Two-Year Results From Pfizer's XELJANZ® (Tofacitinib Citrate) ORAL Start Study Published in The New England Journal of Medicine

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Phase 3 Study ORAL Start Showed XELJANZ Monotherapy Superior to Methotrexate in Inhibiting the Progression of Structural Damage and Reducing Signs and Symptoms of Rheumatoid Arthritis in Methotrexate-Naïve Patients Findings Contribute to Growing Body of Evidence Supporting Efficacy and Safety Profile of XELJANZ as Monotherapy in Rheumatoid Arthritis

Pfizer Inc. (NYSE:PFE) announced today the publication of two-year results from the ORAL Start study in the June 19 issue of The New England Journal of Medicine. ORAL Start is a 24-month Phase 3 study in patients with moderately to severely active rheumatoid arthritis who had not previously received methotrexate. The study showed that XELJANZ (tofacitinib citrate) 5 mg and 10 mg twice daily, as monotherapy (e.g., taken without methotrexate), inhibited the progression of structural damage and reduced the signs and symptoms of rheumatoid arthritis, and was statistically significantly superior to methotrexate on these measures at Month 6 (primary endpoint) and at all measured time points up to 24 months. XELJANZ is not indicated in patients who had not previously received methotrexate. The safety profile of XELJANZ in the ORAL Start study was consistent with that seen previously in the clinical development program.

In the United States, XELJANZ 5 mg tablets are indicated for the treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate. XELJANZ may be used alone or in combination with methotrexate or other non-biologic, disease-modifying antirheumatic drugs (DMARDs). Use of XELJANZ in combination with biologic DMARDs or potent immunosuppressants,

such as azathioprine and cyclosporine, is not recommended. The recommended dose is a 5 mg pill taken twice daily.

“This study showed that XELJANZ taken by itself was statistically significantly superior to methotrexate in measures of clinical, radiographic and functional efficacy rheumatoid arthritis outcomes, and these results were sustained over two years,” said lead investigator Roy M. Fleischmann, MD, professor, Metroplex Clinical Research Center, Dallas, Texas. “These results also add to the information on the efficacy and safety of XELJANZ as monotherapy.”

The ORAL Start study was a 24-month Phase 3 randomized, double-blind, controlled trial in which 956 patients with moderately to severely active rheumatoid arthritis who had not previously received methotrexate were randomized to receive XELJANZ 5 mg or 10 mg twice daily or to methotrexate dose-titrated over 8 weeks to 20 mg weekly. As previously announced, both doses of XELJANZ met the study’s co-primary efficacy endpoints: reduction of progression of radiographic measures of disease as measured by average change from baseline in van der Heijde modified Total Sharp Score (mTSS)[0.18 and 0.04 (both $P<0.001$) for XELJANZ 5 mg and 10 mg twice daily, respectively, versus 0.84 for methotrexate], and clinical response as measured by ACR70 response rates, a measure of at least 70% reduction in signs and symptoms of rheumatoid arthritis [25.5% and 37.7% for XELJANZ 5 mg and 10 mg twice daily, respectively (both $P<0.001$), versus 12.0% for methotrexate], at Month 6. ORAL Start also evaluated improvement in physical function as measured by mean change from baseline in the Health Assessment Questionnaire Disability Index (HAQ-DI)[-0.83 and -0.94 (both $P<0.001$) for XELJANZ 5 mg and 10 mg twice-daily, respectively, versus -0.58 for methotrexate], at Month 6. These results were sustained at all measured time points up to 24 months.

The six- and 12-month radiographic data from this study were recently added to the XELJANZ U.S. label (February, 2014) as part of an FDA approved label update.

“The publication of the ORAL Start data in The New England Journal of Medicine marks the sixth Phase 3 study in the XELJANZ clinical program to be published in a major medical journal,” said Dr. Steven Romano, Global Medicines Development Lead for the Pfizer Global Innovative Pharmaceutical business. “The publication of all of the completed XELJANZ Phase 3 rheumatoid arthritis clinical studies in such respected publications speaks to the significance and clinical relevance of the data for XELJANZ.”

The safety profile of XELJANZ in the ORAL Start study was consistent with that seen previously in the clinical development program. The incidence of adverse events, serious

adverse events and discontinuations due to adverse events were similar across groups. Most adverse events were mild or moderate and the most frequently reported adverse events in all groups were infections. Herpes zoster (shingles) occurred in 4.0% of patients on XELJANZ and 1.1% of patients on methotrexate. Confirmed malignancies developed in five patients treated with XELJANZ and one patient treated with methotrexate. XELJANZ was associated with increases in average serum creatinine and lipid levels.

XELJANZ U.S. Label Information

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.

About Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic, inflammatory autoimmune disease that typically affects the hands and feet, although any joint lined by the synovial membrane can be affected.1 RA causes a range of symptoms, including stiffness and swelling in the joints,2 particularly those in the hands, feet and knees.1 Although the exact cause of RA is unknown,1 it is considered to be an autoimmune disease, because the immune system in people with RA mistakes the body’s healthy tissues for a threat and attacks them.1 Some people are at increased risk of developing RA, including people with a family history of RA, smokers and women.3 Three times as many women are affected by RA compared to men.2 RA affects approximately 23.7 million people4 worldwide and 1.6

million people in the United States.5,6 It can develop at any time during adulthood, but it usually occurs between 40 and 70 years of age.2

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DISCLOSURE NOTICE: The information contained in this release is as of June 18, 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 XELJANZ (tofacitinib citrate), including its potential benefits, that involves substantial risks and uncertainties. Such risks and uncertainties include, among other things, whether and when the FDA will assess the benefit: risk profile of the 10 mg twice-daily dose; 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.

References:

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