Lilly's Lebrikizumab Combined with Topical Corticosteroids Showed Significant Improvements in Disease Severity for Atopic Dermatitis

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Lebrikizumab significantly improved several areas of great importance to patients with atopic dermatitis, including skin and itch, in pivotal combination trial that met all primary and key secondary endpoints

INDIANAPOLIS, April 11, 2022 /PRNewswire/ -- At 16 weeks, 70 percent of patients with moderate-to-severe atopic dermatitis (AD) receiving lebrikizumab combined with standard-of-care topical corticosteroids (TCS) achieved at least 75 percent improvement in overall disease severity (EASI-75*) in the ADhere trial, Eli Lilly and Company (NYSE: LLY) announced today at the 4th Annual Revolutionizing Atopic Dermatitis (RAD) Conference. Lebrikizumab, an investigational IL-13 inhibitor, also showed improvements in itch, sleep interference, and quality of life when combined with TCS, compared to placebo plus TCS.

"Today's ADhere data, together with results from the ADvocate monotherapy studies, demonstrate the potential for lebrikizumab to reduce disease burden and provide relief for people with uncontrolled atopic dermatitis when used either alone or combined with topicals," said Eric Simpson, M.D., M.C.R., Professor of Dermatology and Director of Clinical Research at Oregon Health & Science University in Portland, and principal investigator of ADhere. "Lebrikizumab specifically targets the IL-13 pathway, which plays the central role in this chronic inflammatory disease. These results strengthen our understanding of lebrikizumab in atopic dermatitis and help establish it as a possible new treatment option."

Lebrikizumab is a novel, monoclonal antibody (mAb) that binds to the interleukin 13 (IL-13) protein with high affinity to specifically prevent the formation of IL-13Rα1/IL-4Rα (Type 2 receptor) which blocks downstream signaling through the IL-13 pathway.[1-5] IL-13 plays the central role in Type 2 inflammation in AD.[6,7] In AD, IL-13 underlies the signs and symptoms including skin barrier dysfunction, itch, infection and hard, thickened areas of skin.[8]

Among patients taking lebrikizumab plus TCS, 41 percent achieved clear or almost clear skin (IGA) at 16 weeks compared to 22 percent of patients taking placebo plus TCS. At 16 weeks, 70 percent of patients taking lebrikizumab plus TCS achieved an EASI-75 response compared to 42 percent taking placebo plus TCS. Differences between patients receiving lebrikizumab in combination with TCS and placebo with TCS were observed as early as four weeks for EASI-75.

Patients treated with lebrikizumab plus TCS also achieved statistically significant improvements across key secondary endpoints including skin clearance and itching, interference of itch on sleep, and quality of life measures, compared to placebo with TCS. Clinically meaningful differences were observed as early as four weeks for itch, interference of itch on sleep, and quality of life measures.

Safety results were consistent with prior lebrikizumab studies in AD. Patients taking lebrikizumab plus TCS, compared to placebo plus TCS, reported a higher frequency of adverse events (lebrikizumab plus TCS: 43%, placebo plus TCS: 35%). Most adverse events were mild or moderate in severity and nonserious and did not lead to treatment discontinuation. The most common adverse events for those on lebrikizumab were conjunctivitis (5%) and headache (5%).

"Lilly is working to empower people with skin-related diseases, such as atopic dermatitis, to live their lives to the fullest potential," said Lotus Mallbris, M.D., Ph.D., vice president of global immunology development and medical affairs at Lilly. "We recognize the critical need for more options for people whose disease cannot be controlled with topicals. We look forward to seeing full results from our broader Phase 3 program and advancing lebrikizumab worldwide."

Lilly recently announced 16-week data from the ongoing ADvocate studies, and an encore presentation of results was presented at RAD 2022. Additionally, longer term data from the ADvocate studies will be disclosed in coming months.

"These results are a further step in our commitment to deliver innovative therapies that make a meaningful difference to patients. We look forward to announcing exciting new milestones in the months to come," commented Karl Ziegelbauer, Ph.D., Almirall S.A.'s Chief Scientific Officer.

Lilly has exclusive rights for development and commercialization of lebrikizumab in the United States and the rest of the world outside Europe. Almirall has licensed the rights to develop and commercialize lebrikizumab for the treatment of dermatology indications, including AD, in Europe.

*EASI=Eczema Area and Severity Index, EASI-75=75 percent reduction in EASI from baseline to Week 16

About ADhere and the Phase 3 Program
ADhere is a 16-week randomized, double-blind, placebo-controlled, parallel-group, global, Phase 3 study to evaluate the efficacy and safety of lebrikizumab in combination with TCS initiated in 211 adult and adolescent patients (aged 12 to less than 18 years of age and weighing at least 40 kg) with moderate-to-severe AD. In the study, patients' AD symptoms were inadequately controlled by TCS with or without topical calcineurin inhibitors (TCI). The study was designed to be more reflective of clinical practice and patients were provided with mid-potency TCS (triamcinolone acetonide 0.1% cream), and low-potency TCS (hydrocortisone 1% cream, for use on sensitive skin areas) which could be tapered, stopped or resumed at the patient's discretion.

The primary endpoints were measured by an Investigator Global Assessment (IGA) score of clear (0) or almost clear (1) skin with a reduction from baseline and at least 75 percent change in baseline in the Eczema Area and Severity Index (EASI-75) score at 16 weeks. EASI measures extent and severity of the disease. Key secondary endpoints were measured by EASI, the Pruritus Numeric Rating Scale, Sleep-Loss due to Pruritus and the

Dermatology Life Quality Index.

The U.S. Food and Drug Administration (FDA) granted lebrikizumab Fast Track designation in AD in December 2019. The lebrikizumab Phase 3 program consists of five key global studies including two monotherapy studies (ADvocate 1 and 2), a combination study (ADhere), as well as long-term extension (ADjoin) and adolescent open label (ADore) studies.

About Atopic Dermatitis
Atopic dermatitis (AD), or atopic eczema, is a chronic, relapsing skin disease characterized by intense itching, dry skin and inflammation that can be present on any part of the body.[9] AD is a heterogeneous disease both biologically and clinically, and may be characterized by a highly variable appearance in which flares occur in an unpredictable manner.[10]

Moderate-to-severe AD is characterized by intense itching, which leads to an itch-scratch cycle that further damages the skin.[11] Like other chronic inflammatory diseases, AD is immune-mediated and involves a complex interplay of immune cells and inflammatory cytokines.[9] People living with AD often report symptoms of intense, persistent itch which can be so uncomfortable that it can affect sleep, daily activities and social relationships.

About Lebrikizumab
Lebrikizumab is a novel, investigational, monoclonal antibody designed to bind IL-13 with high affinity to specifically prevent the formation of the IL-13Rα1/IL-4Rα heterodimer complex and subsequent signaling, thereby inhibiting the biological effects of IL-13 in a targeted and efficient fashion. IL-13 is the central pathogenic mediator of AD, promoting type 2 inflammation that drives skin barrier dysfunction, itch, skin thickening and infection.[6-8]

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.

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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 lebrikizumab as a potential treatment for patients with atopic dermatitis and reflects Lilly'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 planned or ongoing studies will be completed as planned, that future study results will be consistent with the results to date, or that lebrikizumab will receive regulatory approvals, or be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's most recent 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.

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