FDA Approves OLUMIANT® (baricitinib) 2-mg Tablets for the Treatment of Adults with Moderately-to-Severely Active Rheumatoid Arthritis

06/01/2018

The approval of OLUMIANT is based on the Phase 3 clinical trial program that demonstrated efficacy for difficult to treat patients1

INDIANAPOLIS, June 1, 2018 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) and Incyte Corporation (NASDAQ: INCY) announced today that the U.S. Food and Drug Administration (FDA) has approved the 2-mg dose of OLUMIANT® (baricitinib), a once-daily oral medication for the treatment of adults with moderately-to-severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more tumor necrosis factor (TNF) inhibitor therapies.[1] Use of OLUMIANT in combination with other Janus kinase (JAK) inhibitors or biologic disease-modifying antirheumatic drugs (bDMARDs), or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.[1] OLUMIANT may be used as monotherapy or in combination with methotrexate (MTX) or other non-biologic DMARDs.[1]

"We are pleased to provide RA patients in the U.S. an effective treatment option with OLUMIANT, as people with RA who have had an inadequate response to TNF inhibitors are generally considered to be some of the most difficult to treat RA patients," said Christi Shaw, president, Lilly Bio-Medicines.

The OLUMIANT clinical trial program included the RA-BEACON study, a randomized, double-blind, placebo-controlled study in which patients were randomly assigned to receive OLUMIANT 2 mg, baricitinib 4 mg or placebo, in addition to conventional DMARDs that they were currently using.[1] This study included 527 patients who had an inadequate response or intolerance to one or more TNF inhibitor therapies.[1] Patients could have had prior therapy with other bDMARDs.[1]

The study results showed that significantly higher ACR20 response rates and improvement in all individual ACR20 component scores were observed at Week 12 with OLUMIANT.[1] The study found that patients treated with OLUMIANT had significantly higher rates of ACR20 response versus placebo-treated patients at Week 12 (49% of OLUMIANT-treated patients versus 27% of placebo-treated patients).[1] OLUMIANT also demonstrated early symptom relief, with ACR20 responses seen as early as Week 1.[1] Patients treated with OLUMIANT reported significant improvements in physical function based on the Health Assessment Questionnaire Disability Index (HAQ-DI) (recording an average score of 1.71 before treatment and 1.31 at Week 12) compared to placebo-treated patients (who recorded an average score of 1.78 before treatment and 1.59 at Week 12).[1]

OLUMIANT is approved with a Boxed Warning for the risk of serious infections, malignancies and thrombosis.[1] Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving OLUMIANT.[1] Lymphoma and other malignancies have been observed in patients treated with OLUMIANT as well.[1] Additionally, thrombosis, including deep venous thrombosis, pulmonary embolism and arterial thrombosis, some fatal, have occurred in patients treated with OLUMIANT.[1] Other warnings and precautions include gastrointestinal perforations, laboratory abnormalities (including neutropenia, lymphopenia, anemia, liver enzyme elevations, and lipid elevations) and a warning against the use of live vaccines with OLUMIANT.[1] The most common adverse events (occurring in greater than or equal to 1% of OLUMIANT 2 mg- and baricitinib 4 mg-treated patients in placebo-controlled trials) included upper respiratory tract infections, nausea, herpes simplex and herpes zoster.[1] See Important Safety Information including Boxed Warning below.

As part of the approval, the companies have agreed to conduct a randomized controlled clinical trial to evaluate the long-term safety of baricitinib in patients with rheumatoid arthritis.

"Despite the advancements we've seen in the RA treatment landscape over the past several decades, many patients are still failing to achieve their disease management goals," said Seth Ginsberg, co-founder and president of CreakyJoints and the Global Healthy Living Foundation. "As it's important for RA patients to have multiple treatment options available to best suit their disease characteristics and experiences, the approval of OLUMIANT is very encouraging for our community."

RA is a chronic, painful and progressive form of arthritis.[2-3] It is estimated that about two-thirds of established RA patients will not reach clinical remission with their first TNF inhibitor therapy, and a significant percentage will not maintain efficacy as time goes on.[4]

"In my clinical practice, I continue to see patients who experience debilitating symptoms and who are waiting for a medicine that may be right for them," said Elizabeth L. Perkins, M.D., Rheumatology Care Center, Birmingham, Alabama. "OLUMIANT is an important option for rheumatologists to help address these patients' unmet needs."

"RA patients continue to experience unique challenges accessing the treatments prescribed by their healthcare providers. Therefore, we are determined to continue our work with stakeholders to demonstrate value across the healthcare system so providers have greater choice in prescribing treatments to fit individual patient needs," said Shaw.

Lilly will launch OLUMIANT in the U.S. by the end of the second quarter of 2018. The price of OLUMIANT will be 60% less than the leading TNF inhibitor.[5] Lilly will be offering a patient support program, Olumiant Together™. For more information about this program, please call 1-844-OLUMIANT.

Incyte is now eligible to receive a $100 million milestone payment from Lilly as a result of the OLUMIANT approval, which Incyte expects to recognize in the second quarter of 2018.

Indications and Usage

OLUMIANT® (baricitinib) 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.

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 antimicrobial 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 moderate or severe renal impairment.

Please click to access full Prescribing Information (http://pi.lilly.com/us/olumiant-uspi.pdf), including Boxed Warning about Serious infections, Malignancies, and Thrombosis, and Medication Guide (http://pi.lilly.com/us/olumiant-us-mg.pdf).

BA HCP ISI 1JUNE2018

About OLUMIANT

OLUMIANT is a once-daily, oral JAK inhibitor 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.[1] 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.[6] 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.[1] OLUMIANT is approved in more than 40 countries.

About Rheumatoid Arthritis

Rheumatoid arthritis is a systemic autoimmune disease characterized by inflammation and progressive destruction of joints.[2,3] Approximately three times as many women as men have the disease.[7] Current treatment of RA includes the use of non-steroidal anti-inflammatory drugs, oral conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) — such as methotrexate, the current standard of care, and injectable, biological disease-modifying

antirheumatic drugs (bDMARDs) that target selected mediators implicated in the pathogenesis of RA.[9,10] Despite current treatment options, many patients do not reach their therapeutic goals.[9,10] There remains an important need to provide additional treatment options to improve overall patient care.

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 (http://www.lilly.com/) and newsroom.lilly.com/social-channels (http://newsroom.lilly.com/social-channels). P-LLY

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 website at www.incyte.com (http://www.incyte.com/).

Follow @Incyte on Twitter at https://twitter.com/Incyte (http://cts.businesswire.com/ct/CT?id=smartlink&url=https%3A%2F%2Ftwitter.com%2FIncyte&esheet=51345944&newsitemid=20160519005741&lan=en-US&anchor=https%3A%2F%2Ftwitter.com%2FIncyte&index=6&md5=fc69c9bcc05fae189e60acc15595e475).

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 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.

1. Olumiant [package insert]. Indianapolis, IN: Eli Lilly and Company; 2018.
2. Klareskog L, Catrina AI, Paget S. *Lancet*. 2009;373:659-672.
3. Hand Clinics, Advances in the Medical Treatment of Rheumatoid Arthritis, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3135413/pdf/nihms305780.pdf (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3135413/pdf/nihms305780.pdf). Accessed April 23, 2018.
4. Curtis JR and Singh JA.*Clin Ther*. 2011;33(6):679-707.
5. Reprinted with permission by First Databank, Inc. All rights reserved. ©2016.
6. Walker JG and Smith MD. *J Rheumatol.* 2005;32;1650-1653.
7. Hunter TM, et al. *Rheumatol Int.* 2017;37:1551–1557.
8. Arthritis Foundation, Rheumatoid Arthritis Treatment, https://www.arthritis.org/about-arthritis/types/rheumatoid-arthritis/treatment.php (https://www.arthritis.org/about-

arthritis/types/rheumatoid-arthritis/treatment.php). Accessed April 23, 2018.
9. Smolen JS, Aletaha D, McInnes IB. *Lancet*. 2016;388:2023-2038.
10. Sustained Rheumatoid Arthritis Remission is Uncommon in Clinical Practice, Arthritis Research & Therapy, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3446437/ (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3446437/). Accessed April 23, 2018.

Refer to: Danielle Neveles; danielle.neveles@lilly.com (mailto:danielle.neveles@lilly.com); 317-796-4564 (Lilly media)

Kevin Hern; hern_kevin_r@lilly.com (mailto:hern_kevin_r@lilly.com); 317-277-1838 (Lilly investors)

Catalina Loveman; cloveman@incyte.com (mailto:cloveman@incyte.com); 302-498-6171 (Incyte media)

Michael Booth, DPhil; mbooth@incyte.com (mailto:mbooth@incyte.com); 302-498-5914 (Incyte investors)