



Lilly Begins Clinical Testing of Therapies for COVID-19

April 10, 2020

- Baricitinib Research Commences in NIH-led Adaptive COVID-19 Treatment Trial - Lilly Starts Phase 2 Trial with Anti-Ang2 in COVID-19

INDIANAPOLIS, April 10, 2020 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today it has entered into an agreement with the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), to study baricitinib as an arm in NIAID's Adaptive COVID-19 Treatment Trial. The study will investigate the efficacy and safety of baricitinib as a potential treatment for hospitalized patients diagnosed with COVID-19, beginning this month in the U.S. with a planned expansion to additional sites including Europe and Asia. Results are expected within the next two months.

Baricitinib, an oral JAK1/JAK2 inhibitor marketed as OLUMIANT[®], is approved in more than 65 countries as a treatment for adults with moderately to severely active rheumatoid arthritis. The U.S. prescribing information includes boxed warnings regarding the use of baricitinib, including warnings about risk for developing serious infections, a risk that may be related to baricitinib's effects on the immune system. Given the inflammatory cascade seen in COVID-19, baricitinib's anti-inflammatory activity has been hypothesized to have a potential beneficial effect in COVID-19 and warrants further study in patients with this infection.

Joining the NIAID study is just one approach Lilly is taking to tackle the COVID-19 global health crisis. Lilly is also announcing today that it will advance LY3127804, an investigational selective monoclonal antibody against Angiopoietin 2 (Ang2), to Phase 2 testing in pneumonia patients hospitalized with COVID-19 who are at a higher risk of progressing to acute respiratory distress syndrome (ARDS). Ang2 is known to be elevated in ARDS patients and Lilly will test whether inhibiting the effects of Ang2 with a monoclonal antibody can reduce the progression to ARDS or the need for mechanical ventilation in COVID-19 patients. This trial will begin later this month at several U.S. centers.

"Lilly is moving at top speed and using all available resources to help fight this pandemic," said Daniel Skovronsky, M.D., Ph.D., Lilly's chief scientific officer and president of Lilly Research Laboratories. "Developing potential therapeutic medicines for COVID-19 is part of our vital and humanitarian mission. To be successful, we must combine resources, data and expertise, with government, academia and other companies. We look forward to seeing the results of baricitinib and anti-Ang2 clinical studies."

"There is an urgent need for new strategies to help hospitalized COVID-19 patients, many of whom will progress to respiratory failure," said Vincent C. Marconi, M.D., professor of medicine and global health at Emory University School of Medicine, one of the U.S. sites for NIAID's ongoing Adaptive COVID-19 Treatment Trial. "This NIAID study presents an important opportunity to test whether baricitinib can help these patients."

Lilly currently does not anticipate shortages for any of its medicines, including baricitinib, which remains widely available in countries where it is approved. Should research efforts for baricitinib in COVID-19 prove successful, Lilly will continue to create adequate supply to support both appropriate clinical and investigational use.

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/mm³) compared to placebo. Avoid initiation or interrupt Olumiant treatment in patients with an ANC <1000 cells/mm³. Evaluate at baseline and thereafter according to routine patient management.

Lymphopenia – Absolute lymphocyte count (ALC) <500 cells/mm³ 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/mm³. 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 ($\geq 1\%$) 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**.

BA HCP ISI 11OCT2019

About OLUMIANT®

OLUMIANT is a once-daily, oral JAK inhibitor approved in the U.S. 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

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.

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. 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 COVID-19, about LY3127804 as a potential treatment for patients with COVID-19, and about the supply of OLUMIANT, and reflects Lilly'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 continue to be commercially successful, that OLUMIANT or LY3127804 will prove to be an effective treatment for COVID-19, or that we can provide an adequate supply of OLUMIANT in all circumstances. For further discussion of these and other risks and uncertainties, see Lilly'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 undertakes 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.

Refer to:

Kristen Basu; basu_kristen_porter@lilly.com; +1-317-447-2199 (media, baricitinib)

Nicole Hebert; nicole_hebert@lilly.com; +1-317-701-9984 (media, Lilly Research Laboratories)

Kevin Hern; hern_kevin_r@lilly.com; +1-317-277-1838 (investors)



 View original content to download multimedia: <http://www.prnewswire.com/news-releases/lilly-begins-clinical-testing-of-therapies-for-covid-19-301038931.html>

SOURCE Eli Lilly and Company