New Safety and Long-Term Efficacy Data from Baricitinib Clinical Trials in Patients with Moderate-to-Severe Rheumatoid Arthritis Presented at EULAR 2017

June 16, 2017

INDIANAPOLIS, June 16, 2017 /CNW/ -- Eli Lilly and Company (NYSE: LLY) and Incyte Corporation (NASDAQ: INCY) today announced a new pooled analysis of data from eight Olumiant® (baricitinib) clinical trials, showing that baricitinib-treated and placebo-treated patients with moderate-to-severe rheumatoid arthritis (RA) had similar rates of serious infection incidents. Additionally, new data from the long-term extension (LTE) of Phase 3 trials showed that two years of baricitinib treatment significantly lowered the rate of joint damage progression and maintained an overall low disease activity (LDA) throughout the treatment period in these patients. These results were presented at an oral presentation and two poster presentations at the Annual European Congress of Rheumatology (EULAR 2017) in Madrid.

"We are pleased to present these data, which support the evidence that baricitinib may be a potential long-term, oral treatment option for people with moderate-to-severe RA, many of whom are not achieving treatment goals with existing therapies," said James McGill, M.D., distinguished medical fellow and global brand development leader, Lilly Bio-Medicines. "We are hopeful that baricitinib may help to meet the needs of healthcare providers and their patients with RA as they work toward achieving overall treatment goals."

Pooled infection data from 8 clinical trials

A pooled analysis of data from eight completed baricitinib clinical trials (four Phase 3, three Phase 2, one Phase 1) and one LTE study showed that there were similar incidence rates (IR) of severe infection events between the baricitinib and placebo groups.

- Specifically, during the first 24 weeks of treatment, in six trials, incidence rates of serious infections in the baricitinib (4 mg) and placebo groups were 3.8 and 4.2 per 100 patient-years (IR/100 PY), respectively. Additionally, the study also showed that in a set of four clinical trials, IRs of serious infections per 100 PY in the 2 mg and 4 mg groups were 4.2 and 5.7, respectively, compared to 5.1 in the placebo group in this set.
- The study also identified that concomitant corticosteroids use, prior biologics use, non-normal BMI, Asian region of enrollment, and advancing age are the key risk factors for serious infections.

"Rheumatoid arthritis is a chronic disease that is often associated with serious infections," said Kevin L. Winthrop, M.D., M.P.H., assistant professor at Oregon Health and Science University. "These results suggest that baricitinib treatment may not increase the incidence of serious infections in patients with moderate-to-severe rheumatoid arthritis compared to placebo."

Efficacy data from long-term extension study

Two presentations from a LTE study of baricitinib in moderate-to-severe RA patients showed the continued efficacy and long-term benefit with two years of treatment.

- Specifically, one of the analyses showed that at two years, progression of structural joint damage, measured by change in the van der Heijde modified total sharp score (mTSS), was significantly lower in patients treated with baricitinib throughout the two-year period compared to those who were first treated with placebo or methotrexate before switching to baricitinib.
- A second analysis of up to two years in a long-term extension study showed that among patients treated with baricitinib for up to three years, the proportion of patients with low disease activity (LDA) at 24 weeks in different treatment groups across trials remained similar or increased up to three years. Additionally, the results also showed that most patients who had responded to treatment before entering the long-term extension study maintained their response throughout the two-year extension period.
    - In this study, achieving a Simplified Disease Activity Index (SDAI) score ≤11 was considered as LDA.

"These data suggest the potential of baricitinib as an option to control the progression of joint damage and overall disease activity, which is important because long-term control is a key goal in chronic inflammatory diseases like rheumatoid arthritis," said Steven Stein, M.D., chief medical officer, Incyte Corporation.

Baricitinib was approved in February 2017 for the treatment of adults with moderate-to-severe RA in the European Union and is marketed as Olumiant®.

INDICATIONS AND USAGE FOR OLUMIANT

Therapeutic indications
Olumiant is indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs. Olumiant may be used as monotherapy or in combination with methotrexate.

IMPORTANT SAFETY INFORMATION FOR OLUMIANT

CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients.
Pregnancy.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Infections
Baricitinib is associated with an increased rate of infections such as upper respiratory tract infections compared to placebo. In treatment naïve patients, combination with methotrexate resulted in increased frequency of infections compared to baricitinib monotherapy. The risks and benefits of treatment with Olumiant should be carefully considered prior to initiating therapy in patients with active, chronic or recurrent infections. If an infection develops, the patient should be monitored carefully and Olumiant therapy should be temporarily interrupted if the patient is not responding to standard therapy. Olumiant treatment should not be resumed until the infection resolves.

Tuberculosis
Patients should be screened for tuberculosis (TB) before starting Olumiant therapy. Olumiant should not be given to patients with active TB. Anti-TB therapy should be considered prior to initiation of Olumiant in patients with previously untreated latent TB.

Haematological Abnormalities
Absolute Neutrophil Count (ANC) < 1 x 10^9 cells/L, Absolute Lymphocyte Count (ALC) < 0.5 x 10^9 cells/L and haemoglobin < 8 g/dL were reported in less than 1% of patients in clinical trials. Treatment should not be initiated, or should be temporarily interrupted, in patients with an ANC < 1 x 10^9 cells/L, ALC < 0.5 x 10^9 cells/L or haemoglobin < 8 g/dL observed during routine patient management.

The risk of lymphocytosis is increased in elderly patients with rheumatoid arthritis. Rare cases of lymphoproliferative disorders have been reported.

Viral Reactivation
Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster, herpes simplex), were reported in clinical studies. Herpes zoster was reported more commonly in patients ≥ 65 years of age who had previously been treated with both biologic and conventional DMARDs. If a patient develops herpes zoster, Olumiant treatment should be temporarily interrupted until the episode resolves.

Screening for viral hepatitis should be performed in accordance with clinical guidelines before starting therapy with Olumiant. Patients with evidence of active hepatitis B or C infection were excluded from clinical trials. Patients, who were positive for hepatitis C antibody but negative for hepatitis C virus RNA, were allowed to participate. Patients with hepatitis B surface antibody and hepatitis B core antibody, without hepatitis B surface antigen, were also allowed to participate; such patients should be monitored for expression of hepatitis B virus (HBV) DNA. If HBV DNA is detected, a liver specialist should be consulted to determine if treatment interruption is warranted.

Vaccination
No data are available on the response to vaccination with live or inactivated vaccines in patients receiving baricitinib. Use with live, attenuated vaccines during, or immediately prior to, Olumiant therapy is not recommended. International treatment guidelines on vaccination in rheumatoid arthritis patients should be followed when varicella zoster vaccination is considered prior to treatment with Olumiant.

Lipids
Dose dependent increases in blood lipid parameters were reported in patients treated with baricitinib compared to placebo. Elevations in LDL cholesterol decreased to pre-treatment levels in response to statin therapy. Lipid parameters should be assessed approximately 12 weeks following initiation of Olumiant therapy and thereafter patients should be managed according to international clinical guidelines for hyperlipidaemia. The effect of these lipid parameter elevations on cardiovascular morbidity and mortality has not been determined.

Hepatic transaminase elevations
Increases in alanine transaminase (ALT) and aspartate transaminase (AST) to ≥ 5 and ≥ 10 x upper limit of normal (ULN) were reported in less than 1 % of patients in clinical trials. In treatment-naïve patients, combination with methotrexate resulted in increased frequency of hepatic transaminase elevations compared with baricitinib monotherapy. If increases in ALT or AST are observed during routine patient management and drug-induced liver injury is suspected, Olumiant should be temporarily interrupted until this diagnosis is excluded.

Malignancy
The risk of malignancies including lymphoma is increased in patients with rheumatoid arthritis. Immunomodulatory medicinal products may increase the risk of malignancies including lymphoma. The clinical data are insufficient to assess the potential incidence of malignancies following exposure to baricitinib. Long-term safety evaluations are ongoing.

Laboratory Monitoring
Please refer to the SmPC for laboratory measures and monitoring guidance.

Immunosuppressive Medicinal Products
Combination with biologic DMARDs or other Janus kinase (JAK) inhibitors is not recommended, as a risk of additive immunosuppression cannot be excluded. Data concerning use of baricitinib with potent immunosuppressive medicinal products (e.g., azathioprine, tacrolimus, ciclosporin) are limited and caution should be exercised when using such combinations.

ADVERSE REACTIONS

Undesirable Effects: Summary of safety profile
The most commonly reported adverse drug reactions (ADRs) occurring in ≥ 2% of patients treated with Olumiant monotherapy or in combination with conventional synthetic DMARDs were increased LDL cholesterol (33.6%), upper respiratory tract infections (14.7%) and nausea (2.8%). Infections reported with Olumiant treatment included Herpes zoster.

Please see Summary of Product Characteristics.

About Olumiant
Olumiant® (baricitinib) is a once-daily oral JAK inhibitor currently in clinical studies for inflammatory and autoimmune diseases. There are four known

JAK enzymes: JAK1, JAK2, JAK3 and TYK2. JAK-dependent cytokines have been implicated in the pathogenesis of a number of inflammatory and autoimmune diseases, suggesting that JAK inhibitors may be useful for the treatment of a broad range of inflammatory conditions, including rheumatoid arthritis.

In December 2009, Lilly and Incyte announced an exclusive worldwide license and collaboration agreement for the development and commercialization of baricitinib and certain follow-on compounds for patients with inflammatory and autoimmune diseases. Baricitinib was submitted for regulatory review seeking marketing approval for the treatment of rheumatoid arthritis in the U.S., European Union and Japan in 2016, and was approved in the EU in February 2017.

About Rheumatoid Arthritis
Rheumatoid arthritis (RA) is an autoimmune disease characterized by inflammation and progressive destruction of joints. More than 23 million people worldwide suffer from RA.[i] Approximately three times as many women as men have the disease.[ii] Current treatment of RA includes the use of non-steroidal anti-inflammatory drugs (NSAIDs), oral conventional disease-modifying antirheumatic drugs (cDMARDs) - such as methotrexate, the current standard of care, and injectable and intravenous biological disease-modifying antirheumatic drugs (bDMARDs) that target selected mediators implicated in the pathogenesis of RA.[iii] Despite current treatment options, many patients do not reach their therapeutic goals or are not able to achieve sustained remission.[iv] There remains an important need to provide additional treatment options to improve overall patient care.

About Baricitinib Phase 3 Trials
Lilly and Incyte conducted four successful pivotal Phase 3 clinical trials of baricitinib in patients with moderate- to-severe active rheumatoid arthritis to support regulatory submission in most countries. Two of the four studies included pre-specified comparisons to approved DMARDs: one to methotrexate (RA-BEGIN) and one to adalimumab (RA-BEAM). An additional Phase 3 study was initiated to support clinical development in China. The clinical trial program includes a wide range of patients including those who are methotrexate-naïve, inadequate responders to methotrexate, inadequate responders to conventional synthetic disease modifying antirheumatic drugs, or inadequate responders to biologic DMARDs including TNF inhibitors. Patients completing any of the Phase 3 studies can enroll in a long-term extension study. For additional information on this clinical trial program, please visit www.clinicaltrials.gov.

About Incyte
Incyte Corporation is a Wilmington, Delaware-based biopharmaceutical company focused on the discovery, development and commercialization of proprietary therapeutics. For additional information on Incyte, please visit the Company's web site at www.incyte.com.

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About Eli Lilly and Company
Lilly is a global healthcare leader that unites caring with discovery to make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at www.lilly.com and newsroom.lilly.com/social-channels.

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This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about baricitinib as a potential treatment for patients with rheumatoid arthritis, and reflects Lilly's and Incyte's current belief. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there can be no guarantee that baricitinib will receive regulatory approvals or be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's and Incyte's most recent respective Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly and Incyte undertake no duty to update forward-looking statements to reflect events after the date of this release.

[i] WHO Global Burden of Disease Report, (table 7, page 32) 2004, http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf (Accessed: May 16, 2017)

[ii] Arthritis Foundation, What is Rheumatoid Arthritis?, http://www.arthritis.org/about-arthritis/types/rheumatoid-arthritis/what-is-rheumatoid-arthritis.php (Accessed: May 16, 2017)

[iii] Arthritis Foundation, Rheumatoid Arthritis Treatment, http://www.arthritis.org/about-arthritis/types/rheumatoid-arthritis/treatment.php (Accessed: May 16, 2017)

[iv] McWilliams DF, Kiely PDW, Young A, Walsh DA. Baseline factors predicting change from the initial DMARD treatment during the first 2 years of rheumatoid arthritis: experience in the ERAN inception cohort. BMC Musculoskeletal Disorders. 2013;14:1-7.

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