FDA Advisory Committee Recommends the Approval of Baricitinib 2mg, but not 4mg, for the Treatment of Moderately-to-Severely Active Rheumatoid Arthritis

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INDIANAPOLIS, April 23, 2018 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) and Incyte Corporation (NASDAQ: INCY) announced today that the U.S. Food and Drug Administration's (FDA) Arthritis Advisory Committee recommended approval of the 2-mg dose of baricitinib, a once-daily oral medication for the treatment of moderately-to-severely active rheumatoid arthritis (RA) for adult patients who have had an inadequate response or intolerance to methotrexate. While the Advisory Committee unanimously supported the efficacy of the 4-mg dose of baricitinib, it did not recommend approval of the 4-mg dose of baricitinib for the proposed indication based on the adequacy of the safety and benefit-risk profiles.

"We are confident that baricitinib, if approved, can help people in the U.S. manage the challenges of living with RA," said Christi Shaw, president of Lilly Bio-Medicines. "While we are disappointed with the Advisory Committee's assessment of the data for the 4-mg dose, we are confident in the positive benefit-risk profile of both the 2-mg and the 4-mg doses. We look forward to continuing our work with the FDA on our New Drug Application (NDA) and are hopeful that baricitinib will receive approval in the coming months."

Baricitinib 2-mg and 4-mg doses are approved in more than 40 countries, including the member states of the European Union and Japan.

For both doses, the Advisory Committee voted to support the assessment that baricitinib's data provide substantial evidence of efficacy. For the 2-mg dose, the Advisory Committee voted in favor of the assessment that baricitinib's safety data adequately support its approval. For the 4-mg dose, the Advisory Committee voted against the assessment that baricitinib's safety data was adequate to support its approval based on the proposed indication.

The Advisory Committee's recommendation was based on baricitinib's global development program, which included four completed Phase 3 studies. In total, 3,492 patients, who represented a range of treatment experiences, received baricitinib in the global RA development program. The Phase 3 studies evaluated baricitinib's treatment impact related to RA signs and symptoms, physical function, joint damage progression and other patient-reported outcomes. The Phase 3 program also evaluated recognized risks for RA patients, including serious infection, malignancy, major adverse cardiovascular events (MACE), venous thromboembolism (VTE), and gastrointestinal perforations, along with key laboratory changes. The safety profile of baricitinib is based on 7,860 patient-years of exposure.

"Despite advances in the management of RA over the last 20 years, which include early treatment, optimized use of traditional therapies for rheumatic disease and the advent of newer medications such as biologics, many patients are still struggling to meet treatment targets, and live with debilitating pain, fatigue and other symptoms of RA," said Peter Taylor, MA, PhD, professor, University of Oxford, an expert who attended the Advisory Committee Meeting. "Baricitinib could be a promising option for RA patients in the U.S. who are not achieving adequate disease control with currently available treatments."

The FDA is not required to follow the Advisory Committee's recommendation, but will consider it during its review of the NDA for baricitinib.

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., the European Union and Japan in 2016. Baricitinib was approved in the EU in February 2017 and in Japan in July 2017. In April 2017, the U.S. Food and Drug Administration issued a Complete Response Letter on the New Drug Application for baricitinib. To date, baricitinib has been approved in more than 40 countries and remains under review in several other markets.

About Rheumatoid Arthritis
Rheumatoid arthritis is a systemic autoimmune disease characterized by inflammation and progressive destruction of joints.[1,2] More than 23 million people worldwide suffer from RA.[3] 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.[4] Despite current treatment options, many patients do not reach their therapeutic goals or sustained remission.[5,6] 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 moderately-to-severely 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 concluded and is under review to support registration 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 were able to 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 www.lilly.com/newsroom/social-channels. P-LLY

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.

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[1]American College of Rheumatology, Rheumatoid Arthritis, http://www.rheumatology.org/practice/clinical/patients/diseases_and_conditions/ra.asp. Accessed April 23, 2018.

[2] Hand Clinics, Advances in the Medical Treatment of Rheumatoid Arthritis, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3135413/pdf/nihms305780.pdf. Accessed April 23, 2018.

[3] 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 April 23, 2018.

[4]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 April 23, 2018.

[5] Rheumatoid arthritis, Lancet, https://www.ncbi.nlm.nih.gov/pubmed/27156434. Accessed April 23, 2018.

[6] Sustained Rheumatoid Arthritis Remission is Uncommon in Clinical Practice, Arthritis Research & Therapy, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3446437/. Accessed April 23, 2018.

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