Patient-reported outcomes across phase 3 studies of baricitinib demonstrate statistically significant improvements in physical function and quality of life symptoms in patients with rheumatoid arthritis (RA)

June 9, 2016

*Pivotal trials show treatment with baricitinib resulted in significant improvements in pain, fatigue and ability to perform daily activities compared to methotrexate - the current standard of care - and adalimumab (Humira®)**

INDIANAPOLIS, June 9, 2016 /CNW/ -- Eli Lilly and Company (NYSE: LLY) and Incyte Corporation (NASDAQ: INCY) today announced that in two phase 3 trials patients with rheumatoid arthritis (RA) treated with baricitinib reported significant improvements in quality of life symptoms and other patient-reported outcomes compared to methotrexate or adalimumab (Humira®). Patients with RA also reported improvement in productivity at work. In these studies, significant improvements in patient-reported measures, including pain, physical function, tiredness and morning joint stiffness, were observed as early as one week after initial treatment with baricitinib. These findings were presented today at the Annual European Congress of Rheumatology (EULAR 2016) in London.

Key findings include:

- In the phase 3 RA-BEGIN trial:
  - At 24 weeks, 81 percent of patients receiving baricitinib monotherapy and 79 percent of patients receiving baricitinib plus methotrexate had clinically meaningful improvement in physical function compared with 70 percent among those receiving methotrexate alone ($p < 0.05$). Clinically meaningful improvement was defined as an improvement in Health Assessment Questionnaire-Disability Index (HAQ-DI) score of ≥0.22.
  - At 52 weeks, 68 percent of patients on baricitinib monotherapy and 72 percent of patients on baricitinib in combination with methotrexate saw clinically meaningful improvements in physical function compared to 57 percent of those treated with methotrexate alone ($p < 0.05$).
  - At 24 and 52 weeks, baricitinib (as monotherapy or in combination with methotrexate) was also associated with significant improvement in pain, and clinically meaningful improvement in fatigue and the physical health components of the quality of life assessment compared with methotrexate alone.
- In the phase 3 RA-BEAM trial, where all patients received background methotrexate therapy:
  - At 12 weeks, 75 percent of patients treated with baricitinib reported clinically meaningful improvement in physical function compared with 71 percent of patients on adalimumab ($p=0.302$). Clinically meaningful improvement was defined as an improvement in HAQ-DI score of ≥0.22.
  - At 24 weeks, 73 percent of patients treated with baricitinib reported clinically meaningful improvement in physical function compared with 64 percent of patients on adalimumab ($p < 0.05$).
  - At 52 weeks, 68 percent of patients treated with baricitinib reported clinically meaningful improvement in physical function compared with 58 percent of patients on adalimumab ($p < 0.01$).
  - At 52 weeks, baricitinib was also associated with significant improvement in pain, and clinically meaningful improvement in fatigue and the physical health components of quality of life compared with adalimumab.
- An analysis of the phase 3 trials found that in each study, patients taking baricitinib have less impairment in work productivity and daily activities compared to patients taking the comparator.

"Our extensive phase 3 clinical trial program demonstrates that baricitinib could, if approved, offer a potentially significant improvement in the treatment of rheumatoid arthritis," said Terence Rooney, M.D., medical director, rheumatoid arthritis, Lilly Bio-Medicines. "In these studies, baricitinib demonstrated superiority on a variety of efficacy measures compared to the leading biologic, adalimumab, as well as the current oral standard of care, methotrexate. Additionally, patients reported their personal experience with baricitinib, further highlighting its positive impact on patients' daily lives and activities."

Physical function was measured using the patient-reported HAQ-DI questionnaire that assesses the ability of a patient to perform daily activities like dressing, eating, walking, grip, etc. Quality of life assessment was made by using the Medical Outcomes Study 36-Item Short Form Health Survey Version 2 Acute, or SF-36, which is a patient-reported survey that measures overall health quality based on physical and psychological functioning.

RA-BEGIN demonstrated that in RA patients who had limited or no previous treatment with any disease-modifying antirheumatic drugs (DMARDs), baricitinib used as monotherapy or in combination with methotrexate showed statistically significant improvements in the physical quality of life measures, as measured by the SF-36, when compared to methotrexate alone. Reported improvements in patient quality of life symptoms were accompanied by an increase in physical function, and decreased pain and fatigue. All the improvements with baricitinib were statistically significant at week 24 and week 52, compared to methotrexate alone.

The RA-BEGIN study included patients who had limited or no prior treatment with methotrexate, and were naïve to other conventional or biologic DMARDs. Part of a larger phase 3 program of more than 3,000 RA patients at various points in the RA treatment continuum, RA-BEGIN enrolled

nearly 600 patients who were randomized to one of the following treatment groups:

- Once-weekly oral methotrexate monotherapy
- 4 mg once-daily oral baricitinib monotherapy
- 4 mg once-daily oral baricitinib in combination with once-weekly oral methotrexate.

"Left untreated or uncontrolled, rheumatoid arthritis can dramatically impact patients' quality of life," said Steven Stein, M.D., chief medical officer, Incyte Corporation. "Patients and physicians alike deserve better treatment options beyond today's standard of care. If approved, baricitinib has the potential to become an oral drug option that may improve the clinical symptoms of the disease, as well as patients' ability to perform daily activities at home and at work."

The pivotal phase 3 trial, RA-BEAM, showed that RA patients who had previously responded inadequately to methotrexate and were not treated with any biologic, experienced significant improvement in the physical quality of life measures when taking baricitinib compared to patients treated with adalimumab or placebo. Reported improvements in patient quality of life were accompanied by an increase in physical function, and decreased pain and fatigue. The improvements in physical function, pain and physical quality of life with baricitinib were statistically significant at week 24 and week 52, compared to adalimumab.

RA-BEAM was a 52-week trial of 1,305 patients who had active, moderate-to-severe RA, despite ongoing treatment with methotrexate. Patients were randomized to placebo once-daily (n=488), baricitinib 4 mg once-daily (n=487) or adalimumab 40 mg biweekly (n=330). All patients received background methotrexate. At week 24, patients taking placebo were crossed over to the baricitinib treatment group.

In the baricitinib RA development program, no increases in adverse events leading to study drug discontinuation, malignancies, or serious infections were seen for baricitinib vs. placebo or active comparators during the controlled periods of the program. Herpes zoster was reported more frequently for baricitinib vs. placebo. The incidence rates of malignancy, serious infection and herpes zoster did not increase over time including long-term observations.

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.[i,ii] More than 23 million people worldwide suffer from RA.[iii] 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.[iv] Despite current treatment options, many patients do not reach their therapeutic goals or sustained remission.[v,vi] 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 anti-rheumatic 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-BEGIN and RE-BEAM trials, 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 American College of Rheumatology, Rheumatoid Arthritis, http://www.rheumatology.org/practice/clinical/patients/diseases_and_conditions/ra.asp (Accessed: May 16, 2016)
ii Hand Clinics, *Advances in the Medical Treatment of Rheumatoid Arthritis*, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3135413/pdf/nihms305780.pdf (Accessed: May 16, 2016)
iii 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, 2016)
iv 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: May 16, 2016)
v Rheumatoid arthritis, *Lancet,* https://www.ncbi.nlm.nih.gov/pubmed/27156434 (Accessed: May 19, 2016)
vi Sustained rheumatoid arthritis remission is uncommon in clinical practice, *Arthritis Research & Therapy*, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3446437/ (Accessed: May 19, 2016)