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Pfizer Announces Detailed Results Of ORAL Sync Showing Investigational Compound Tofacitinib Reduces Signs And Symptoms And Improves Physical Function In Patients With Moderate-To-Severe Active Rheumatoid Arthritis, With Results Seen As Early As Two Weeks

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Pfizer Also Presents Results of a Separate Phase 2 Trial, Study A3921109, Evaluating Atorvastatin in Patients with Moderate-to-Severe Active Rheumatoid Arthritis Taking Tofacitinib Data to Be Presented at 12th Annual Congress of the European League Against Rheumatism in London

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(BUSINESS WIRE)--Pfizer Inc. (NYSE:PFE) today announced data from ORAL Sync (A3921046) and Study A3921109, two clinical trials of tofacitinib (development code: CP-690,550), an investigational, novel, oral JAK inhibitor, being studied in rheumatoid arthritis (RA). Top-line results of ORAL Sync, a pivotal Phase 3 trial, were announced earlier this year. A separate trial, Study A3921109, evaluated the safety and efficacy of atorvastatin versus placebo in reducing LDL cholesterol (LDL-C) in moderate-to-severe active RA patients taking tofacitinib. Detailed results of these studies are being presented as late-breaking abstracts at the 12th Annual Congress of the European League Against Rheumatism (EULAR).

“The results of ORAL Sync are encouraging, with tofacitinib plus background traditional DMARDs showing clinically meaningful reductions in the signs and symptoms of RA with statistically significant separation from placebo at both doses by the second week of treatment,” said Joel M. Kremer, M.D., head of the Division of Rheumatology at Albany Medical College and director of research of The Center for Rheumatology in Albany, New York.

ORAL Sync Trial Design and Results

ORAL Sync is a completed 12-month Phase 3 study that enrolled 792 patients with moderate-to-severe active RA who had a previous inadequate response to a traditional or biologic disease- modifying anti-rheumatic drug (DMARD) and were randomized to receive tofacitinib 5 mg or 10 mg twice a day (BID) or placebo added to background traditional DMARD(s), including methotrexate (MTX). At Month 3, non-responder placebo patients were advanced to tofacitinib 5 or 10 mg BID. At Month 6, the remaining placebo patients were advanced to

tofacitinib.

ORAL Sync met its primary efficacy endpoints by showing statistically significant changes versus placebo in reducing signs and symptoms of RA, as measured by ACR20 response rates at six months; in improving physical function, as measured by mean change in HAQ-DI at three months; and in reaching DAS 28-4(ESR) <2.6 (DAS-defined remission) at six months. See details in the table below.

Primary and Selected Secondary Efficacy Endpoints (Month 6; HAQ-DI Month 3)

Treatment Group	**ACR20(±) (%)**	**ACR50 (%)**	**ACR70 (%)**	**HAQ-DI(±) mean change from baseline**	**DAS28-4 (ESR)2.6(±)(%)**	**DAS28-4 (ESR) mean change from baseline**
5 mg	52.7***	33.8***	13.2***	-0.46***	11.0**	-2.2***
10 mg	58.3***	36.6***	16.2***	-0.56***	14.8***	-2.5***
Placebo	31.2	12.7	3.2	-0.21	2.7	-1.6

± Primary efficacy endpoint; **p<0.001; ***p<0.0001

Onset of action, as measured by statistically significant ACR20 or HAQ-DI responses versus placebo, was seen by Week 2.

In ORAL Sync, a comparable incidence of adverse events (AEs) and serious adverse events (SAEs) was seen across treatment groups during Months 0-3 and the incidence of these events did not appear to increase thereafter. There was a higher incidence of discontinuations due to AEs in tofacitinib treatment groups over Months 0-6. See details in the table below. The majority of AEs were mild and the most frequently reported class of AEs throughout the study was infections and infestations. Serious infectious events (SIEs) were reported for two (5 mg BID) and four (10 mg BID) patients in Months 0-3 and one patient each in the placebo-to-5 mg BID and placebo-to-10 mg BID groups during Months 3-6. There were four deaths, one of which was assessed by the investigator as study drug related, and four opportunistic infections in the study (all events in the tofacitinib treatment groups).

Safety: n (%)

Treatment Group	**AEs 0-3 Months**	**SAEs 0-3 Months**	**AEs 3-6 Months**	**SAEs 3-6 Months**	**D/C (AEs) 0-6 Months**
5 mg	166	9 (2.9)	121	5 (1.6)	13 (4.2)

	(52.7)		(38.4)		
10 mg	173	8 (2.5)	124	7 (2.2)	15 (4.7)
	(54.4)		(39.0)		
Placebo	97 (61.0)	6 (3.8)	21 (25.9)	0	3 (1.9)

D/C (discontinuation)

Among patients treated with tofacitinib, dose-dependent decreases in mean neutrophil counts and increases in mean LDL, HDL and total cholesterol were observed. Most cases of neutropenia were mild and there were no cases of life-threatening neutropenia. Changes in neutrophils and lipids were observed during Months 0-3 and stabilized thereafter. Transaminase increases and small increases in serum creatinine were also observed.

“Pfizer is encouraged by the efficacy and safety findings from ORAL Sync, which showed that tofacitinib may be an oral option for patients not responding adequately to traditional DMARDs,” said Yvonne Greenstreet, senior vice president and head of the Medicines Development Group for Pfizer’s Specialty Care Business Unit.

Study A3921109 Trial Design and Results

Study A3921109 is a completed 12-week Phase 2 study that enrolled 111 patients to evaluate the efficacy and safety of atorvastatin treatment versus placebo in reducing LDL-C in RA patients taking tofacitinib. After receiving 10 mg BID tofacitinib open-label for six weeks, patients were randomized to receive atorvastatin 10 mg once daily (50 patients) or placebo (47 patients) in a double-blind manner in addition to open-label tofacitinib 10 mg BID for six weeks. Concomitant MTX or other background DMARDs were not allowed. The primary endpoint of the study was the percent change in mean LDL-C from baseline (Week 6) to Week 12.

In patients on tofacitinib, the addition of atorvastatin 10 mg resulted in a statistically significant 35 percent reduction in mean LDL-C compared to a 5.8 percent increase in LDL-C in the placebo group at Week 12, with median LDL-C achieved in the ATP-III optimal target range (<100 mg/dL) in the atorvastatin group at Week 12. The ATP-III (Adult Treatment Panel) are guidelines developed by the National Heart, Lung and Blood Institute to evaluate target blood cholesterol levels.

The median LDL-C level increased at Week 6 after treatment with tofacitinib in both groups and then decreased after randomization in the atorvastatin group to values below tofacitinib pre-treatment levels. A similar pattern was observed in apolipoprotein B, triglycerides and total cholesterol levels, with decreases to below pre-treatment levels. HDL-C and apolipoprotein A-1 increased with tofacitinib treatment and continued to trend upward during the last six weeks of the study regardless of treatment group.

After six weeks of tofacitinib treatment, 76 percent of patients exhibited ACR20 response. By Week 12, the atorvastatin group had an ACR20 response rate of 82.6 percent versus the placebo group with 65.2 percent. Given the size of the study, the significance of a higher numeric ACR score in the atorvastatin group is unclear.

The safety profile of tofacitinib in this study was similar to that seen in other studies of tofacitinib in patients with RA and no significant differences were seen between treatment groups, including effect on serum transaminases. The most common classes of treatment emergent AEs throughout the study were infections/infestations and gastrointestinal disorders. Three SAEs were reported during the course of the study, one case each of pneumonia, right hip arthritis aggravation and bacterial pneumonia. None of these cases occurred in patients receiving atorvastatin.

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 1.3 million people in the U.S. [1] and one percent of the adult population worldwide.[2]

About Tofacitinib

Tofacitinib is a novel, oral Janus kinase (JAK) inhibitor that is being investigated as a targeted immunomodulator and disease-modifying therapy for RA. More than 4,000 RA patients have been treated with tofacitinib in clinical trials to date. Unlike more recent therapies for RA, which are directed at extracellular targets such as pro-inflammatory cytokines, tofacitinib takes a novel approach, targeting the intracellular signaling pathways that operate as hubs in the inflammatory cytokine network.

Pfizer is studying tofacitinib for RA in the Phase 3 ORAL (Oral Rheumatoid Arthritis Phase 3 TriaLs) program at more than 350 locations in 35 countries worldwide. The ORAL Trials program consists of five completed pivotal trials and one ongoing Phase 3 trial. In addition, tofacitinib is being investigated in an ongoing long-term open-label treatment study.

Pfizer is also studying orally administered tofacitinib in psoriasis, inflammatory bowel disease (Crohn’s disease and ulcerative colitis) and renal transplant, and topical tofacitinib in both psoriasis and dry eye disease.

Important U.S. Prescribing Information for Lipitor (atorvastatin calcium)

LIPITOR is a prescription medicine that is used along with a low-fat diet, and when diet and exercise are not enough to lower the LDL ("bad" cholesterol) and triglycerides in your blood. It can raise HDL ("good" cholesterol) as well. LIPITOR can lower the risk for heart attack, stroke, certain types of heart surgery, and chest pain in patients who have heart disease or risk factors for heart disease such as age, smoking, high blood pressure, low HDL, or family history of early heart disease.

LIPITOR can lower the risk for heart attack or stroke in patients with diabetes and risk factors such as diabetic eye or kidney problems, smoking, or high blood pressure.

LIPITOR is not for everyone. It is not for those with liver problems. And it is not for women who are nursing, pregnant or may become pregnant.

Patients taking LIPITOR should tell their doctor if they feel any new muscle pain or weakness. This could be a sign of rare but serious muscle side effects. Patients should tell their doctor about all medications they take. This may help avoid serious drug interactions. Doctors should do blood tests to check your liver function before and during treatment and may adjust the dose. Common side effects are diarrhea, upset stomach, muscle and joint pain, and changes in some blood tests.

For additional product information, visit www.Lipitor.com.

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DISCLOSURE NOTICE: The information contained in this release is as of May 24, 2011. 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 product in development, tofacitinib, including its potential benefits as a treatment for rheumatoid arthritis, certain other diseases and renal transplant, that involves substantial risks and uncertainties. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development; decisions by regulatory authorities regarding whether and when to approve any drug applications that may be filed for tofacitinib 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, 2010 and in its reports on Form 10-Q and Form 8-K.

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[1] Arthritis Today. "What is Rheumatoid Arthritis." Accessed 24 February 2011. Available at: http://www.arthritistoday.org/conditions/rheumatoid-arthritis/all-about-ra/what-is-ra.php.

[2] Rubbert-Roth A, Finckh A. Treatment options in patients with rheumatoid arthritis failing initial TNF inhibitor therapy: a critical review. Arthritis Res Ther. 2009; 11(Suppl 1): S1.Published online 2009 April 6. doi: 10.1186/ar2662.

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