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New Ulcerative Colitis Data for XELJANZ® (tofacitinib) at Upcoming Gastroenterology Congresses

Monday, October 16, 2017 - 09:10am

Pfizer Inc. (NYSE:PFE) announced today that a total of 10 abstracts on XELJANZ® (tofacitinib) in ulcerative colitis (UC) will be presented at the World Congress of Gastroenterology at the American College of Gastroenterology (WCOG at ACG2017) (October 13-18, Orlando, Florida) and the 25th United European Gastroenterology (UEG) Week (October 28–November 1, Barcelona, Spain).
“We are pleased to share this informative data with the gastroenterology community as it deepens our knowledge of tofacitinib in UC and the multi-faceted needs of patients living with the condition,” said Michael Corbo, Chief Development Officer, Inflammation & Immunology, Pfizer Global Product Development.

Pfizer-sponsored research for tofacitinib, which is not currently approved for the treatment of UC, will be presented at the WCOG at ACG2017 and UEG Week. The data include the following presentations:

WCOG at ACG2017 (Times shown in EDT)

Poster Presentations
• Symptomatic Improvement within 3 Days with Tofacitinib Induction Therapy in Patients with Ulcerative Colitis: Results from OCTAVE Induction 1 and 2 [#P418, Sunday, October 15, 2017: 3:30-7:00p.m.]
• Efficacy of Tofacitinib in Patients with Ulcerative Colitis by Prior Tumor Necrosis Factor Inhibitor Treatment Status: Results from OCTAVE Induction and Maintenance Studies [#P449; Sunday, October 15, 2017: 3:30-7:00p.m.]
• Tofacitinib for Maintenance Therapy in Patients with Active Ulcerative Colitis in the Phase 3 OCTAVE Sustain Trial: Results by Local and Central Endoscopic Assessments [#P416; Sunday, October 15, 2017: 3:30-7:00p.m.]
• The Effectiveness of Zoster Vaccine in Patients Subsequently Treated with Tofacitinib [#P2163, Tuesday, October 17, 2017: 10:30a.m.-4:30p.m.]
• Tofacitinib, an Oral Janus Kinase Inhibitor, in the Treatment of Ulcerative Colitis: Open-Label, Long-Term Extension Study [#P2129; Tuesday, October 17, 2017: 10:30a.m.-4:30p.m.]
• An Updated Analysis of In Vitro Cytokine Inhibition Profiles of a Number of Janus Kinase Inhibitors at Clinically Meaningful Concentrations [#P2154; Tuesday, October 17, 2017: 10:30a.m.-4:30p.m.]
• Integrated Safety Analyses of Tofacitinib in Ulcerative Colitis Clinical Trials [#P2146; Tuesday, October 17, 2017: 10:30a.m.-4:30p.m.]
• Pregnancy Outcomes in the Tofacitinib Ulcerative Colitis OCTAVE Studies [#P2155; Tuesday, October 17, 2017: 10:30a.m.-4:30p.m.]

Oral Presentation
• Herpes Zoster Infection in Patients with Ulcerative Colitis Receiving Tofacitinib [#78, Wednesday, October 18, 2017: 9:20-9:30a.m.]

UEG Week (Times shown in UTC)

Poster Presentations
• Comparative Efficacy and Safety of Tofacitinib and Biologics as Induction Therapy for Moderately to Severely Active Ulcerative Colitis: A Systematic Review and Network Meta-Analysis [#P0407, Monday, October 30, 2017: 9:00a.m.-5:00p.m.]
• Pregnancy Outcomes in the Tofacitinib Ulcerative Colitis OCTAVE Studies [#P0394; Monday, October 30, 2017: 9:00a.m.-5:00p.m.] Encore presentation from the WCOG at ACG2017

Oral Presentations
• Tofacitinib, an Oral Janus Kinase Inhibitor, in the Treatment of Ulcerative Colitis: Open-Label, Long-Term Extension Study [#OP095; Monday, October 30, 2017: 3:45-5:15p.m.] Encore presentation from the WCOG at ACG2017
• Tofacitinib for Maintenance Therapy in Patients with Active Ulcerative Colitis in the Phase 3 OCTAVE Sustain Trial: Results by Local and Central Endoscopic Assessments [#OP059; Monday, October 30, 2017: 2:00-3:30p.m.] Encore presentation from the WCOG at ACG2017
• An Updated Analysis of In Vitro Cytokine Inhibition Profiles of a Number of Janus Kinase Inhibitors at Clinically Meaningful Concentrations [#OP222; Tuesday, October 31, 2017: 10:30a.m.-12:00p.m.] Encore presentation from the WCOG at ACG2017
• Integrated Safety Analyses of Tofacitinib in Ulcerative Colitis Clinical Trials [#OP353; Wednesday, November 1, 2017: 10:30a.m.-12:00p.m.] Encore presentation from the WCOG at ACG2017

About Ulcerative Colitis

UC is a chronic, debilitating and often misunderstood inflammatory bowel disease that affects millions of people worldwide. [1,2] Symptoms of UC can include chronic diarrhea with blood and mucus, abdominal pain and cramping, fever and weight loss. [3a,4] While the exact cause of UC is unknown, it is believed to be the result of complex interactions between multiple factors that include genetic predisposition and an exaggerated immune response to a microbial trigger.[5] UC can have a significant effect on work, family and social activities. [6] Despite receiving treatment, half of patients continue to experience symptoms.[7] Under these circumstances, surgery to remove the colon (colectomy), may be considered for some patients.[3b]

About Tofacitinib
Tofacitinib is a Janus kinase (JAK) inhibitor. Applications for tofacitinib for the treatment of moderately to severely active UC are currently under review by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA). It is not currently approved for the treatment of UC.
As the developer of tofacitinib, Pfizer is a leader in JAK science and is committed to enhancing understanding of tofacitinib through robust clinical development programs in the treatment of immune-mediated inflammatory conditions.

INDICATION
Rheumatoid Arthritis
• XELJANZ/XELJANZ XR (tofacitinib) is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate. It may be used as monotherapy or in combination with methotrexate or other nonbiologic disease-modifying antirheumatic drugs (DMARDs).
• Limitations of Use: Use of XELJANZ/XELJANZ XR in combination with biologic DMARDs or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

IMPORTANT SAFETY INFORMATION
BOXED WARNING: SERIOUS INFECTIONS AND MALIGNANCY
SERIOUS INFECTIONS

Patients treated with XELJANZ/XELJANZ XR are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.
If a serious infection develops, interrupt XELJANZ/XELJANZ XR until the infection is controlled.
Reported infections include:
• Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before XELJANZ/XELJANZ XR use and during therapy. Treatment for latent infection should be initiated prior to XELJANZ/XELJANZ XR use.
• Invasive fungal infections, including cryptococcosis and pneumocystosis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.
• Bacterial, viral, and other infections due to opportunistic pathogens.
The risks and benefits of treatment with XELJANZ/XELJANZ XR should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.
Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with XELJANZ/XELJANZ XR, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

MALIGNANCIES
Lymphoma and other malignancies have been observed in patients treated with XELJANZ. Epstein Barr Virus-associated post-transplant lymphoproliferative disorder has been observed at an increased rate in renal transplant patients treated with XELJANZ and concomitant immunosuppressive medications.

WARNINGS AND PRECAUTIONS
SERIOUS INFECTIONS

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ/XELJANZ XR in patients with an active, serious infection, including localized infections. Consider the risks and benefits of treatment before initiating XELJANZ/XELJANZ XR in patients:
• with chronic or recurrent infection;
• who have been exposed to tuberculosis (TB);
• with a history of a serious or an opportunistic infection;
• who have lived or traveled in areas of endemic TB or mycoses; or
• with underlying conditions that may predispose them to infection.
Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with XELJANZ/XELJANZ XR. XELJANZ/XELJANZ XR should be interrupted if a patient develops a serious infection, an opportunistic infection, or sepsis.

Caution is also recommended in patients with a history of chronic lung disease, or in those who develop interstitial lung disease, as they may be more prone to infection.
Risk of infection may be higher with increasing degrees of lymphopenia and consideration should be given to lymphocyte counts when assessing individual patient risk of infection.

Tuberculosis
Evaluate and test patients for latent or active infection prior to and per applicable guidelines during administration of XELJANZ/XELJANZ XR. Consider anti-TB therapy prior to administration of

XELJANZ/XELJANZ XR in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed, and for patients with a negative test for latent TB but who have risk factors for TB infection. Treat patients with latent TB with standard therapy before administering XELJANZ/XELJANZ XR.

Viral Reactivation
Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster), was observed in clinical studies with XELJANZ. Screening for viral hepatitis should be performed in accordance with clinical guidelines before starting therapy with XELJANZ/XELJANZ XR. The risk of herpes zoster is increased in patients treated with XELJANZ/XELJANZ XR and appears to be higher in patients treated with XELJANZ in Japan and Korea.
MALIGNANCY and LYMPHOPROLIFERATIVE DISORDERS

Consider the risks and benefits of XELJANZ/XELJANZ XR treatment prior to initiating therapy in patients with a known malignancy other than a successfully treated non-melanoma skin cancer (NMSC) or when considering continuing XELJANZ/XELJANZ XR in patients who develop a malignancy.

In the 7 controlled rheumatoid arthritis clinical studies, 11 solid cancers and 1 lymphoma were diagnosed in 3328 patients receiving XELJANZ with or without DMARD, compared to 0 solid cancers and 0 lymphomas in 809 patients in the placebo with or without DMARD group during the first 12 months of exposure. Lymphomas and solid cancers have also been observed in the long-term extension studies in rheumatoid arthritis patients treated with XELJANZ.
In Phase 2B controlled dose-ranging trials in de-novo renal transplant patients, all of whom received induction therapy with basiliximab, high-dose corticosteroids, and mycophenolic acid products, Epstein Barr Virus-associated post-transplant lymphoproliferative disorder was observed in 5 out of 218 patients treated with XELJANZ (2.3%) compared to 0 out of 111 patients treated with cyclosporine.
Other malignancies were observed in clinical studies and the post-marketing setting including, but not limited to, lung cancer, breast cancer, melanoma, prostate cancer, and pancreatic cancer.

Non-Melanoma Skin Cancer
Non-melanoma skin cancers (NMSCs) have been reported in patients treated with XELJANZ. Periodic skin examination is recommended for patients who are at increased risk for skin cancer.
GASTROINTESTINAL PERFORATIONS
Gastrointestinal perforations have been reported in XELJANZ rheumatoid arthritis clinical trials, although the role of JAK inhibition is not known. 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).
LABORATORY ABNORMALITIES

Lymphocyte Abnormalities
Treatment with XELJANZ was associated with initial lymphocytosis at 1 month of exposure followed by a gradual decrease in mean lymphocyte counts of approximately 10% during 12 months of therapy. Counts less than 500 cells/mm3 were associated with an increased incidence of treated and serious infections. Avoid initiation of XELJANZ/XELJANZ XR treatment in patients with a count less than 500 cells/mm3. In patients who develop a confirmed absolute lymphocyte count less than 500 cells/mm3, treatment with XELJANZ/XELJANZ XR is not recommended. Monitor lymphocyte counts at baseline and every 3 months thereafter.

Neutropenia
Treatment with XELJANZ was associated with an increased incidence of neutropenia (less than 2000 cells/mm3) compared to placebo. Avoid initiation of XELJANZ/XELJANZ XR treatment in patients with an ANC less than 1000 cells/mm3. For patients who develop a persistent ANC of 500-1000 cells/mm3, interrupt

XELJANZ/XELJANZ XR dosing until ANC is greater than or equal to 1000 cells/mm3. In patients who develop an ANC less than 500 cells/mm3, treatment with XELJANZ/XELJANZ XR is not recommended. Monitor neutrophil counts at baseline and after 4-8 weeks of treatment and every 3 months thereafter.

Anemia
Avoid initiation of XELJANZ/XELJANZ XR treatment in patients with a hemoglobin level less than 9 g/dL. Treatment with XELJANZ/XELJANZ XR should be interrupted in patients who develop hemoglobin levels less than 8 g/dL or whose hemoglobin level drops greater than 2 g/dL on treatment. Monitor hemoglobin at baseline and after 4-8 weeks of treatment and every 3 months thereafter.

Liver Enzyme Elevations
Treatment with XELJANZ was associated with an increased incidence of liver enzyme elevation compared to placebo. Most of these abnormalities occurred in studies with background DMARD (primarily methotrexate) therapy.
Routine monitoring of liver tests and prompt investigation of the causes of liver enzyme elevations is recommended to identify potential cases of drug-induced liver injury. If drug-induced liver injury is suspected, the administration of XELJANZ/XELJANZ XR should be interrupted until this diagnosis has been excluded.

Lipid Elevations
Treatment with XELJANZ was associated with increases in lipid parameters, including total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol. Maximum effects were generally observed within 6 weeks.
Assess lipid parameters approximately 4-8 weeks following initiation of XELJANZ/XELJANZ XR therapy, and manage patients according to clinical guidelines for the management of hyperlipidemia.

VACCINATIONS
Avoid use of live vaccines concurrently with XELJANZ/XELJANZ XR. The interval between live vaccinations and initiation of tofacitinib therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. A varicella virus-naïve patient experienced dissemination of the vaccine strain of varicella zoster virus 16 days after vaccination with live attenuated virus vaccine which was 2 days after 5 mg twice daily treatment with tofacitinib. The patient recovered after discontinuation of tofacitinib and treatment with antiviral medication. Update immunizations in agreement with current immunization guidelines prior to initiating XELJANZ/XELJANZ XR therapy.

GENERAL
Specific to XELJANZ XR
Caution should be used when administering XELJANZ XR to patients with pre-existing severe gastrointestinal narrowing. There have been rare reports of obstructive symptoms in patients with known strictures in association with the ingestion of other drugs utilizing a non-deformable extended release formulation.

HEPATIC and RENAL IMPAIRMENT
Use of XELJANZ/XELJANZ XR in patients with severe hepatic impairment is not recommended. The recommended dose in patients with moderate hepatic impairment or with moderate or severe renal impairment is XELJANZ 5 mg once daily.

ADVERSE REACTIONS
The most common serious adverse reactions were serious infections. The most commonly reported adverse reactions during the first 3 months in controlled clinical trials with XELJANZ 5 mg twice daily and placebo, respectively, (occurring in greater than or equal to 2% of patients treated with XELJANZ with or without DMARDs) were upper respiratory tract infections (4.5%, 3.3%), headache (4.3%, 2.1%), diarrhea (4.0%, 2.3%),

and nasopharyngitis (3.8%, 2.8%).

USE IN PREGNANCY
There are no adequate and well-controlled studies in pregnant women and the estimated background risks of major birth defects and miscarriage for the indicated population is unknown. Based on animal studies, tofacitinib has the potential to affect a developing fetus. Women of reproductive potential should be advised to use effective contraception.

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 health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care 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, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and 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 October 16, 2017. 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 adult patients with moderately to severely active UC (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; uncertainties regarding the commercial success of XELJANZ and XELJANZ XR; whether and when any applications for the potential indication may be filed with regulatory authorities in any additional jurisdictions; whether and when the FDA and the EMA will approve the applications pending for the potential indication and whether and when regulatory authorities in any jurisdictions may approve any such other applications and/or any other applications that are pending or may be filed for XELJANZ or XELJANZ XR, 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, 2016 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.

[1]Loftus E. Clinical Epidemiology of Inflammatory Bowel Disease:
Incidence, Prevalence, and Environmental Influences. Gastroenterology. 2004;126:1504–1517.
[2]Kappelman MD, et al. Recent trends in the prevalence of Crohn’s disease and ulcerative colitis in a

commercially insured US population. Digestive Diseases and Sciences. 2013;58:519–525.

[3]Crohn’s & Colitis Foundation. Updated IBD Factbook. 2014. http://www.crohnscolitisfoundation.org/assets/pdfs/updatedibdfactbook.pdf. Accessed 14 September 2017.

a) Page 6/ Column 1/ Table 1

b) Page 13/ Column 1/ Lines 8-9

[4]Crohn’s & Colitis Foundation. What is Ulcerative Colitis? http://www.crohnscolitisfoundation.org/what-are-crohns-and-colitis/what-is-ulcerative-colitis/?referrer=https://www.google.com/ Accessed 14 September 2017.

[5]Sartor RB. Mechanisms of Disease: pathogenesis of Crohn's disease and ulcerative colitis. Nature Clinical Practice Gastroenterology & Hepatology. 2006;3:390-407.

[6]Louis E, Roughly A, Thakkar R, et al. Impact of ulcerative colitis on patient quality of life in a real-world clinical setting. Presented at ECCO Congress 2013, Vienna, Austria. P180. https://www.ecco-ibd.eu/index.php/publications/congress-abstract-s/abstracts-2013/item/p180-impact-of-ulcerative-colitis-on-patient-quality-of-life-in-a-real-world-clinical-setting.html.

[7]Moss A. Residual inflammation and ulcerative colitis in remission. Gastroenterology & Hepatology. 2014; Volume 10, Issue 3: 181-183.

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