CHMP Recommends Approval of Lilly and Incyte's OLUMIANT® (baricitinib) as the First and Only Centrally-Authorized Treatment for Adults with Severe Alopecia Areata (AA)

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INDIANAPOLIS, May 20, 2022 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) and Incyte (NASDAQ:INCY) announced today that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has issued a positive opinion for OLUMIANT® (baricitinib) for the treatment of adults with severe alopecia areata (AA).

This opinion marks the first step toward European regulatory approval of OLUMIANT for patients with severe AA, and it is now referred to the European Commission for final action. If approved, OLUMIANT would be the first centrally-authorized oral treatment and first JAK inhibitor for patients with severe AA in the European Union. The European Commission's decision is expected in the next one to two months.

"Alopecia areata is an often-misunderstood autoimmune disease that can lead to unpredictable hair loss, ranging from bald patches to complete loss of all hair. The disease carries significant psychosocial burden and can impact patients of any race, ethnicity, or age, with many experiencing alopecia in their early to mid-20s," said Bianca Maria Piraccini, M.D., Ph.D., professor and head of the Dermatology Unit at the University of Bologna. "As there has never been a centrally-authorized therapy for alopecia areata, I'm delighted about Lilly's potential to provide this oral medicine with statistically significant and clinically meaningful Phase 3 clinical trial results for adults with severe alopecia areata across Europe."

The positive opinion was based on Lilly's Phase 3 BRAVE-AA1 and BRAVE-AA2 trials evaluating the efficacy and safety of OLUMIANT in 1,200 patients with severe AA, the largest Phase 3 clinical trial program with completed primary endpoints. Severe AA was defined as having a Severity of Alopecia Tool (SALT) score ≥50 (≥50% scalp hair loss). The primary endpoint was the proportion of patients achieving SALT ≤20 (i.e., 80% or more scalp hair coverage) at Week 36. Across both studies, 1 out of 3 patients treated with OLUMIANT 4-mg achieved 80% or more scalp hair coverage (BRAVE-AA1=35.2% [n=99]; BRAVE-AA2=32.5% [n=76]), compared to 1 out of 20 patients (5.3%, n=10) and 1 out of 50 patients (2.6%, n=4) taking placebo in BRAVE-AA1 and BRAVE-AA2, respectively (p≤0.001 for all comparisons to placebo).

Achievement of full regrowth or regrowth with minimal gaps in eyebrow and eyelash hair was also seen at 36 weeks with OLUMIANT 4-mg for 1 in 3 patients who at baseline had significant gaps or no notable eyebrows or eyelashes, as compared to patients taking placebo (BRAVE-AA1: 4-mg dose: eyebrow=31.4% [n=59]; eyelash=33.5% [n=56]; placebo: eyebrow=3.2% [n=4]; eyelash=3.1% [n=3]; BRAVE-AA2: 4-mg dose: eyebrow=34.8% [n=56]; eyelash=34.3% [n=48]; placebo: eyebrow=4.5% [n=5]; eyelash=5.6% [n=5]; p≤0.001 for all comparisons to placebo). Eyebrow and eyelash hair loss was evaluated using the Clinician-Reported Outcome (ClinRO) Measure for Eyebrow Hair Loss™ and ClinRO Measure for Eyelash Hair Loss™ – novel, clinically-validated tools developed by Lilly.

The Phase 3 BRAVE-AA clinical program also evaluated the safety profile of OLUMIANT, and no new safety signals were observed. Few patients discontinued treatment due to adverse events (2.6% or less across both studies), and the majority of treatment-emergent adverse events were mild or moderate in severity.

"We're proud of today's CHMP opinion as it reflects our commitment to immunological diseases with high unmet need," said Patrik Jonsson, Lilly senior vice president, president of Lilly Immunology and Lilly USA, and chief customer officer. "This is a significant step for OLUMIANT on the path to becoming the first and only centrally-authorized medicine in Europe for adults with severe alopecia areata. We eagerly anticipate additional regulatory decisions around the world this year."

In February 2022, the U.S. Food and Drug Administration (FDA) granted priority review for OLUMIANT in adults with severe AA. Lilly expects additional regulatory decisions in the U.S. and Japan in 2022.

About OLUMIANT®

OLUMIANT, a once-daily, oral JAK inhibitor, was discovered by Incyte and licensed to Lilly. It is approved in the U.S. and more than 75 countries as a treatment for adults with moderate to severe rheumatoid arthritis and is approved in more than 50 countries, including the European Union and Japan, for the treatment of adult patients with moderate to severe atopic dermatitis who are candidates for systemic therapy. FDA approval was granted for OLUMIANT for the treatment of certain hospitalized adult patients with COVD-19 in May 2022. Marketing authorization for OLUMIANT in COVID-19 has been granted in six other countries including Japan and Switzerland. Baricitinib is authorized for emergency use in eight countries. Over 400,000 patients have been treated with OLUMIANT for approved indications, in addition to nearly one million patients with COVID-19 worldwide. The U.S. FDA-approved labeling for OLUMIANT includes a Boxed Warning for Serious Infections, Mortality, Malignancy, Major Adverse Cardiovascular Events, and Thrombosis. See the full Prescribing Information here. OLUMIANT is being investigated in alopecia areata (AA), juvenile idiopathic arthritis (JIA) and in pediatric patients with atopic dermatitis (AD).

In December 2009, Lilly and Incyte announced an exclusive worldwide license and collaboration agreement for the development and commercialization of OLUMIANT and certain follow-on compounds for patients with inflammatory and autoimmune diseases.

Indications and Usage for OLUMIANT (baricitinib) tablets (in the United States)

OLUMIANT 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. Limitations of Use: Not recommended for use in combination with other JAK inhibitors, biologic disease-modifying antirheumatic drugs (DMARDs), or with potent immunosuppressants such as azathioprine and cyclosporine.

OLUMIANT is indicated for the treatment of coronavirus disease 2019 (COVID-19) in hospitalized adults requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

IMPORTANT SAFETY INFORMATION FOR OLUMIANT (baricitinib) tablets

WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS, AND THROMBOSIS

SERIOUS INFECTIONS

Patients treated with Olumiant are at risk for developing serious infections that may lead to hospitalization or death. Most patients with rheumatoid arthritis (RA) 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. Olumiant should not be given to patients with active tuberculosis. Test patients, except those with COVID-19, for latent TB before initiating Olumiant and during therapy. If positive, start treatment for latent infection 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.

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 localized disease, and were often taking concomitant immunosuppressants such as methotrexate or corticosteroids.

Avoid use of 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.

The risks and benefits of treatment with Olumiant in COVID-19 patients with other concurrent infections should be considered.

Consider anti-TB therapy prior to initiation of 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.

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.

MORTALITY

In a large, randomized, postmarketing safety study in RA patients 50 years of age and older with at least one cardiovascular risk factor comparing another Janus kinase (JAK) inhibitor to tumor necrosis factor (TNF) blockers, a higher rate of all-cause mortality, including sudden cardiovascular death, was observed with the JAK inhibitor.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Olumiant.

MALIGNANCIES

Lymphoma and other malignancies have been observed in patients treated with Olumiant. In RA patients treated with another JAK inhibitor, a higher rate of malignancies (excluding non-melanoma skin cancer [NMSC]) was observed when compared with TNF blockers. Patients who are current or past smokers are at additional increased risk. A higher rate of lymphomas was observed in patients treated with the JAK inhibitor compared to those treated with TNF blockers. A higher rate of lung cancers and an additional increased risk of overall malignancies were observed in current or past smokers treated with the JAK inhibitor compared to those treated with TNF blockers.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Olumiant, particularly in patients with a known malignancy (other than successfully treated NMSC), patients who develop a malignancy, and patients who are current or past smokers.

NMSCs have been reported in patients treated with Olumiant. Periodic skin examination is recommended for patients who are at increased risk for skin cancer.

MAJOR ADVERSE CARDIOVASCULAR EVENTS

In RA patients 50 years of age and older with at least one cardiovascular risk factor treated with another JAK inhibitor, a higher rate of major adverse cardiovascular events (MACE) (defined as cardiovascular death, myocardial infarction [MI], and stroke) was observed when compared with TNF blockers. Patients who are current or past smokers are at additional increased risk. Discontinue Olumiant in patients that have experienced a myocardial infarction or stroke.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Olumiant, particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Inform patients about the symptoms of serious cardiovascular events and the steps to take if they occur.

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. In RA patients 50 years of age and older with at least one cardiovascular risk factor treated with another JAK inhibitor, a higher rate of thrombosis was observed when compared with TNF blockers. Avoid Olumiant in patients at risk. Discontinue Olumiant and promptly evaluate patients with symptoms of thrombosis.

GASTROINTESTINAL PERFORATIONS

Gastrointestinal perforations have been reported in Olumiant clinical studies, although the role of JAK inhibition in these events is not known. Monitor Olumiant-treated 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. Evaluate at baseline and thereafter according to routine patient management.

In patients with RA, avoid initiation or interrupt Olumiant treatment in patients with an ANC <1000 cells/mm^3. In patients with COVID-19, avoid initiation or interrupt Olumiant treatment in patients with an ANC <500 cells/mm^3.

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. Evaluate at baseline and thereafter according to routine patient management.

In patients with RA, avoid initiation or interrupt Olumiant treatment in patients with an ALC <500 cells/mm^3. In patients with COVID-19, avoid initiation or interrupt Olumiant treatment in patients with an ALC <200 cells/mm^3.

Anemia – Decreases in hemoglobin levels to <8 g/dL were reported in Olumiant clinical trials. Evaluate at baseline and thereafter according to routine patient management.

In patients with RA, avoid initiation or interrupt Olumiant treatment in patients with hemoglobin <8 g/dL. In patients with COVID-19, there is limited information regarding use of Olumiant in patients with hemoglobin less than 8 g/dL.

Liver Enzyme Elevations – Olumiant treatment was associated with increased incidence of liver enzyme elevation compared to placebo. Increases of alanine transaminase (ALT) ≥5x upper limit of normal (ULN) and increases of aspartate transaminase (AST) ≥10x ULN were observed 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 in patients with RA. Manage patients according to clinical guidelines for the management of hyperlipidemia.

VACCINATIONS

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

HYPERSENSITIVITY

Reactions such as angioedema, urticaria, and rash that may reflect drug hypersensitivity have been observed in patients receiving Olumiant, including serious reactions. If a serious hypersensitivity reaction occurs, promptly discontinue Olumiant while evaluating the potential causes of the reaction.

ADVERSE REACTIONS

In RA trials, the most common adverse reactions (≥1%) reported with Olumiant were: upper respiratory tract infections, nausea, herpes simplex, and herpes zoster.

In COVID-19 trials, the most common adverse reactions (≥1%) reported with Olumiant were: ALT ≥3x ULN, AST ≥3x ULN, thrombocytosis (platelets >600,000 cells/mm^3), creatine phosphokinase >5x ULN, neutropenia (ANC <1000 cells/mm^3), DVT, PE, and urinary tract infection.

PREGNANCY AND LACTATION

Limited data on Olumiant use in pregnant women are not sufficient to inform a drug-associated risk for major birth defects or miscarriage. Advise women with RA not to breastfeed during treatment with Olumiant.

HEPATIC AND RENAL IMPAIRMENT

Olumiant is not recommended in patients with RA and severe hepatic impairment or severe renal impairment (estimated glomerular filtration rate [eGFR] <30 mL/min/1.73m^2).

Olumiant should only be used in patients with COVID-19 and severe hepatic impairment if the potential benefit outweighs the potential risk. Olumiant is

not recommended in patients with COVID-19 who are on dialysis, have end-stage renal disease, or with eGFR <15 mL/min/1.73m^2.

Please click to access full Prescribing Information, including Boxed Warning about Serious Infections, Mortality, Malignancy, Major Adverse Cardiovascular Events, and Thrombosis, and Medication Guide.

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About Lilly
Lilly unites caring with discovery to create medicines that make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help more than 47 million people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges, redefining diabetes care, treating obesity and curtailing its most devastating long-term effects, advancing the fight against Alzheimer's disease, providing solutions to some of the most debilitating immune system disorders, and transforming the most difficult-to-treat cancers into manageable diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit Lilly.com and Lilly.com/newsroom or follow us on Facebook, Instagram, Twitter and LinkedIn.

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.

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Lilly Cautionary Statement Regarding Forward-Looking Statements

This press release 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 possible treatment for other conditions and reflects Lilly's and Incyte's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development, and commercialization. Among other things, there can be no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with the results to date, and 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.

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