November 2, 2016

New data from pivotal RA-BEACON study show significant improvement in patient-reported outcomes in rheumatoid arthritis patients treated with baricitinib compared to placebo

Phase 3 trial results published in Annals of the Rheumatic Diseases demonstrate baricitinib's significant efficacy in patients with inadequate response to conventional and biologic DMARDs

INDIANAPOLIS, Nov. 2, 2016 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) and Incyte Corporation (NASDAQ: INCY) announced today that new data from RA-BEACON - a pivotal phase 3 study of baricitinib in the treatment of moderate-to-severe rheumatoid arthritis (RA) - showed baricitinib demonstrated significant improvement in patient-reported outcomes and health-related quality of life (HRQOL) measures, fatigue and pain compared with placebo. The results of the study were published in *Annals of the Rheumatic Diseases*. The global trial is part of the ongoing study of baricitinib, a once-daily oral medication currently under regulatory review for the treatment of moderate-to-severe RA.

The RA-BEACON study included patients who had insufficient response or intolerance to previous treatment with biologic disease-modifying antirheumatic drugs (bDMARDs), including tumor necrosis factor (TNF) inhibitors. In these patients, treatment with baricitinib through 24 weeks significantly improved most patient-reported outcomes compared with placebo, and patients receiving baricitinib 4 mg showed the most rapid and greatest change. Previously, baricitinib has also shown significant clinical efficacy in these patients.[i]

HRQOL was assessed using the 36-Item Short Form Health Survey (SF-36), a patient-reported instrument that collects information in multiple domains, including physical function, bodily pain, general health, limitation in role, vitality and social functioning. The SF-36 reports physical and mental component scores. Results of the study showed that:

- At week 12, a clinically important improvement (≥5) in the physical component score was achieved by
  - 49 percent (p≤0.001) of patients taking baricitinib 2 mg;
  - 53 percent (p≤0.001) of patients taking baricitinib 4 mg; and
  - 32 percent of patients in the placebo group.
- At week 24, a clinically important improvement (≥5) in the physical component score was achieved by
  - 39 percent (p≤0.001) of patients taking baricitinib 2mg;
  - 45 percent (p≤0.001) of patients taking baricitinib 4 mg; and
  - 21 percent of patients in the placebo group.

"These positive results from the RA-BEACON study, which assessed outcomes that impact health-related quality of life, fatigue and pain, reinforce baricitinib's potential to address an unmet need for patients with rheumatoid arthritis whose previous treatment with biologics failed," said Terence Rooney, M.D., Lilly's senior medical director for baricitinib. "If approved, baricitinib may help address some of the challenges patients with rheumatoid arthritis who are not achieving remission or low disease activity with their current biologic therapy face when performing daily activities."

At week 4, in patients treated with baricitinib (2 mg and 4 mg doses), the improvement in the physical component score of SF-36 was statistically significant compared to the improvement seen in the placebo group. This improvement was sustained through week 24 for both baricitinib doses.

Both doses of baricitinib (2 mg and 4 mg) also significantly improved fatigue as early as week 4 compared to placebo, and the greater improvement compared to placebo was maintained throughout the study. The study also showed that baricitinib treatment resulted in significant reductions in the duration of morning joint stiffness as early as week 1 (for 4 mg dose) compared to placebo, and the greater improvement compared to placebo was maintained throughout the study. There were also significant improvements in physical functioning and pain in the baricitinib-treated groups at week 12 and week 24, compared with placebo.

The differences in improvement in Patient's Global Assessment of Disease Activity and disability were evident as early as week 1 in the baricitinib-treated groups versus placebo. For patient's assessment of pain, only baricitinib 4 mg was shown to be statistically significantly different from placebo at week 1.

"In addition to symptoms associated with inflammation, patients with RA commonly suffer from impaired physical function and fatigue, which can significantly impact their quality of life," said Steven Stein, M.D., chief medical officer, Incyte Corporation. "It's encouraging to see that treatment with baricitinib, at both doses studied, improves the debilitating symptoms experienced by patients with RA, especially in those for whom biologic DMARDs have not been effective."

The RA-BEACON study enrolled 527 patients who previously had failed at least one TNF inhibitor, and included 199 patients who also had received prior treatment with one or more non-anti-TNF biologic agents. Patients received baricitinib 4 mg (n=177) or 2 mg (n=174) or placebo (n=176) daily, in addition to their existing background therapies, for 24 weeks. Clinical efficacy and safety results from the RA-BEACON study were published earlier this year in the *New England Journal of Medicine*.[i]

In RA-BEACON, through 24 weeks, 77 percent of patients on baricitinib 4 mg and 71 percent of patients on baricitinib 2 mg experienced treatment-emergent adverse events (AEs), compared to 64 percent of patients in the placebo group. Discontinuation rates due to AEs were 6 percent, 4 percent and 4 percent, respectively. The most common AEs reported for baricitinib-treated patients included headache, upper respiratory infections and nasopharyngitis. There were no cases of tuberculosis or gastrointestinal perforations. Rates of serious adverse events (SAEs) were 10 percent for baricitinib 4 mg, 4 percent for baricitinib 2 mg and 7 percent for placebo. One death was reported in the baricitinib 4 mg dose group (stroke). A large majority of patients completing this 6-month trial opted to participate in a long-term extension study.

About Baricitinib
Baricitinib is a once-daily oral highly selective JAK1 and JAK2 inhibitor currently in late-stage 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. Baricitinib demonstrates approximately 100-fold greater potency of inhibition against JAK1 and JAK2 than JAK3 in kinase assays.

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 Q1 2016, and is being studied in phase 2 trials for atopic dermatitis and systemic lupus erythematosus.

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

About Baricitinib Phase 3 Trials
Lilly and Incyte conducted four pivotal phase 3 clinical trials of baricitinib in patients with moderately-to-severely active rheumatoid arthritis to support regulatory submission in most countries. 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 disease-modifying antirheumatic drugs, or inadequate responders to TNF inhibitors. Patients completing any of the five 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 rheumatoid arthritis and the RA-BEACON trial, and reflects Lilly 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 future study results will be consistent with study findings to-date, or that baricitinib will receive regulatory approvals or prove to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's and Incyte's most recent Form 10-K and 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] Baricitinib in Patients with Refractory Rheumatoid Arthritis, *New England Journal of Medicine*, http://www.nejm.org/doi/full/10.1056/NEJMoa1507247 (Accessed September 15, 2016)

[ii] American College of Rheumatology, Rheumatoid Arthritis, http://www.rheumatology.org/practice/clinical/patients/diseases_and_conditions/ra.asp (Accessed: September 15, 2016)

[iii] Hand Clinics, *Advances in the Medical Treatment of Rheumatoid Arthritis*, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3135413/pdf/nihms305780.pdf (Accessed: September 15, 2016)

[iv] 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 September 15, 2016)

[v] Arthritis Foundation, Medications for Rheumatoid Arthritis, http://www.arthritistoday.org/about-arthritis/types-of-arthritis/rheumatoid-arthritis/treatment-plan/medication-overview/ra-medications.php (Accessed: September 15, 2016)

[vi] Rheumatoid arthritis, *Lancet,* https://www.ncbi.nlm.nih.gov/pubmed/27156434 (Accessed: September 15, 2016)

[vii] Sustained rheumatoid arthritis remission is uncommon in clinical practice, *Arthritis Research & Therapy*, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3446437/ (Accessed: September 15, 2016)

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