Lilly Receives FDA Breakthrough Therapy Designation for Baricitinib for the Treatment of Alopecia Areata

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Recognition reinforces baricitinib's potential to be the first FDA-approved medicine for individuals living with alopecia areata

INDIANAPOLIS, March 16, 2020 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) and Incyte Corporation (NASDAQ: INCY) announced today that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation to baricitinib for the treatment of alopecia areata (AA), an autoimmune disorder that can cause unpredictable hair loss on the scalp, face and other areas of the body. The Breakthrough Therapy designation aims to expedite the development and review of drugs that are intended to treat a serious condition when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over already available therapies on a clinically significant endpoint(s).

"Patients with AA currently do not have any FDA-approved treatment options available to them," said Lotus Mallbris, M.D., Ph.D., vice president of immunology development at Lilly. "AA not only causes hair loss but also may be a psychosocial burden for people living with this disease. At Lilly, we aspire to create new medicines that can give hope to patients. We look forward to working with the FDA to further explore baricitinib's potential to become the first approved treatment option for these individuals."

The FDA Breakthrough Therapy designation is based on the positive Phase 2 results of Lilly's adaptive Phase 2/3 study BRAVE-AA1, which evaluated treatment with baricitinib versus placebo in adult patients with AA. In the Phase 2 portion of the BRAVE-AA1 study up to Week 36, there were no new safety signals with no serious adverse events reported. The reported treatment-emergent adverse events (TEAEs) were mild or moderate and the most common included upper respiratory tract infections, nasopharyngitis and acne.

Based on the interim results of the Phase 2 part of the study, the Phase 3 portion of BRAVE-AA1 and an additional Phase 3 double-blind study (BRAVE-AA2), are currently assessing the efficacy and safety of the 2-mg and 4-mg doses of baricitinib relative to placebo.

"There are millions of people around the world affected by and living with AA," said Dory Kranz, president and CEO of the National Alopecia Areata Foundation. "We're encouraged by baricitinib's potential to be one of the first FDA-approved medicines to treat AA."

Baricitinib is currently approved for the treatment of adults with moderately to severely active rheumatoid arthritis (RA). More than 100,000 patients have experience using baricitinib, which is approved in over 65 countries including the U.S., member states of the EU and Japan. It is marketed as OLUMIANT®.

Indication and Usage for OLUMIANT (baricitinib) tablets (in the United States) for RA patients

OLUMIANT® (baricitinib) 2-mg is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more tumor necrosis factor (TNF) antagonist therapies. Limitation of Use: Use of OLUMIANT in combination with other JAK inhibitors, biologic disease-modifying antirheumatic drugs (DMARDs), or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

IMPORTANT SAFETY INFORMATION FOR OLUMIANT (baricitinib) TABLETS

WARNING: SERIOUS INFECTIONS, MALIGNANCY, AND THROMBOSIS

***SERIOUS INFECTIONS*: Patients treated with Olumiant are at risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. If a serious infection develops, interrupt Olumiant until the infection is controlled. Reported infections include:**

- **Active tuberculosis (TB), which may present with pulmonary or extrapulmonary disease. Test patients for latent TB before initiating Olumiant and during therapy. Treatment for latent infection should be considered prior to Olumiant use.**
- **Invasive fungal infections, including candidiasis and pneumocystosis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.**
- **Bacterial, viral, and other infections due to opportunistic pathogens.**

Carefully consider the risks and benefits of Olumiant prior to initiating therapy in patients with chronic or recurrent infection.

Closely monitor patients for the development of signs and symptoms of infection during and after treatment with Olumiant including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy.

***MALIGNANCIES*: Lymphoma and other malignancies have been observed in patients treated with Olumiant.**

***THROMBOSIS*: Thrombosis, including deep venous thrombosis (DVT) and pulmonary embolism (PE), has been observed at an increased incidence in patients treated with Olumiant compared to placebo. In addition, there were cases of arterial thrombosis. Many of these adverse events were serious and some resulted in death. Patients with symptoms of thrombosis should be promptly evaluated.**

WARNINGS AND PRECAUTIONS

SERIOUS INFECTIONS: The most common serious infections reported with Olumiant included pneumonia, herpes zoster and urinary tract infection.

Among opportunistic infections, tuberculosis, multidermatomal herpes zoster, esophageal candidiasis, pneumocystosis, acute histoplasmosis, cryptococcosis, cytomegalovirus and BK virus were reported with Olumiant. Some patients have presented with disseminated rather than local disease and were often taking concomitant immunosuppressants such as methotrexate or corticosteroids. Avoid Olumiant in patients with an active, serious infection, including localized infections. Consider the risks and benefits of treatment prior to initiating Olumiant in patients:

- with chronic or recurrent infection
- who have been exposed to TB
- with a history of a serious or an opportunistic infection
- who have resided or traveled in areas of endemic tuberculosis or endemic mycoses; or
- with underlying conditions that may predispose them to infection.

Closely monitor patients for infections during and after Olumiant treatment. Interrupt Olumiant if a patient develops a serious infection, an opportunistic infection, or sepsis. Do not resume Olumiant until the infection is controlled.

Tuberculosis – Before initiating Olumiant evaluate and test patients for latent or active infection and treat patients with latent TB with standard antimycobacterial therapy. Olumiant should not be given to patients with active TB. Consider anti-TB therapy prior to initiating Olumiant in patients with a history of latent or active TB in whom an adequate course of treatment cannot be confirmed, and for patients with a negative test for latent TB but who have risk factors for TB infection. Monitor patients for TB during Olumiant treatment.

Viral Reactivation – Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster), were reported in clinical studies with Olumiant. If a patient develops herpes zoster, interrupt Olumiant treatment until the episode resolves.

The impact of Olumiant on chronic viral hepatitis reactivation is unknown. Screen for viral hepatitis in accordance with clinical guidelines before initiating Olumiant.

MALIGNANCY AND LYMPHOPROLIFERATIVE DISORDERS: Malignancies were observed in Olumiant clinical studies. Consider the risks and benefits of Olumiant prior to initiating therapy in patients with a known malignancy other than a successfully treated non-melanoma skin cancer (NMSC) or when considering continuing Olumiant in patients who develop a malignancy. NMSCs were reported in patients treated with Olumiant. Periodic skin examination is recommended for patients who are at increased risk for skin cancer.

THROMBOSIS: Thrombosis, including DVT and PE, has been observed at an increased incidence in Olumiant-treated patients compared to placebo. In addition, arterial thrombosis events in the extremities have been reported in clinical studies with Olumiant. Many of these adverse events were serious and some resulted in death. There was no clear relationship between platelet count elevations and thrombotic events. Use Olumiant with caution in patients who may be at increased risk of thrombosis. If clinical features of DVT/PE or arterial thrombosis occur, evaluate patients promptly and treat appropriately.

GASTROINTESTINAL PERFORATIONS: Gastrointestinal perforations have been reported in Olumiant clinical studies, although the role of JAK inhibition in these events is not known. Use Olumiant with caution in patients who may be at increased risk for gastrointestinal perforation (e.g., patients with a history of diverticulitis). Promptly evaluate patients who present with new onset abdominal symptoms for early identification of gastrointestinal perforation.

LABORATORY ABNORMALITIES:

Neutropenia – Olumiant treatment was associated with an increased incidence of neutropenia (absolute neutrophil count [ANC] <1000 cells/mm^3) compared to placebo. Avoid initiation or interrupt Olumiant treatment in patients with an ANC <1000 cells/mm^3. Evaluate at baseline and thereafter according to routine patient management.

Lymphopenia – Absolute lymphocyte count (ALC) <500 cells/mm^3 were reported in Olumiant clinical trials. Lymphocyte counts less than the lower limit of normal were associated with infection in patients treated with Olumiant, but not placebo. Avoid initiation or interrupt Olumiant treatment in patients with an ALC <500 cells/mm^3. Evaluate at baseline and thereafter according to routine patient management.

Anemia – Decreases in hemoglobin levels to <8 g/dL were reported in Olumiant clinical trials. Avoid initiation or interrupt Olumiant treatment in patients with hemoglobin <8 g/dL. Evaluate at baseline and thereafter according to routine patient management.

Liver Enzyme Elevations – Olumiant treatment was associated with increased incidence of liver enzyme elevation compared to placebo. Increases to ≥5x and ≥10x upper limit of normal were observed for both ALT and AST in patients in Olumiant clinical trials.

Evaluate at baseline and thereafter according to routine patient management. Promptly investigate the cause of liver enzyme elevation to identify potential cases of drug-induced liver injury. If increases in ALT or AST are observed and drug-induced liver injury is suspected, interrupt Olumiant until this diagnosis is excluded.

Lipid Elevations – Treatment with Olumiant was associated with increases in lipid parameters, including total cholesterol, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol. Assess lipid parameters approximately 12 weeks following Olumiant initiation. Manage patients according to clinical guidelines for the management of hyperlipidemia.

VACCINATIONS: Avoid use of live vaccines with Olumiant. Update immunizations in agreement with current immunization guidelines prior to initiating Olumiant therapy.

ADVERSE REACTIONS
Adverse reactions (≥1%) include: upper respiratory tract infections (16.3%, 14.7%, 11.7%), nausea (2.7%, 2.8%, 1.6%), herpes simplex (0.8%, 1.8%, 0.7%) and herpes zoster (1.0%, 1.4%, 0.4%) for Olumiant 2 mg, baricitinib 4 mg, and placebo, respectively.

USE IN SPECIFIC POPULATIONS

PREGNANCY AND LACTATION: No information is available to support the use of Olumiant in pregnancy or lactation. Advise women not to breastfeed during treatment with Olumiant.

HEPATIC AND RENAL IMPAIRMENT: Olumiant is not recommended in patients with severe hepatic impairment or in patients with severe renal impairment.

Please click to access full Prescribing Information, including Boxed Warning about Serious infections, Malignancies, and Thrombosis, and Medication Guide.

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About OLUMIANT®
OLUMIANT is a once-daily, oral JAK inhibitor approved in more than 65 countries for the treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more TNF inhibitor therapies, and approved outside of the U.S. for patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more DMARDs.[i] 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.[ii] OLUMIANT has greater inhibitory potency at JAK1, JAK2 and TYK2 relative to JAK3; however, the relevance of inhibition of specific JAK enzymes to therapeutic effectiveness is not currently known.[i]

About Alopecia Areata
Alopecia areata (AA) is a common autoimmune skin disease which results in hair loss on the scalp, face and sometimes other areas of the body. AA often first appears during childhood and can be different for everyone who has it. People of all ages, males/females and all ethnic groups can develop AA.

About Lilly in Dermatology
By following the science through unchartered territory, we continue Lilly's legacy of delivering innovative medicines that address unmet needs and have significant impacts on people's lives around the world. Skin-related diseases are more than skin deep. We understand the devastating impact this can have on people's lives. At Lilly, we are relentlessly pursuing a robust dermatology pipeline to provide innovative, patient-centered solutions so patients with skin-related diseases can aspire to live life without limitations.

About Eli Lilly and Company
Lilly is a global healthcare leader that unites caring with discovery to create medicines that 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.

About Incyte
Incyte is a Wilmington, Delaware-based, global biopharmaceutical company focused on finding solutions for serious unmet medical needs through the discovery, development and commercialization of proprietary therapeutics. For additional information on Incyte, please visit Incyte.com and follow @Incyte. P-LLY

This press release also contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about OLUMIANT (baricitinib) as a treatment for patients with rheumatoid arthritis and as a potential treatment for patients with alopecia areata, 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 OLUMIANT 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 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] Olumiant Prescribing Information, 2019.
[ii] Walker JG and Smith MD. J Rheumatol. 2005;32;1650-1653.

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