Lilly and Incyte's Baricitinib Improved Hair Regrowth for Alopecia Areata Patients in Second Phase 3 Study

April 20, 2021

- Results from two studies (BRAVE-AA1 and BRAVE-AA2) show statistically significant improvement in scalp hair regrowth across both baricitinib dosing groups, compared to placebo

- Program data will support a submission to achieve a potential first-in-disease regulatory approval

- Safety profile is consistent with the known safety findings for baricitinib

INDIANAPOLIS, April 20, 2021 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) and Incyte (NASDAQ: INCY) announced today results from a second Phase 3 trial (BRAVE-AA1) evaluating the efficacy and safety of once-daily baricitinib 2-mg and 4-mg in adults with severe alopecia areata (AA). The data are consistent with findings from the first Phase 3 clinical trial, BRAVE-AA2, top-lined earlier this year. In both investigational trials, a statistically significant proportion of patients treated with baricitinib achieved the primary endpoint of hair regrowth across the two dosing regimens at Week 36 compared to patients treated with placebo. AA is an autoimmune disease that causes patchy hair loss on the scalp, face and sometimes on other areas of the body that can progress, and currently has no therapies approved by the U.S. Food and Drug Administration (FDA).

"There is a pressing need for approved treatment options for people suffering from alopecia areata as existing topicals and steroids do not provide meaningful improvement for many patients," said Maryanne Senna, M.D., dermatologist and assistant professor of dermatology at Harvard Medical School and clinical trial investigator of BRAVE-AA1. "I am pleased to see such positive results from these important trials of baricitinib offering a much-needed potential breakthrough treatment option for this disease."

The BRAVE-AA trial program was designed to evaluate the efficacy and safety of baricitinib in adult patients with severe AA. The program consists of two trials: BRAVE-AA1 and BRAVE-AA2. BRAVE-AA1 is a multicenter, randomized, double-blind, placebo-controlled adaptive Phase 2/3 trial. Based on interim results of the Phase 2 portion of BRAVE-AA1 at Week 12, baricitinib 2-mg and 4-mg once-daily doses were selected for further evaluation in the Phase 3 portion of the study. BRAVE-AA2 is a multicenter, randomized, double-blind, placebo-controlled study evaluating the baricitinib 2-mg and 4-mg dosing regimens versus placebo. Both studies included adults with severe alopecia, defined in the BRAVE clinical trials as a Severity of Alopecia Tool (SALT) score ≥ 50 (i.e., who had ≥ 50% scalp hair loss), in addition to a current episode of AA lasting at least six months but no more than eight years.

BRAVE-AA1 and BRAVE-AA2 Study Results

In both studies, over the nine-month treatment period, patients with severe AA treated with baricitinib 2-mg and 4-mg doses experienced significantly greater scalp hair regrowth compared to patients treated with placebo based on physician's assessment.

Results of BRAVE-AA1 showed that at Week 36, the proportion of patients reaching 80 percent or more scalp hair coverage was achieved by 35 percent ($p \leq 0.001$) of patients treated with baricitinib 4-mg/day, 22 percent ($p \leq 0.001$) of patients treated with baricitinib 2-mg/day and five percent of patients in the placebo group, meeting the primary endpoint.

BRAVE-AA2 showed that at Week 36 the proportion of patients reaching 80 percent or more scalp hair coverage was achieved by 33 percent ($p \leq 0.001$) of patients treated with baricitinib 4-mg/day, 17 percent ($p \leq 0.001$) of patients treated with baricitinib 2-mg/day and three percent of patients in the placebo group, meeting the primary endpoint.

Across both studies, the proportion of patients self-reporting at least 80 percent scalp hair coverage was significantly greater in the 2-mg and 4-mg groups compared to placebo ($p \leq 0.001$) by Week 36.

The most common treatment-emergent adverse events (TEAEs) in BRAVE-AA1 and BRAVE-AA2 included upper respiratory tract infections, headache and acne. No deaths or venous thromboembolic events (VTEs) were reported in the trials. The safety profile of baricitinib in the two studies was consistent with its known safety profile in patients with rheumatoid arthritis (RA) and atopic dermatitis (AD).

Lilly will present detailed data from these studies at scientific meetings later this year and submit the results to peer-reviewed journals. Based on these results, Lilly plans to submit a supplemental New Drug Application (sNDA) to the FDA for baricitinib in AA in the second half of 2021, followed by submissions to other regulatory agencies around the world. In Q1 2020, baricitinib received Breakthrough Therapy designation from the FDA for the treatment of AA.

"The positive results from our Phase 3 trials of baricitinib in alopecia areata bring us one step closer to potentially providing an approved treatment option to people affected by this serious autoimmune disease," said Lotus Mallbris, M.D., Ph.D., vice president of immunology development at Lilly. "We look forward to discussing with global regulators data from the BRAVE-AA clinical trial program for this important potential treatment, which could be the first approved for people living with alopecia areata."

Baricitinib is an oral JAK inhibitor discovered by Incyte and licensed to Lilly. Baricitinib is approved and commercially available as OLUMIANT in the U.S. and more than 70 countries as a treatment for adults with moderately to severely active RA and in Europe and Japan for the treatment of adult patients with moderate to severe AD who are candidates for systemic therapy. AA is the second potential treatment indication in dermatology for baricitinib.

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. 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.

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 of ALT ≥5x upper limit of normal (ULN) and increases of 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. 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.

HYPERSENSITIVITY: Reactions such as angioedema, urticaria, and rash that may reflect drug sensitivity 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
Most common adverse reactions include: upper respiratory tract infections (16.3%, 11.7%), nausea (2.7%, 1.6%), herpes simplex (0.8%, 0.7%) and herpes zoster (1.0%, 0.4%) for Olumiant 2 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 the U.S. and more than 70 countries as a treatment for adults with moderate to severe rheumatoid arthritis and was recently approved in the European Union and Japan for the treatment of adult patients with moderate to severe atopic dermatitis who are candidates for systemic therapy. The U.S. FDA-approved labeling for Olumiant includes a Boxed Warning for Serious Infections, Malignancy, 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 baricitinib and certain follow-on compounds for patients with inflammatory and autoimmune diseases.

About Alopecia Areata

Alopecia areata (AA) is an autoimmune disease that causes patchy hair loss on the scalp, face and sometimes on other areas of the body that can progress. 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 health care 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 lilly.com and lilly.com/newsroom. 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.

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 atopic dermatitis and as a potential treatment for patients with alopecia areata, 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 research, 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.

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View original content to download multimedia:http://www.prnewswire.com/news-releases/lilly-and-incytes-baricitinib-improved-hair-regrowth-for-alopecia-areata-patients-in-second-phase-3-study-301272086.html

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