Lilly and Incyte's Oral JAK1 and JAK2 Inhibitor, Baricitinib, Showed Positive Results in Phase IIb Study in Patients with Active Rheumatoid Arthritis

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Results presented as a late breaker at EULAR 2012

BERLIN, June 8, 2012 /PRNewswire via COMTEX/ --Eli Lilly and Company (NYSE: LLY) and Incyte Corporation (Nasdaq: INCY) announced the presentation of 12-week results from a Phase IIb study of baricitinib, formerly LY3009104 (INCB28050), an orally available janus kinase (JAK) inhibitor, in patients with active rheumatoid arthritis (RA). The results were presented as a late-breaking oral presentation at the European League Against Rheumatism's (EULAR) Annual European Congress of Rheumatology *[EULAR abstract LB0005: 12-Week Results of a Phase IIb Dose-Ranging Study of LY3009104 (INCB028050), an Oral JAK1/JAK2 Inhibitor, in Combination with Traditional DMARDs in Patients with Rheumatoid Arthritis].*

The Phase IIb randomized double-blind, placebo-controlled, dose-ranging study, known as JADA, involved a total of 301 patients with active RA on stable doses of methotrexate. Patients were randomized to receive either placebo or one of four once-daily doses of baricitinib (1 mg, 2 mg, 4 mg or 8 mg) for 12 weeks.

Primary Endpoint Achieved

The Phase IIb trial achieved the primary endpoint by demonstrating a statistically significant difference in the American College of Rheumatology 20 (ACR20) response between the combined 4 mg and 8 mg baricitinib groups (76 percent) compared with placebo (41 percent) after 12 weeks of treatment ($p<0.001$). Statistically significant improvement was observed at the first assessment point after two weeks of treatment and was sustained through week 12.

Summary of Secondary Endpoints

A statistically significant difference in response for the ACR20, ACR50 and ACR70 secondary endpoints was observed with the 1 mg, 4 mg and 8 mg dose groups compared with placebo.

ACR20

- 8 mg: 78 percent ($p<0.001$)
- 4 mg: 75 percent ($p<0.001$)
- 2 mg: 54 percent (not significant)
- 1 mg: 57 percent ($p<0.05$)
- Placebo: 41 percent

ACR50

- 8 mg: 40 percent ($p<0.001$)
- 4 mg: 35 percent ($p<0.001$)
- 2 mg: 17 percent (not significant)
- 1 mg: 31 percent ($p<0.05$)
- Placebo: 10 percent

ACR70

- 8 mg: 20 percent ($p<0.001$)
- 4 mg: 23 percent ($p<0.001$)
- 2 mg: 8 percent (not significant)
- 1 mg: 12 percent ($p<0.05$)
- Placebo: 2 percent

Safety Results

The most common treatment-emergent adverse event class was infections, with a similar rate observed among patients in the placebo group (12 percent) and patients receiving baricitinib (14 percent). One patient in the placebo group was diagnosed with an opportunistic infection of toxocariasis. No deaths or opportunistic infections occurred in the active treatment groups.

There were seven serious adverse events reported in six patients (two events in the placebo group, four in the 2 mg group and one in the 8 mg group).

Dose-dependent changes in laboratory tests (hemoglobin, neutrophil, serum creatinine, LDL and HDL) were observed, with greater changes being observed in the 8 mg baricitinib group.

A copy of the EULAR oral presentation can be accessed at: Link to Presentation.

Trial Design and Status

This Phase IIb trial consists of three parts: Part A, Part B and an open-label extension. Part A was randomized, double-blind and placebo-controlled. Patients randomized to baricitinib received one of four doses administered once daily for 12 weeks.

In Part B, patients initially randomized to placebo or the 1 mg baricitinib dose were re-randomized to receive either 4 mg once daily or 2 mg twice daily for 12 weeks. Patients initially randomized to the 2 mg, 4 mg and 8 mg doses continued therapy for an additional 12 weeks.

Patients completing Part B were eligible to continue in an open-label extension arm on either the 4 mg or 8 mg once daily doses of baricitinib for 52 additional weeks.

Part B of the study has completed and data analysis is underway. Patients are continuing to participate in the open-label long-term extension of the trial.

About JAK Inhibition

There are four known JAK enzymes: JAK1, JAK2, JAK3 and TYK2. These enzymes are critical components of signaling mechanisms utilized by a number of cytokines and growth factors, including those that are elevated in RA patients. Cytokines such as interleukin-6, 12, and 23 signal through the JAK pathway and have been clinically validated as therapeutic targets in inflammatory diseases. Additional JAK-dependent cytokines have also been implicated in a number of inflammatory and autoimmune diseases suggesting that JAK inhibitors may be useful for the treatment of a broad range of inflammatory conditions.

About Baricitinib

Baricitinib is an orally administered selective JAK1 and JAK2 inhibitor that is JAK3-sparing. Currently, baricitinib is in Phase II development as a treatment for rheumatoid arthritis and psoriasis.

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 inflammatory and autoimmune diseases.

About Rheumatoid Arthritis

The disease is characterized by abnormal immune mechanisms that lead to joint inflammation and swelling with progressive destruction of joints. In addition to affecting the joints, RA can also affect connective tissue in the skin and organs of the body. [1]

Current treatment of RA includes the use of non-steroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs such as methotrexate, and the newer injectable biological response modifiers that target tumor necrosis factor, a pro-inflammatory cytokine implicated in the pathogenesis of RA.

About Eli Lilly and Company

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers - through medicines and information - for some of the world's most urgent medical needs. Additional information about Lilly is available at www.lilly.com.

About Incyte

Incyte Corporation is a Wilmington, Delaware-based biopharmaceutical company focused on the discovery, development and commercialization of proprietary small molecule drugs for oncology and inflammation. For additional information on Incyte, please visit the Company's website at www.incyte.com.

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[1] Arthritis Foundation, What is Rheumatoid Arthritis, http://www.arthritis.org/types-what-is-rheumatoid-arthritis.php (Accessed: May 1, 2012).

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