New Analyses of Phase 3 Trials Show Improvements in Rheumatoid Arthritis Symptoms Following Treatment with Baricitinib Across Diverse Population of Patients

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Three post-hoc analyses of two phase 3 studies showed improvements in rheumatoid arthritis symptoms in patients irrespective of age, BMI and number of previously used conventional synthetic DMARDs

INDIANAPOLIS, Nov. 14, 2016 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) and Incyte Corporation (NASDAQ: INCY) today announced new data analyses of two phase 3 trials, RA-BUILD and RA-BEAM, showing that baricitinib treatment resulted in improvements in rheumatoid arthritis (RA) symptoms across a diverse population of patients with RA regardless of age, body mass index (BMI) and previous treatment with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs). Findings were presented today at the American College of Rheumatology (ACR)/Association of Rheumatology Health Professionals (ARHP) Annual Meeting in Washington DC, November 11-16, 2016.

"Multiple patient characteristics may impact the effectiveness of rheumatoid arthritis treatment," said James McGill, M.D., distinguished medical fellow and global brand development leader, Lilly Bio-Medicines. "What these data showed is that regardless of a patient's age, body mass index or previous experience with conventional synthetic DMARDs, treatment with baricitinib resulted in improvement in rheumatoid arthritis symptoms. This gives us tremendous hope for how this oral medication may work in a real-world setting, if approved."

Key findings include:

- Results from a post-hoc analysis of the phase 3 RA-BUILD and RA-BEAM studies evaluating elderly patients found that age did not affect baricitinib's efficacy as measured by ACR20, Health Assessment Questionnaire-Disability Index (HAQ-DI), Disease Activity Score 28 C-Reactive Protein (DAS28-CRP) and Simplified Disease Activity Index (SDAI).
    - At week 12, in the baricitinib 4 mg group, 67 percent of patients younger than 65 years and 68 percent of patients 65 years or older achieved an ACR20 response, meaning a 20 percent improvement across various aspects of RA. In the group that received placebo, 40 percent of patients younger than 65 years and 43 percent of patients 65 years or older achieved an ACR20 response.
    - The percentage of patients reporting an adverse event (AE) was higher in patients 65 years or older. The overall rates of AEs, serious adverse events (SAEs), and serious infections were similar between patients treated with placebo and baricitinib in patients younger than 65 years and patients 65 years or older. Additional safety information regarding RA-BUILD and RA-BEAM are provided in the study description below.
- Results from a post-hoc analysis of the phase 3 RA-BUILD and RA-BEAM studies evaluating the effect of baseline BMI on the response to baricitinib in patients who had insufficient response to previous csDMARDs found that baricitinib improved clinical outcomes compared to placebo regardless of baseline BMI as measured by ACR20, ACR50, ACR70, DAS28-CRP, SDAI and Clinical Disease Activity Index (CDAI). The proportion of patients who reached low disease activity or remission, including progression in structural joint damage, improved compared to placebo across the different BMI groups.
    - Proportion of patients in the low, middle and high BMI groups who achieved an ACR20 response were 68.4 percent, 68 percent and 64.7 percent, respectively. ACR50 and ACR70 responses (meaning a 50 percent and 70 percent improvement across various aspects of RA, respectively) were also improved compared to placebo across the BMI groups. As has been shown for other DMARDs, baricitinib treatment effect for patients with higher BMI was numerically smaller than for patients with lower BMI.
    - Additional safety information regarding RA-BUILD and RA-BEAM are provided in the study description below.
- Results from a post-hoc analysis of the phase 3 RA-BUILD and RA-BEAM studies evaluating whether the number of previous csDMARD failures altered patients' response to baricitinib found that baricitinib demonstrated improvement in RA symptoms irrespective of the number of previous csDMARDs used or the present use of oral corticosteroids as measured by ACR20, ACR50, ACR70, radiographic progression, SDAI and DAS28-ESR.
    - At week 12, in the baricitinib 4 mg groups that previously used methotrexate alone, methotrexate + 1 csDMARD and methotrexate + ≥2 csDMARDs, 67.9 percent, 67.3 percent and 66.9 percent of patients achieved an ACR20 response, respectively. ACR50 responses were also similar across the groups (42.5 percent, 42.9 percent and 39.2 percent, respectively) and ACR70 responses were 21.4 percent, 19.5 percent and 13.3 percent respectively.
    - The rates of SAEs and discontinuation due to AEs were comparable regardless of the number of csDMARDs used and corticosteroid use. Additional safety information regarding RA-BUILD and RA-BEAM are provided in the study description below.

"These data add to the breadth of evidence supporting baricitinib's efficacy profile across a wide range of patient populations," said Steven Stein, M.D., chief medical officer, Incyte Corporation. "If approved, we believe that baricitinib has the potential to become an effective once-daily oral treatment

option for patients with rheumatoid arthritis who may not respond well to other treatments — age, BMI or previous csDMARDs use notwithstanding."

RA-BUILD
The RA-BUILD study enrolled 684 patients with moderate-to-severe RA who previously had an inadequate response to, or were intolerant of, at least one csDMARD and had not received a biologic disease-modifying antirheumatic drug (bDMARD). Patients received either once-daily baricitinib (2 mg or 4 mg) or placebo, in addition to their background therapy.

In RA-BUILD, the incidence of SAEs with baricitinib treatment, including serious infections, was similar to placebo. There were no gastrointestinal perforations in the study. A single case of tuberculosis was reported in a patient receiving baricitinib. The most common adverse events observed were consistent with previous studies of baricitinib in RA. Discontinuation rates due to adverse events were similar between treatment groups.

RA-BEAM
The 52-week RA-BEAM study randomized 1,307 patients who had active, moderate-to-severe RA, despite ongoing treatment with methotrexate. Patients were randomized to once-daily placebo (n=488), once-daily baricitinib 4 mg (n=487) or biweekly adalimumab 40 mg (n=330). All patients received background methotrexate. At week 24, patients taking placebo were crossed over to the baricitinib treatment group.

In RA BEAM, compared to placebo, serious adverse events rates were similar for baricitinib and lower for adalimumab; serious infection rates were similar across groups. There were no cases of gastrointestinal perforations. One event of tuberculosis was reported in each of the baricitinib and adalimumab groups. The most common adverse events observed with baricitinib were nasopharyngitis and bronchitis. Discontinuations due to adverse events occurred with similar frequency across treatment groups.

About Baricitinib
Baricitinib is a once-daily oral selective JAK 1 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.

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 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 patients with rheumatoid arthritis and the RA-BUILD and RA-BEAM trials, and reflects Lilly's and Incyte's current beliefs. 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 the results to date or that baricitinib will achieve its primary study endpoints or receive regulatory approvals. 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 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.