April 14, 2017

U.S. FDA Issues Complete Response Letter for Baricitinib

INDIANAPOLIS--(BUSINESS WIRE)-- Eli Lilly and Company (NYSE:LLY) and Incyte Corporation (NASDAQ:INCY) announced today that the U.S. Food and Drug Administration (FDA) has issued a complete response letter for the New Drug Application (NDA) of the investigational medicine baricitinib, a once-daily oral medication for the treatment of moderate-to-severe rheumatoid arthritis (RA).

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The letter indicates that the FDA is unable to approve the application in its current form. Specifically, the FDA indicated that additional clinical data are needed to determine the most appropriate doses. The FDA also stated that additional data are necessary to further characterize safety concerns across treatment arms. The companies disagree with the Agency's conclusions. The timing of a resubmission will be based on further discussions with the FDA.

"We are disappointed with this action. We remain confident in the benefit/risk of baricitinib as a new treatment option for adults with moderate-to-severe RA," said Christi Shaw, president of Lilly Bio-Medicines. "We will continue to work with the FDA to determine a path forward and ultimately bring baricitinib to patients in the U.S."

Lilly and Incyte submitted the NDA for baricitinib to the FDA in January 2016, and in January 2017 announced the FDA's three-month extension to allow time for review of additional data analyses.

Lilly is reaffirming both its financial guidance for 2017 and its mid-term guidance for the remainder of this decade. Incyte is evaluating the impact of the complete response on its previously-issued milestone and R&D expense guidance for 2017; any update will be provided on its Q1 2017 earnings call.

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, and was approved in the EU in February 2017. It is being studied in phase 2 trials for atopic dermatitis and systemic lupus erythematosus, and a phase 3 trial for patients with psoriatic arthritis is expected to be initiated in 2017.

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 biologic DMARDs 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 achieve its primary endpoints, receive regulatory approvals, 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 December 5, 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 December 5, 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. Acce Accessed December 5, 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 December 5, 2016.

[v] Rheumatoid arthritis, *Lancet,* https://www.ncbi.nlm.nih.gov/pubmed/27156434. Accessed December 5, 2016.

[vi] Sustained rheumatoid arthritis remission is uncommon in clinical practice, *Arthritis Research & Therapy*, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3446437/. Accessed December 5, 2016.

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Source: Incyte Corporation