory applications seeking expansion of the XELJANZ (tofacitinib citrate) label to include a PsA indication.

About Psoriatic Arthritis

Psoriatic Arthritis (PsA) is a chronic inflammatory multisystem disease.[i] The symptoms of PsA often overlap with skin inflammation as observed in psoriasis and other forms of inflammatory arthritis, including: pain and swelling of the joints; inflammation of the sites where tendons or ligaments insert into the bone; inflammation of the spine, reduced range of motion; and inflammation of the fingers and toes.[ii],[iii] Up to 30 percent of people living with psoriasis may develop PsA.[iv],[v] An estimated 3 million people in the U.S. and Europe combined have PsA.[vi] Disease prevalence may even be higher because it is often misdiagnosed or goes undiagnosed altogether.[vii],[viii],[ix] PsA may also impact health-related quality of life (HRQoL). Many PsA patients indicate that their disease has resulted in marked physical limitations and impaired emotional well-being, as well as general fatigue.[x]

About XELJANZ (tofacitinib citrate) and XELJANZ XR (tofacitinib citrate) extended-release

XELJANZ®/XELJANZ XR® is a prescription medicine called a Janus kinase (JAK) inhibitor. XELJANZ XR 11 mg is the first and only once-daily oral JAK inhibitor for the treatment of moderate to severe rheumatoid arthritis (RA).

As the developer of XELJANZ/XELJANZ XR, Pfizer is a leader in JAK innovation. XELJANZ/XELJANZ XR does not require injections or infusions. XELJANZ/XELJANZ XR can be taken with or without methotrexate.

XELJANZ is approved in more than 45 countries around the world for the treatment of moderate to severe RA as a second-line therapy after failure of one or more disease-modifying antirheumatic drugs (DMARDs).

Pfizer is committed to advancing the science of JAK inhibition and enhancing understanding of XELJANZ through a robust clinical development program. The efficacy and safety profile of XELJANZ has been studied in approximately 6,200 patients with moderate to severe RA, amounting to more than 19,400 patient-years of drug exposure in the global clinical development program.

XELJANZ is the only JAK inhibitor included in the *2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis*.[xi]

XELJANZ/XELJANZ XR U.S. Label Information

XELJANZ/XELJANZ XR is a prescription medicine called a Janus kinase (JAK) inhibitor. XELJANZ/XELJANZ XR is used to treat adults with moderately to severely active rheumatoid arthritis in which methotrexate did not work well. XELJANZ/XELJANZ XR may be used as a single agent or in combination with methotrexate (MTX) or other non-biologic disease-modifying antirheumatic drugs (DMARDs). Use of XELJANZ/XELJANZ XR in combination with biologic DMARDs or potent immunosuppressants, such as azathioprine and cyclosporine, is not recommended.

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

· It is not known if XELJANZ/XELJANZ XR is safe and effective in children.

Important Safety Information

· **XELJANZ/XELJANZ XR can lower the ability of the immune system to fight infections. Some people can have serious infections while taking XELJANZ/XELJANZ XR, 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/XELJANZ XR, and monitor them closely for signs and symptoms of TB and other infections during treatment. People should not start taking XELJANZ/XELJANZ XR if they have any kind of infection unless their healthcare provider tells them it is okay.**

· **People may be at a higher risk of developing shingles.**

· **XELJANZ/XELJANZ XR may increase the risk of certain cancers by changing the way the immune system works. Lymphoma and other cancers, including skin cancers, can happen in patients taking XELJANZ/XELJANZ XR.**

· The risks and benefits of treatment should be considered prior to initiating XELJANZ/XELJANZ XR 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/XELJANZ XR. Update immunizations in agreement with current immunization guidelines prior to initiating XELJANZ/XELJANZ XR 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/XELJANZ XR can get tears in their stomach or intestines. This happens most often in people who also take nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, or methotrexate.

· XELJANZ/XELJANZ XR should be used with caution in patients who may be at increased risk for gastrointestinal perforation (e.g., patients with a history of diverticulitis), or who have a narrowing within their digestive track. 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/XELJANZ XR 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/XELJANZ XR and while they are taking XELJANZ/XELJANZ XR, to check for these side effects. Normal cholesterol levels are important to good heart health. Healthcare providers may stop XELJANZ/XELJANZ XR treatment because of changes in blood cell counts or liver test results.

· Use of XELJANZ/XELJANZ XR 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/XELJANZ XR will harm an unborn baby. To monitor the outcomes of pregnant women exposed to XELJANZ/XELJANZ XR, 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/XELJANZ XR 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/XELJANZ XR. Healthcare providers may do blood tests before and during treatment with XELJANZ/XELJANZ XR.

· 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/XELJANZ XR, 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 healthcare products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer healthcare 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. For more information, please visit us at www.pfizer.com. In addition, to learn more, follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

DISCLOSURE NOTICE: The information contained in this release is as of April 5, 2016. 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 potential new indication for XELJANZ for the treatment of adults with active psoriatic arthritis (the "potential indication"), 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 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 applications for the potential indication may be filed with regulatory authorities in any jurisdictions; whether and when regulatory authorities in any jurisdictions may approve such applications and/or any other applications that are pending for XELJANZ, 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 XELJANZ and XELJANZ XR, including the potential indication; 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, 2015 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.

[i] Ritchlin CT, Kavanaugh A, Gladman DD, et al. Treatment recommendations for psoriatic arthritis. *Ann Rheum Dis*. 2009;68(9):1387-1394.

[ii] National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health, US Department of Health and Human Services. Psoriatic arthritis overview. NIH publication 14–AR-8001. http://www.niams.nih.gov/health_info/Psoriatic_Arthritis/psoriatic-arthritis.pdf. Published October 2014.

[iii] National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health, US Department of Health and Human Services. Psoriatic arthritis overview. NIH publication 14–AR-8001. http://www.niams.nih.gov/health_info/Psoriatic_Arthritis/psoriatic-arthritis.pdf. Published October 2014.

[iv] Van de Kerkhof PCM, Reich K, Kavanaugh A, et al. Physician perspectives in the management of psoriasis and psoriatic arthritis: results from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis survey. *J Eur Acad Dermatol Venereol*. 2015.

[v] Helliwell P, Coates L, Chandran V, et al. Qualifying unmet needs and improving standards of care in psoriatic arthritis. *Arthritis Care Res (Hoboken)*. 2014;66(12):1759-1766.

[vi] Data on File. Decision Resources Group. Table 1-4 : Number of Total Prevalent Cases of Psoriatic Arthritis in the Major Pharmaceutical Markets, 2013-2023. United States and Europe, 2016.

[vii] Van de Kerkhof PCM, Reich K, Kavanaugh A, et al. Physician perspectives in the management of psoriasis and psoriatic arthritis: results from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis survey. *J Eur Acad Dermatol Venereol*. 2015.

[viii] Helliwell P, Coates L, Chandran V, et al. Qualifying unmet needs and improving standards of care in psoriatic arthritis. *Arthritis Care Res (Hoboken)*. 2014;66(12):1759-1766.

[ix] National Psoriasis Foundation. 2011 Survey Panel Snapshot. http://www.psoriasis.org/document.doc?id=1782. Accessed July 15, 2015.

[x] Helliwell P, Coates L, Chandran V, et al. Qualifying unmet needs and improving standards of care in psoriatic arthritis. *Arthritis Care Res (Hoboken)*. 2014;66(12):1759-1766.

[xi] Singh, J. A., Saag, K. G., Bridges, S. L., et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis & Rheumatology. doi: 10.1002/art.39480.

Media Contact: Steven Danehy 978-273-3946 Steven.Danehy@pfizer.com Investor Contact: Chuck Triano 212-733-3901 Charles.E.Triano@pfizer.com