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Lilly and Incyte Provide Update on Baricitinib

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INDIANAPOLIS , July 25, 2017 /PRNewswire/ -- Eli Lilly and Company (NYSE : LLY) and Incyte Corporation (NASDAQ: INCY) announced today that a resubmission to the U.S. Food and Drug Administration (FDA) for the New Drug Application (NDA) for baricitinib, a once-daily oral medication for the treatment of moderate-to-severe rheumatoid arthritis (RA), will be delayed beyond 2017. The companies will be further discussing the path forward with the agency and evaluating options for resubmission, including the potential for an additional clinical study, as requested by the FDA . The length of time to a resubmission for the NDA will depend on which option the companies pursue and further FDA discussions, but is anticipated to be a minimum of 18 months.

"We disagree with the FDA's conclusions, and believe the existing comprehensive clinical data demonstrate there is a positive benefit/risk profile that supports baricitinib's approval as a new treatment option for people suffering from RA in the United States ," said Christi Shaw, president of Lilly Bio-Medicines. "We are disappointed that resubmission will not occur this year, but are committed to bringing baricitinib to people with RA and we will work with the FDA on the path forward."

The FDA has indicated that a new clinical study is necessary for a resubmission in order to further characterize the benefit/risk across doses, in light of the observed imbalance in thromboembolic events that occurred during the placebo-controlled period of the RA clinical program. This request for an additional clinical study does not impact the ongoing clinical trials for baricitinib.

The NDA for RA contained the results of four positive Phase 3 clinical trials that met their primary endpoints and in which 3,100 patients were enrolled, across the full spectrum of RA patients from treatment-naïve to highly-treatment refractory. Thromboembolic events - diagnosed as deep venous thrombosis (DVT) and pulmonary embolism (PE) - were reported in five patients receiving baricitinib during the controlled period of two of seven completed Phase 2 or Phase 3 trials in RA. Although an imbalance was observed during the placebo controlled period of the RA clinical trials, the rate of these events in the overall baricitinib clinical program was consistent with that seen among the general population of treated RA patients.

In the European Union , where baricitinib 2-mg and 4-mg tablets have been approved since February 2017 , the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) recently agreed to update the label with a precaution for patients who have risk factors for DVT and PE. In Japan , where baricitinib was also recently approved, the label includes a similar precaution.

About Baricitinib

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. Baricitinib was approved in the EU in February 2017 . In April 2017 , the U.S. Food and Drug Administration issued a Complete Response Letter on the New Drug Application for baricitinib. Baricitinib was also approved in Kuwait and Switzerland in June 2017 and approved in Japan in July 2017 for the treatment of RA. Baricitinib remains under review in other markets. It is also being studied in Phase 2 trials for atopic dermatitis and systemic lupus erythematosus. The Phase 3 trial for psoriatic arthritis has been delayed and will not begin in 2017 as previously expected.

About Rheumatoid Arthritis

Rheumatoid arthritis is a systemic 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 synthetic disease-modifying antirheumatic drugs (csDMARDs), 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 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 bDMARDs 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 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 baricitinib will receive regulatory approval 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 American College of Rheumatology, Rheumatoid Arthritis, http://www.rheumatology.org/practice/clinical/patients/diseases_and_conditions/ra.asp. Accessed July 21, 2017 .

ⁱⁱ Hand Clinics, *Advances in the Medical Treatment of Rheumatoid Arthritis*, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3135413/pdf/nihms305780.pdf>. Accessed July 21, 2017 .

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 July 21, 2017 .

^{iv} Arthritis Foundation, Medications for Rheumatoid Arthritis, <http://www.arthritis.org/about-arthritis/types-of-arthritis/rheumatoid-arthritis/treatment-plan/medication-overview/ra-medications.php>. Accessed July 21, 2017 .

^v Rheumatoid arthritis, *Lancet*, <https://www.ncbi.nlm.nih.gov/pubmed/27156434>. Accessed July 21, 2017 .

^{vi} Sustained rheumatoid arthritis remission is uncommon in clinical practice, *Arthritis Research & Therapy*, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3446437/>. Accessed July 21, 2017 .

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