Pfizer Announces 11 Abstracts for Tofacitinib to Be Presented at the European League Against Rheumatism (EULAR) 2013 Annual Meeting

Sunday, May 12, 2013 - 06:30pm

Additional Analyses Further Evaluate Safety and Efficacy of Tofacitinib in Rheumatoid Arthritis

"The JAK Inhibitor Tofacitinib Suppresses Synovial JAK1-STAT1 Signaling in Rheumatoid Arthritis"

(BUSINESS WIRE)--Pfizer Inc. (NYSE: PFE) announced today that 11 abstracts for tofacitinib will be presented at the European League Against Rheumatism (EULAR) 2013 Annual Meeting being held June 12-15 in Madrid, Spain. The brand name for tofacitinib is XELJANZ® (ZEL' JANS').

Highlights include:

Comparison of monotherapy vs. combination therapy with tofacitinib

A meta-analysis of four Phase 3 trials (ORAL Sync, Standard, Scan and Solo) assessed whether there were relative differences in efficacy or safety between mono- and combination therapy with tofacitinib in patients with moderate-to-severe rheumatoid arthritis (RA) who had an inadequate response (IR) to disease-modifying antirheumatic drugs (DMARDs). The results showed no statistically significant differences in efficacy or safety whether tofacitinib was administered as monotherapy or in combination with nonbiologic DMARDs in DMARD-IR patients. Definitive conclusions about the relative differences cannot be made based on this meta-analysis and would require a randomized clinical trial directly comparing mono- and combination therapy. "Tofacitinib, an Oral Janus Kinase Inhibitor: Post-Hoc Analyses of Efficacy and Safety of Monotherapy Versus

Combination Therapy in a Phase 3 Rheumatoid Arthritis Population" [Abstract #0228; Thursday, June 13, 2013].

Patient-reported outcome (PRO) results from Phase 3 ORAL Start study

Results from a 12-month interim analysis of patient-reported outcomes from the 24-month Phase 3 ORAL Start study (A3921069) in methotrexate (MTX)-naïve patients with moderate-to-severe RA showed significant improvements in patient-reported outcomes, including pain, physical function and fatigue, in patients who received tofacitinib 5 mg or 10 mg twice daily (BID) monotherapy compared to MTX. In addition, a significant improvement in health-related quality of life was also seen in the 10 mg BID group versus MTX. "Oral START: Effects of the Oral JAK Inhibitor Tofacitinib Monotherapy Versus Methotrexate On Patient Reported Outcomes in The Phase 3 Oral START Trial of Active Rheumatoid Arthritis" [Abstract #0258; Thursday, June 13, 2013].

An analysis of cardiovascular (CV) biomarkers from Phase 2 and 3 studies

An analysis of three Phase 2 and 3 studies of tofacitinib explored changes in biomarkers relevant to lipid biochemistry and cardiovascular (CV) risk in moderate-to-severe RA patients treated with tofacitinib or placebo. The results showed that tofacitinib induced increases in biomarkers, including lecithin-cholesterol acyltransferase (LCAT) and paraoxonase, and decreases in biomarkers, including serum amyloid A (SAA) and high-density lipoprotein (HDL)-associated SAA, potentially implicating Janus kinase (JAK)-dependent pathways in structural and functional modifications of lipoprotein particles, thereby suggesting a potential for reduction in CV risk in patients treated with tofacitinib. Consequences on vascular co-morbidity require further investigation. "Effects of Tofacitinib on Lipid Biomarkers in Patients with Active Rheumatoid Arthritis" [Abstract #0137; Friday, June 14, 2013].

Analysis of lymphocyte count and risk of infection

An analysis of the relationship between lymphocyte counts and the risk of infection associated with tofacitinib treatment showed lymphocyte counts of less than 0.5 x 1000/mm3 were infrequent but were associated with an increased risk of serious infections. These data help inform appropriate lymphocyte monitoring. "Relationship between Lymphocyte Count and Risk of Infection in Rheumatoid Arthritis Patients Treated with Tofacitinib" [Abstract #0252; Thursday, June 13, 2013].

Additional abstracts accepted for presentation include:

A post-hoc analysis from the Phase 3 ORAL Start study evaluating tofacitinib efficacy, including inhibition of structural damage, in patients with early RA (defined by disease duration of <6 months), versus MTX in MTX-naïve patients with moderate-to-severe

active RA. “Tofacitinib Monotherapy is Effective in Methotrexate-Naïve Patients with Disease Duration Less Than 6 Months: A Post-Hoc Analysis of Early Rheumatoid Arthritis Subjects in a Phase 3 Trial” [Abstract #0225; Thursday, June 13, 2013]. Efficacy and safety analysis of moderate-to-severe RA patients transitioning directly from adalimumab to tofacitinib in a clinical trial setting: “Tofacitinib, An Oral Janus Kinase Inhibitor, in a Rheumatoid Arthritis Open-Label Extension Study Following Adalimumab Therapy in a Phase 3 Randomized Clinical Trial” [Abstract #0046; Hall 4; Thursday, June 13, 2013 at 11:20 a.m. CEST/ 5:20 a.m. EST]. A network meta-analysis comparing efficacy and safety of tofacitinib relative to biologic DMARDs in tumor necrosis factor-IR patients: “Tofacitinib Versus Biologic Treatments In Patients With Active Rheumatoid Arthritis Who Have Had An Inadequate Response To Tumor Necrosis Factor Inhibitors -- A Network Meta-Analysis” [Abstract #0115; Saturday, June 15, 2013]. Assessment of responses of two standard vaccines in RA patients treated with tofacitinib: “Evaluation of Influenza and Pneumococcal Vaccine Responses in Rheumatoid Arthritis Patients using tofacitinib” [Abstract #0163; Hall 8; Friday, June 14 at 10:50 a.m. CEST/4:50 a.m. EST]. Comparison of tofacitinib safety between nonbiologic DMARD-IR and biologic DMARD-IR populations: “Tofacitinib, An Oral Janus Kinase Inhibitor: Safety Comparison In Patients With Rheumatoid Arthritis And An Inadequate Response To Nonbiologic Or Biologic Disease Modifying Anti-Rheumatic Drugs” [Abstract #0238; Thursday, June 13, 2013]. Assessment of hemoglobin changes and the relationship to patient-reported fatigue or vitality: “Hemoglobin Changes And Relationship Between Anemia And Fatigue Or Vitality In Rheumatoid Arthritis Patients Treated With Tofacitinib” [Abstract #0241; Thursday, June 13, 2013]. Human mechanistic Phase 2A study assessing how tofacitinib alters synovial biology and inflammatory biomarkers in RA: “The JAK Inhibitor Tofacitinib Suppresses Synovial JAK1-STAT1 Signaling in Rheumatoid Arthritis” [Abstract #0253; Friday, June 14, 2013 at 10:20 a.m. CEST/4:20 a.m. EST].

Safety findings observed in the overall tofacitinib RA program include serious and other important infections, including tuberculosis and herpes zoster; malignancies, including lymphoma; gastrointestinal perforations; decreased neutrophil and lymphocyte counts; liver enzyme elevations; and lipid elevations.

The most common serious adverse events were serious infections. The most commonly reported adverse events were upper respiratory tract infections, headache, diarrhea and nasopharyngitis.

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 can be painful and disabling1 causing swelling, stiffness and loss of function in the joints.1 RA affects 23.7 million people worldwide.2 Although multiple treatments are available, up to one-third of patients do not adequately respond, and about half stop responding to any particular DMARD within five years.3,4,5,6,7,8 As a result, there remains a need for additional options.

About XELJANZ (tofacitinib citrate)

XELJANZ is a novel, oral Janus kinase (JAK) inhibitor for the treatment of RA. XELJANZ is approved in the United States, Japan and Russia for the treatment of adults with moderate-to-severe active RA with previous treatment history, and is the first approved RA treatment in a new class of medicines known as Janus kinase (JAK) inhibitors.

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DISCLOSURE NOTICE: The information contained in this release is as of May 13, 2013. 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 tofacitinib, including its potential benefits and risks as well as clinical trial data relating to tofacitinib and the potential implications of such data. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data, and the

need for additional clinical studies to confirm certain results discussed in this release; whether and when regulatory authorities in jurisdictions in which applications for tofacitinib for the treatment of moderate-to-severe rheumatoid arthritis are pending or will be submitted will approve 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/A for the fiscal year ended December 31, 2012 and in its reports on Form 10-Q and Form 8-K.

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1 Lee DM, Weinblatt ME. Rheumatoid arthritis. Lancet. 2001; 358:903–911.

2 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.

3 Klareskog L, Van der Heijde D, de Jager J, et al. Therapeutic effect of the combination of etanercept and methotrexate compared with each treatment alone in patients with rheumatoid arthritis: double-blind randomized controlled trial. The Lancet 2004. 363: 675-681

4 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

5 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.

6 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.

7 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.

8 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.