

Baricitinib Meets Primary Endpoint in Phase 2 Study of Patients with Moderate-to-Severe Atopic Dermatitis

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- Results presented at EADV show baricitinib significantly improved clinical and patient-reported outcomes compared to placebo in moderate-to-severe atopic dermatitis patients
- Improvements seen as early as first week of treatment in baricitinib-treated group
- Lilly will initiate a Phase 3 clinical program for moderate-to-severe atopic dermatitis later this year

INDIANAPOLIS, Sept. 14, 2017 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) and Incyte Corporation (NASDAQ: INCY) today announced new safety and efficacy data from a Phase 2 study of baricitinib in people with moderate-to-severe atopic dermatitis (AD). The results showed that baricitinib in combination with a mid-potency topical corticosteroid (TCS) significantly improved the signs and symptoms of AD compared to TCS alone. The results were presented in an oral presentation today at the European Academy of Dermatology and Venereology (EADV) Annual Meeting in Geneva, Switzerland.

"Atopic dermatitis has a significant impact on the quality of life, including the emotional and social wellbeing of people with the disease," said James McGill, M.D., distinguished medical fellow and global brand development leader, Lilly Bio-Medicines. "Baricitinib demonstrated clinical efficacy in a Phase 2 study in atopic dermatitis. The study was designed to understand the safety and efficacy of baricitinib in patients refractory to topical steroids. In this population, baricitinib was able to achieve improvement in both itch and skin inflammation. Based on these data, we plan to initiate a Phase 3 clinical program for atopic dermatitis later this year."

After 16 weeks of treatment, 61 percent of patients treated with 4-mg of baricitinib in combination with TCS (n=38) achieved a 50 percent or greater reduction in their overall disease severity as measured by the Eczema Area and Severity Index (EASI-50), compared to 37 percent of patients treated with TCS alone (n=49), (p<0.05). Among patients treated with 2-mg of baricitinib in combination with TCS (n=37), 57 percent achieved EASI-50, although these results were not statistically different compared to treatment with TCS alone (p=0.065). At four weeks, 68 percent of patients treated with 4-mg baricitinib in combination with TCS and 62 percent of patients treated with 2-mg of baricitinib in combination with TCS achieved EASI-50, compared to 16 percent of patients treated with TCS alone (p<0.001).

"Importantly, in this study, patients had to fail four weeks of supervised therapy with a mid-potency topical corticosteroid before randomization, selecting for a difficult to treat patient population," said Emma Guttman-Yassky, M.D., Ph.D., Sol and Clara Kest professor of dermatology, vice chair Department of Dermatology, director of the Center for Excellence in Eczema and director of the Laboratory of Inflammatory Skin Diseases in the Department of Dermatology at Icahn School of Medicine at Mount Sinai Medical Center in New York. "These new results suggest that baricitinib may have the potential to become an oral treatment option for patients suffering from atopic dermatitis who are unable to achieve adequate control with TCS."

During the treatment period, treatment-emergent adverse events (TEAE) occurred in 49 percent of patients treated with TCS, 46 percent and 71 percent of the 2-mg and 4-mg baricitinib in combination with TCS groups, respectively. The most common TEAEs in the 4-mg baricitinib in combination with TCS group were upper respiratory tract infections and nasopharyngitis, headache, and increases in asymptomatic laboratory changes, namely increases in creatine phosphokinase (CPK).

INDICATIONS AND USAGE FOR OLUMIANT

Therapeutic Indications

Baricitinib was approved in February 2017 for the treatment of adults with moderate-to-severe-active rheumatoid arthritis in the European Union and is marketed as Olumiant

IMPORTANT SAFETY INFORMATION FOR OLUMIANT BASED ON THE EU APPROVED SUMMARY OF PRODUCT CHARACTERISTICS

CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients.
Pregnancy.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Infections

Baricitinib is associated with an increased rate of infections such as upper respiratory tract infections compared to placebo. In treatment naïve patients, combination with methotrexate resulted in increased frequency of infections compared to baricitinib monotherapy. The risks and benefits of treatment with Olumiant should be carefully considered prior to initiating therapy in patients with active, chronic or recurrent infections. If an infection develops, the patient should be monitored carefully and Olumiant therapy should be temporarily interrupted if the patient is not responding to standard therapy. Olumiant treatment should not be resumed until the infection resolves.

Tuberculosis

Patients should be screened for tuberculosis (TB) before starting Olumiant therapy. Olumiant should not be given to patients with active TB. Anti-TB therapy should be considered prior to initiation of Olumiant in patients with previously untreated latent TB.

Haematological Abnormalities

Absolute Neutrophil Count (ANC) < 1 x 10⁹ cells/L, Absolute Lymphocyte Count (ALC) < 0.5 x 10⁹ cells/L and haemoglobin < 8 g/dL were reported in less than 1% of patients in clinical trials. Treatment should not be initiated, or should be temporarily interrupted, in patients with an ANC < 1 x 10⁹

cells/L, ALC < 0.5 × 10⁹ cells/L or haemoglobin < 8 g/dL observed during routine patient management.

The risk of lymphocytosis is increased in elderly patients with rheumatoid arthritis. Rare cases of lymphoproliferative disorders have been reported.

Viral Reactivation

Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster, herpes simplex), were reported in clinical studies. Herpes zoster was reported more commonly in patients ≥ 65 years of age who had previously been treated with both biologic and conventional DMARDs. If a patient develops herpes zoster, Olumiant treatment should be temporarily interrupted until the episode resolves.

Screening for viral hepatitis should be performed in accordance with clinical guidelines before starting therapy with Olumiant. Patients with evidence of active hepatitis B or C infection were excluded from clinical trials. Patients, who were positive for hepatitis C antibody but negative for hepatitis C virus RNA, were allowed to participate. Patients with hepatitis B surface antibody and hepatitis B core antibody, without hepatitis B surface antigen, were also allowed to participate; such patients should be monitored for expression of hepatitis B virus (HBV) DNA. If HBV DNA is detected, a liver specialist should be consulted to determine if treatment interruption is warranted.

Vaccination

No data are available on the response to vaccination with live or inactivated vaccines in patients receiving baricitinib. Use with live, attenuated vaccines during, or immediately prior to, Olumiant therapy is not recommended. International treatment guidelines on vaccination in rheumatoid arthritis patients should be followed when varicella zoster vaccination is considered prior to treatment with Olumiant.

Lipids

Dose dependent increases in blood lipid parameters were reported in patients treated with baricitinib compared to placebo. Elevations in LDL cholesterol decreased to pre-treatment levels in response to statin therapy. Lipid parameters should be assessed approximately 12 weeks following initiation of Olumiant therapy and thereafter patients should be managed according to international clinical guidelines for hyperlipidaemia. The effect of these lipid parameter elevations on cardiovascular morbidity and mortality has not been determined.

Hepatic transaminase elevations

Increases in alanine transaminase (ALT) and aspartate transaminase (AST) to ≥ 5 and ≥ 10 x upper limit of normal (ULN) were reported in less than 1% of patients in clinical trials. In treatment-naïve patients, combination with methotrexate resulted in increased frequency of hepatic transaminase elevations compared with baricitinib monotherapy. If increases in ALT or AST are observed during routine patient management and drug-induced liver injury is suspected, Olumiant should be temporarily interrupted until this diagnosis is excluded.

Malignancy

The risk of malignancies including lymphoma is increased in patients with rheumatoid arthritis. Immunomodulatory medicinal products may increase the risk of malignancies including lymphoma. The clinical data are insufficient to assess the potential incidence of malignancies following exposure to baricitinib. Long-term safety evaluations are ongoing.

Venous Thromboembolism

Events of deep venous thrombosis (DVT) and pulmonary embolism (PE) have been reported in patients receiving baricitinib. Olumiant should be used with caution in patients with risk factors for DVT/PE, such as older age, obesity, a medical history of DVT/PE, or patients undergoing surgery and immobilisation. If clinical features of DVT/PE occur, Olumiant treatment should be temporarily interrupted and patients should be evaluated promptly, followed by appropriate treatment.

Laboratory Monitoring

Please refer to the SmPC for laboratory measures and monitoring guidance.

Immunosuppressive Medicinal Products

Combination with biologic DMARDs or other Janus kinase (JAK) inhibitors is not recommended, as a risk of additive immunosuppression cannot be excluded. Data concerning use of baricitinib with potent immunosuppressive medicinal products (e.g., azathioprine, tacrolimus, ciclosporin) are limited and caution should be exercised when using such combinations.

ADVERSE REACTIONS

Undesirable Effects: Summary of Safety Profile

The most commonly reported adverse drug reactions (ADRs) occurring in ≥ 2% of patients treated with Olumiant monotherapy or in combination with conventional synthetic DMARDs were increased LDL cholesterol (33.6%), upper respiratory tract infections (14.7%) and nausea (2.8%). Infections reported with Olumiant treatment included Herpes zoster.

Please see [Summary of Product Characteristics](#) for additional information.

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. Baricitinib remains under review in other markets. It is also being studied for the treatment of atopic dermatitis and systemic lupus erythematosus. The Phase 3 program for psoriatic arthritis is expected to begin in 2018.

About Atopic Dermatitis

Atopic dermatitis (AD), a serious form of eczema, is a chronic, relapsing skin disease characterized by intense itching, dry skin and inflammation that can be present on any part of the body.¹ AD is a heterogeneous disease both clinically and biologically, but may be characterized by chronic baseline

symptoms of itch, redness and skin damage that are often punctuated with episodic, sometimes unpredictable, flares or exacerbations.^{2,3} AD affects approximately 1-3 percent of adults worldwide.⁴

Moderate-to-severe AD is characterized by intense itching, resulting in visibly damaged skin, sleep loss and a significant impact on patients' quality of life. AD patients often experience anxiety, depression and reduced self-esteem.⁵ Like other chronic inflammatory diseases, AD is immune-mediated and involves a complex interplay of immune cells and inflammatory cytokines.⁶

About the Baricitinib Phase 2 Clinical Trial in Atopic Dermatitis

The safety and efficacy of baricitinib in patients with moderate-to-severe AD was evaluated in a Phase 2 randomized, double-blind, placebo-controlled study over 16 weeks (NCT02576938). In the trial, 124 patients were randomized 4:3:3 to placebo or baricitinib 2-mg or 4-mg once daily dose. All patients received background Triamcinolone 0.1% cream for four weeks prior to randomization, and throughout the trial as indicated by the product label and the treating physician. The primary objective of the study was the proportion of patients achieving a $\geq 50\%$ improvement in EASI scores (EASI-50). The study also compared the SCORing Atopic Dermatitis (SCORAD) score and EASI total score percent change from baseline (CFB) between groups. Patient-reported outcomes (PROs) assessed at each visit included Dermatology Life Quality Index (DLQI), Itch Numeric Rating Scale (NRS) and Patient Oriented Eczema Measure (POEM).

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 atopic dermatitis, and reflects Lilly's and Incyte's current belief. 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 receive additional regulatory approvals, or be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's and Incyte's most recent 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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² Thijs JL, Strickland I, Bruijnzeel-Koomen C, et. al. Moving toward endotypes in atopic dermatitis: identification of patient clusters based on serum biomarker analysis. *The Journal of Allergy and Clinical Immunology*. 2017.

³ Langan SM, Thomas KS, Williams HC. What is meant by "flare" in atopic dermatitis? A systematic review and proposal. *Arch Dermatol*. 2006;142:1190-1196.

⁴ Nutten S. Atopic dermatitis: global epidemiology and risk factors. *Annals of Nutrition and Metabolism*. 2015;66(suppl 1): 8-16.

⁵ Yosipovitch G, Papoiu AD. What causes itch in atopic dermatitis? *Current Allergy and Asthma Reports*. 2008;8:306-311.

⁶ Weidinger, S, Novak, N. Atopic dermatitis. *The Lancet* Volume 387. 2016;10023:1109-1122.

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