Lilly's lebrikizumab demonstrated significant skin improvement and itch relief when combined with topical corticosteroids in people with atopic dermatitis in third Phase 3 study

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- Study met all primary and key secondary endpoints
- Safety profile consistent with prior lebrikizumab studies in atopic dermatitis
- Global regulatory submissions to occur next year based on data from the Phase 3 clinical trial program

INDIANAPOLIS, Dec. 21, 2021 /PRNewswire/ -- Lebrikizumab, an IL-13 inhibitor, significantly improved disease severity when combined with topical corticosteroids (TCS) in people with moderate-to-severe atopic dermatitis (AD) in Eli Lilly and Company's (NYSE: LLY) third pivotal Phase 3 trial (ADhere). By Week 16, the study met all primary and key secondary endpoints for patients on the lebrikizumab combination arm.

Lebrikizumab is a novel, investigational monoclonal antibody (mAb) that binds soluble IL-13 with high affinity, has high bioavailability, a long half-life and blocks IL-13 signaling.[1-5] In people with AD, the IL-13 protein—a central pathogenic mediator in the disease—is overexpressed, driving multiple aspects of AD pathophysiology by promoting T-helper type 2 (Th2) cell inflammation and resulting in skin barrier dysfunction, itch, infection, flares and hard, thickened areas of skin.[6,7]

"AD is often complex and challenging to treat, as many patients need help controlling their symptoms when topical steroids alone are not enough," said Eric Simpson, M.D., M.C.R., Professor of Dermatology and Director of Clinical Research at Oregon Health & Science University in Portland and a principal investigator of the ADhere study. "I'm encouraged by the aggregate efficacy and safety data which have demonstrated the potential for lebrikizumab as both monotherapy and combination therapy to address unmet needs and improve care for people living with persistent itch and inflamed skin caused by AD."

The primary endpoints were Investigator Global Assessment (IGA) score of clear (0) or almost clear (1) skin with a reduction of at least two points from baseline and at least a 75 percent change from baseline in the Eczema Area and Severity Index (EASI) score, both at Week 16. Lebrikizumab in combination with TCS also achieved all key secondary endpoints versus placebo in combination with TCS in patients with AD, including skin improvement, itch relief, improvement in interference of itch on sleep, and quality of life. Key secondary endpoints were measured by EASI, the Pruritus Numeric Rating Scale, Sleep-Loss due to Pruritus, and the Dermatology Life Quality Index.

Safety results in the 16-week placebo-controlled ADhere study were consistent with the 16-week period of the two monotherapy studies in the lebrikizumab Phase 3 program for AD. The most common adverse events (AEs) included conjunctivitis and headache for lebrikizumab-treated patients.

In August 2021, Lilly announced top-line data from ADvocate 1 and ADvocate 2 showing lebrikizumab as a monotherapy met primary and all key secondary endpoints including itch, interference of itch on sleep and quality of life at Week 16.

"Physicians treating atopic dermatitis continue to need new options for their patients along with current standard of care, given the heterogeneity of disease and variable outcomes for patients' signs and symptoms," said Lotus Mallbris, M.D., Ph.D., vice president of global immunology development and U.S. and global medical affairs at Lilly. "These results add to the growing body of evidence from our robust Phase 3 clinical trial program for lebrikizumab and support the hypothesis that targeting the IL-13 pathway is critical in treating AD and helping improve outcomes for these patients. We look forward to continuing to evaluate lebrikizumab's clinical utility in the ongoing studies in the hopes of making this medicine available to those who still have unmet needs."

Additional data analyses from ADhere, along with results from two monotherapy Phase 3 trials, ADvocate 1 and ADvocate 2, are planned for future scientific congresses in 2022. Pending successful completion of the ongoing ADvocate 1 and ADvocate 2 monotherapy trials, Lilly and Almirall intend to begin U.S., EU and other regulatory submissions next year.

"These results validate the important role that IL-13 cytokine inhibitors play in AD treatment and the success of lebrikizumab in this study represents another key achievement in our journey to offer treatment advances in AD for patients and healthcare professionals," stated 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 rest of world outside Europe. Almirall has licensed the rights to develop and commercialize lebrikizumab for the treatment of dermatology indications, including AD, in Europe.

About ADhere and the Phase 3 Program
ADhere is a 16-week randomized, double-blind, placebo-controlled, parallel-group, Phase 3 study to evaluate the efficacy and safety of lebrikizumab in combination with TCS in 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 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 ongoing, global studies including two monotherapy studies, today's ADhere combination study as well as long-term extension (ADjoin) and adolescent open label (ADore) trials.

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.[8] 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.[9]

Moderate-to-severe AD is characterized by intense itching, which leads to an itch-scratch cycle that further damages the skin.[10] Like other chronic inflammatory diseases, AD is immune-mediated and involves a complex interplay of immune cells and inflammatory cytokines.[8] 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 a central pathogenic mediator that drives multiple aspects of the pathophysiology underlying the range of signs and symptoms of AD by promoting type 2 inflammation and mediating its effects on tissue, resulting in skin barrier dysfunction, itch, skin thickening and infection.[6]

About Lilly in Dermatology
By following the science through uncharted 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 portfolio and emerging pipeline, which includes small molecules and biologics such as a JAK, an IL-17 and an IL-13 inhibitor.

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

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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