Pfizer Announces Data For Investigational Compound Tofacitinib In Rheumatoid Arthritis To Be Presented At The American College Of Rheumatology 2012 Annual Meeting

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Phase 3 Study ORAL Start Showed Tofacitinib Monotherapy Superior to Methotrexate in Inhibiting Structural Damage and Reducing Signs and Symptoms of RA in Methotrexate-Naïve Patients Results from ORAL Scan Showed Tofacitinib Maintained Efficacy, Including Inhibition of Structural Damage, through 24 Months Long-Term Efficacy and Safety Data of Tofacitinib Over Four Years Will Also Be Presented

"Herpes Zoster And Tofacitinib Therapy In Patients With Rheumatoid Arthritis"

(BUSINESS WIRE)--Pfizer Inc. (NYSE: PFE) announced today that 14 abstracts for tofacitinib, an investigational oral Janus kinase (JAK) inhibitor for the treatment of adults with moderate-to-severe active rheumatoid arthritis (RA), will be presented at the American College of Rheumatology (ACR) / Association of Rheumatology Health Professionals (ARHP) 2012 Annual Meeting, which is being held November 9-14 in Washington, D.C.

Tofacitinib is currently under review for the treatment of moderate–to-severe active RA by several regulatory agencies around the world, including in the United States, Europe and Japan. The FDA has provided an anticipated Prescription Drug User Fee Act (PDUFA) date of November 21, 2012. If approved, tofacitinib would be the first RA treatment in a new class of medicines known as JAK inhibitors and the first new oral disease-modifying antirheumatic drug (or DMARD) for RA in more than 10 years.

Results Being Presented for Phase 3 Studies, ORAL Start and ORAL Scan; Long-Term Safety and Efficacy Data Up To 48 months will also be Presented

ORAL Start (A3921069), an ongoing Phase 3, two-year study in methotrexate (MTX)-naïve patients with moderate-to-severe active RA randomized to receive tofacitinib 5 or 10 mg twice-daily (BID) as monotherapy or MTX, met its primary endpoints at both the 5 and 10 mg BID doses. In this study, tofacitinib monotherapy was found to be superior to MTX, with statistically significant changes shown in inhibiting structural damage as measured by change from baseline in van der Heijde modified Total Sharp Score (mTSS) and in reducing signs and symptoms of RA as measured by ACR70 response rates, both assessed at six months. Secondary endpoints, including ACR20 and ACR50 responses, DAS-defined remission (DAS28-4(ESR) <2.6), and mean change in HAQ-DI, were statistically significantly greater with tofacitinib versus MTX at all time points. No new safety signals emerged in the study and the overall safety profile of tofacitinib remained consistent with that seen previously in the RA clinical development program. Results are from a pre-specified planned analysis at one year. “Radiographic, Clinical and Functional Comparison of Tofacitinib Monotherapy Versus Methotrexate in Methotrexate-Naïve Patients with Rheumatoid Arthritis”[Abstract #27194; Tuesday, November 13, 2012 at 2:45 p.m. EST] Results from a two-year analysis of ORAL Scan (A3921044), a completed Phase 3 study in patients with moderate-to-severe active RA who had an inadequate response to MTX, will also be presented. Patients were randomized to receive tofacitinib 5 or 10 mg BID or placebo, in each case with background MTX. Primary outcomes from the one-year analysis from ORAL Scan were previously reported at the ACR 2011 Annual Scientific Meeting.1,2 The two-year analysis evaluated consistency of the efficacy and safety profile of tofacitinib 5 or 10 mg BID in patients who remained on active treatment through 24 months. The two-year results showed that patients on tofacitinib maintained improvements in efficacy including reductions in signs and symptoms, inhibition of structural damage, and improvements in physical function through month 24. No new safety signals emerged. “Tofacitinib, an Oral Janus Kinase Inhibitor, in Combination with Methotrexate Reduced the Progression of Structural Damage in Patients with Rheumatoid Arthritis: Year 2 Efficacy and Safety Results From a 24-Month Phase 3 Study” [Abstract #26718; Monday, November 12, 2012]. Data from a pooled analysis of two long-term, open-label extension studies (NCT00413699, NCT00661661) involving patients with moderate-to-severe RA who had participated in randomized Phase 2 or 3 studies of tofacitinib dosed at 5 or 10 mg BID showed a consistent safety profile and sustained efficacy over 48 months. Safety and efficacy were similar for patients receiving tofacitinib as monotherapy or with background nonbiologic disease-modifying antirheumatic drugs (DMARDs). Primary endpoints were adverse events and confirmed laboratory safety data.

Secondary endpoints included ACR responses, DAS28-4(ESR) and HAQ-DI. “Tofacitinib, an Oral Janus Kinase Inhibitor, in the Treatment of Rheumatoid Arthritis: Open Label, Long-Term Extension Safety and Efficacy Up To 48 Months” [Abstract #27156; Monday, November 12, 2012].

The overall safety profile of tofacitinib was consistent across all aforementioned trials. Notable safety findings observed in the tofacitinib RA program include serious and other important infections, including tuberculosis and herpes zoster; malignancies, including lymphoma; gastrointestinal perforations; decreased neutrophil and lymphocyte counts; and lipid elevations. The most common serious adverse events were serious infections. The most commonly reported adverse events were upper respiratory tract infections, headache, nasopharyngitis and diarrhea.

Additional Tofacitinib Efficacy and Safety Data, including Inhibition of Structural Damage, Remission Rates, Patient-Reported Outcomes and Dosing to be Presented

The following data will also be presented:

Radiographic Analyses

A sensitivity analysis of ORAL Scan: “Trimmed Analysis: A New Approach to the Analysis of Sharp Score Data in the Assessment of the Progression of Patients with Rheumatoid Arthritis” [Abstract #26935; Monday, November 12, 2012] A post-hoc analysis of radiographic progression in RA patients prone to develop structural damage: “Tofacitinib Inhibits Radiographic Progression in Patients with Rheumatoid Arthritis Prone to Develop Structural Damage: A Post-Hoc Analysis of a Phase 3 Trial” [Abstract #26976; Tuesday, November 13, 2012 at 4:45 p.m. EST]
Additional Efficacy Data

Prediction of low disease activity: “Tofacitinib And Adalimumab Achieve Similar Rates Of Low Disease Activity In Rheumatoid Arthritis — Lack Of Improvement In Disease Activity Score By 3 Months Predicts Low Likelihood Of Low Disease Activity At 1 Year” (NCT00853385) [Abstract #28067; Monday, November 12, 2012] Remission rates: “Remission Rates With Tofacitinib Treatment In Rheumatoid Arthritis: A Comparison Of Various Remission Criteria” [Abstract #27787; Sunday, November 11, 2012 at 3:00 p.m. EST] Patient-reported outcomes in ORAL Step and ORAL Scan: “Effects of Tofacitinib On Patient-Reported Outcomes in Patients with Active Rheumatoid Arthritis Receiving Stable-Dose Methotrexate” (NCT00960440 and NCT00847613) [Abstract #27211; Monday, November 12, 2012]
Dosing

Dose-related safety and efficacy: “Tofacitinib, An Oral Janus Kinase Inhibitor: Analyses Of Efficacy And Safety Of 10 Versus 5mg Twice Daily In A Pooled Phase 3 And Long-Term Extension Rheumatoid Arthritis Population” [Abstract #26731; Tuesday, November 13 at 2:30 p.m. EST]

Additional Safety Data

Effects on cholesterol: “Effects Of Tofacitinib On Lipid Profiles And Cholesterol And Lipoprotein Kinetics In Patients With Rheumatoid Arthritis” [Abstract #27669; Monday, November 12, 2012] ORAL Sequel vaccine sub-study: “Evaluation Of Influenza And Pneumococcal Vaccine Responses In Patients With Rheumatoid Arthritis Receiving Tofacitinib” (NCT00413699) [Abstract #27391; Monday, November 12, 2012] Tuberculosis screening: “Tuberculosis And Tofacitinib Therapy In Patients With Rheumatoid Arthritis” [Abstract #26735, Monday, November 12, 2012] Herpes zoster logistic regression analysis: “Herpes Zoster And Tofacitinib Therapy In Patients With Rheumatoid Arthritis” [Abstract #26957; Tuesday, November 13 at 3:45 p.m. EST] Meta-analysis of certain side effects: “Meta-Analysis Of Malignancies, Serious Infections, And Serious Adverse Events With Tofacitinib Or Biologic Treatment In Rheumatoid Arthritis Clinical Trials” [Abstract #27741; Monday, November 12, 2012 at 5:15 p.m. EST]
About Rheumatoid Arthritis

Rheumatoid arthritis is a chronic inflammatory autoimmune disease that typically affects the hands and feet, although any joint lined by a synovial membrane may be affected. RA affects approximately 1.6 million Americans3,4 and 23.7 million people worldwide.5 Although multiple treatments are available, many patients do not adequately respond. Specifically, up to one-third of patients do not adequately respond and about half stop responding to any particular DMARD within five years.6,7,8,9,10,11 There remains a need for additional options.

About Tofacitinib

Tofacitinib is a novel, oral JAK inhibitor that is being investigated as a targeted immunomodulator and disease-modifying therapy for RA. Unlike recent therapies for RA, which are directed at extracellular targets such as pro-inflammatory cytokines, tofacitinib takes a novel approach targeting the intracellular pathways that operate as hubs in the inflammatory cytokine network.

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DISCLOSURE NOTICE: The information contained in this release is as of September 17, 2012. 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 that involves substantial risks and uncertainties about a potential indication for a product in development, tofacitinib, as a treatment for moderate- to -severe active RA that is under review by regulatory authorities in various markets, including the United States, Europe and Japan. Such risks and uncertainties include, among other things, (i) the uncertainties inherent in research and development; (ii) decisions by regulatory authorities regarding whether and when to approve drug applications that have been or may be filed for tofacitinib for moderate- to -severe active RA, as well as their decisions regarding labeling and other matters that could affect its availability or commercial potential; and (iii) 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, 2011 and in its reports on Form 10-Q and Form 8-K.

1 van der Heijde, D. et al. Arthritis Rheum 2011; 63 (Suppl 10): S1017-1018.

2 Pfizer. (2011). Pfizer Announces Detailed Pivotal Data for Investigational Compound Tofacitinib in Rheumatoid Arthritis to be Presented at American College of Rheumatology 2011 Annual Scientific Meeting [Press release]. Available at http://www.pfizer.com/news/press_releases/pfizer_press_release.jsp?guid=20110908005788en&

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4 Howden, L., Meyer, J., 2010 U.S. Census Bureau results --- U.S. Census Bureau, 2010 Census Summary File 1

5 World Health Organization, “The Global Burden of Disease, 2004 Update.” Accessed 13 March 2012. Available at http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf.

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7 Keystone, E, Kavanaugh A, Sharp J, et al. Radiographic, clinical and functional outcomes of treatment with adalimumab (a human anti-tumor necrosis factor monoclonal antibody) in patients with active rheumatoid arthritis receiving concomitant methotrexate therapy. Arthritis & Rheumatism 2004. 50: 1400-1411

8 Lipsky, P, Van der Heijde, D, St. Clair, W. Infliximab and methotrexate in the treatment of rheumatoid arthritis. The New England Journal of Medicine 2000. 1594-1602.

9 Duclos M, Gossec L, Ruyssen-Witrand A, et al. Retention rates of tumor necrosis factor blockers in daily practice in 770 rheumatic patients. J Rheumatol 2006; 33:2433-8.

10 Maradit-Kremers H, Nicola PJ, Crowson CS, et al. Patient, disease, and therapy-related factors that influence discontinuation of disease-modifying antirheumatic drugs: a population-based incidence cohort of patients with rheumatoid arthritis. J Rheumatol 2006; 33(2):248-55.

11 Blum MA, Koo D, Doshi JA. Measurement and rates of persistence with and adherence to biologics for rheumatoid arthritis: a systematic review. Clin Ther 2011;33(7):901-913.

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