FDA Approves Lilly and Incyte's OLUMIANT® (baricitinib) for the Treatment of Certain Hospitalized Patients with COVID-19

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OLUMIANT is the first and only JAK inhibitor FDA-approved for the treatment of COVID-19 in certain hospitalized adults requiring various degrees of oxygen support

INDIANAPOLIS, May 11, 2022 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) and Incyte (NASDAQ: INCY) announced today the U.S. Food and Drug Administration (FDA) has approved OLUMIANT® (baricitinib) for the treatment of COVID-19 in hospitalized adults requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) with a recommended dose of 4-mg once daily for 14 days or until hospital discharge, whichever comes first.

"More than two years into the pandemic, COVID-19 is still hospitalizing many people and burdening our healthcare system. I'm grateful to have OLUMIANT as a treatment option for those who require various degrees of respiratory support, from supplemental oxygen to mechanical ventilation or ECMO," said Andre Kalil, M.D., M.P.H., Professor of Medicine at the University of Nebraska Medical Center and principal investigator of the Adaptive COVID-19 Treatment Trial 2 (ACTT-2) sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH). "I'm encouraged by the FDA's full approval of OLUMIANT for the treatment of these patients based on results from the rigorous, placebo-controlled, double-blind, randomized trials. While there are therapies currently available, there is still an urgent need for more options to help improve outcomes for patients hospitalized due to COVID-19."

The FDA's approval is supported by results from two randomized, double-blind, placebo-controlled Phase 3 studies (ACTT-2 and COV-BARRIER, including the COV-BARRIER OS 7 addendum study), announced previously. No new safety signals potentially related to the use of OLUMIANT were identified in the studies.

"Nearly one million people with COVID-19 have been treated with OLUMIANT (baricitinib) in approximately 15 countries worldwide," said Patrik Jonsson, Lilly senior vice president, president of Lilly Immunology and Lilly USA, and chief customer officer. "Today's full approval reflects both our confidence in OLUMIANT's role in treating these hospitalized patients and Lilly's tireless efforts to support the medical community and patients in the ongoing fight against COVID-19."

Baricitinib has been available in the U.S. under Emergency Use Authorization (EUA) since November 2020. An EUA will remain in place for hospitalized pediatric patients 2 to less than 18 years old who require various degrees of oxygen support. The emergency authorization is not an approval and is temporary for the duration where circumstances justify the authorization. For additional information about the authorized use, please see the FDA Letter of Authorization, Fact Sheet for Healthcare Providers and Fact Sheet for Patients, Parents and Caregivers.

Lilly has submitted applications for regulatory approval or authorization to multiple regulatory agencies around the world and anticipates further regulatory decisions to follow.

The U.S. FDA-approved labeling for OLUMIANT carries a boxed warning for risk of serious infections, mortality, malignancy, major adverse cardiovascular events (MACE) and thrombosis. Patients treated with OLUMIANT are at an increased risk of serious bacterial, fungal, viral and opportunistic infections leading to hospitalization or death, including tuberculosis. Higher rates of all-cause mortality and MACE have been observed with another JAK inhibitor versus tumor necrosis factor (TNF) blockers. Malignancies and thrombosis have occurred in patients treated with OLUMIANT and higher rates of each have been observed with another JAK inhibitor versus TNF blockers. Consider the risks and benefits of treatment prior to initiating or continuing therapy with OLUMIANT. **Please see additional Important Safety Information below.**

OLUMIANT is a once-daily, oral JAK inhibitor discovered by Incyte and licensed to Lilly. To learn more about OLUMIANT, please visit www.OLUMIANT.com. OLUMIANT is available in the U.S. as 1-mg and 2-mg tablets through Lilly's authorized specialty distributors.

About ACTT-2 (COVID I) Study
ACTT-2 was a randomized, double-blind, placebo-controlled clinical trial of certain hospitalized adults with confirmed SARS-CoV-2 infection that compared treatment with OLUMIANT and remdesivir (combination group; n=515) to treatment with placebo and remdesivir (placebo group; n=518). Patients treated with the combination received OLUMIANT 4-mg once daily (orally) for 14 days or until hospital discharge, whichever was first, and remdesivir 200-mg on Day 1 and 100-mg once-daily (via intravenous infusion) on subsequent days for a total treatment duration of 10 days or until hospital discharge, whichever was first.

The primary endpoint, for the intent to treat population, was time to recovery within 29 days after randomization. Recovery was defined as being discharged from the hospital without limitations on activities, being discharged from the hospital with limitations on activities and/or requiring home oxygen, or hospitalized but not requiring supplemental oxygen and no longer requiring medical care. The key secondary endpoint was clinical status on Day 15, as assessed on an 8-point ordinal scale.

About COV-BARRIER (COVID II) Study
COV-BARRIER was a randomized, double-blind, placebo-controlled clinical trial of certain hospitalized adults with confirmed SARS-CoV-2 infection that compared treatment with OLUMIANT 4-mg once daily (n=764) with placebo (n=761). OLUMIANT was administered for 14 days or until hospital discharge, whichever came first. Patients could remain on background standard of care, as defined per local guidelines.

Patients requiring invasive mechanical ventilation or ECMO at baseline were enrolled in an exploratory addendum study of COV-BARRIER. These patients were not included in the main COV-BARRIER study population and were analyzed separately.

The primary endpoint was the proportion of patients who died or progressed to non-invasive ventilation/high-flow oxygen or invasive mechanical ventilation within the first 28 days of the study. Patients who required non-invasive ventilation/high-flow oxygen at baseline needed to worsen by at least 1 point on an 8-point ordinal scale to progress. A key secondary endpoint was all-cause mortality by Day 28.

About COV-BARRIER OS 7 Addendum Study
The COV-BARRIER OS 7 addendum study was an exploratory, randomized, double-blind, placebo-controlled substudy of COV-BARRIER in certain hospitalized adults with confirmed SARS-CoV-2 infection requiring invasive mechanical ventilation or ECMO at baseline. This substudy compared treatment with OLUMIANT 4-mg once daily + standard of care (SOC) (n=51) with placebo + SOC (n=50). All patients received SOC in keeping with local clinical practice for COVID-19 management. OLUMIANT was administered for 14 days or until hospital discharge, whichever occurred first. All endpoints in this substudy are considered exploratory, including the prespecified endpoint of all-cause mortality by Day 28.

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

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 rheumatoid arthritis 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 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 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 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. Marketing authorization for the treatment of hospitalized patients with COVID-19 and approval has been granted for OLUMIANT in multiple countries. To date, nearly one million patients worldwide with COVID-19 have been treated with OLUMIANT (baricitinib). 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.

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.

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. P-LLY

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 COVID-19 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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