Lilly's lebrikizumab significantly improved skin clearance and itch in people with moderate-to-severe atopic dermatitis in two Phase 3 trials

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- Primary and all key secondary endpoints including itch, interference of itch on sleep and quality of life were met at Week 16 in two pivotal Phase 3 trials in lebrikizumab clinical trial program

- Safety profile consistent with prior lebrikizumab studies in atopic dermatitis

INDIANAPOLIS, Aug. 16, 2021 /PRNewswire/ -- Lebrikizumab led to significant improvements with at least 75 percent skin clearance in more than half of people with moderate-to-severe atopic dermatitis (AD), as measured by EASI, in Eli Lilly and Company's (NYSE: LLY) ADvocate 1 and ADvocate 2 Phase 3 clinical trials. In the top-line results from these two studies of lebrikizumab as a monotherapy in AD, primary and all key secondary endpoints, including skin clearance and itch improvement, were met at Week 16. Lebrikizumab is a novel monoclonal antibody (mAb) that binds soluble IL-13 with high affinity, has high bioavailability, a long half-life and blocks IL-13 signaling. [1-4] The U.S. Food and Drug Administration (FDA) has granted Fast Track designation to lebrikizumab for moderate-to-severe AD in adult and adolescent patients (aged 12 to less than 18 years of age and weighing at least 40 kg). Fast Track designation is granted for a medicine that is intended to treat a serious condition and data demonstrate the potential to address an unmet medical need.

AD, also known as atopic eczema, is a chronic inflammatory skin disorder caused by skin barrier dysfunction and dysregulation of the immune response. 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. 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 and hard, thickened areas of skin.[5,6]

"AD is a heterogenous disease with signs and symptoms varying greatly between patients, underscoring the need for additional treatment options with different mechanisms of action," said Jonathan Silverberg, M.D., Ph.D., M.P.H., associate professor of dermatology at George Washington University School of Medicine and Health Sciences in Washington, DC, and a principal investigator of the ADvocate 2 trial. "Data from the studies showed lebrikizumab's effect on skin clearance and its potential to address a key driver for this disease as well as provide improvements in itch, sleep disturbance and quality of life."

ADvocate 1 and ADvocate 2 are ongoing 52-week randomized, double-blind, placebo-controlled, parallel-group, Phase 3 studies designed to evaluate lebrikizumab as monotherapy 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. The primary efficacy endpoints were assessed at 16 weeks in the two studies and were measured by an Investigator Global Assessment (IGA) score of clear (0) or almost clear (1) skin with a reduction of at least two points from baseline at Week 16 and at least a 75 percent or greater change from baseline in their Eczema Area and Severity Index (EASI) score at Week 16.

Lebrikizumab also achieved key secondary endpoints versus placebo in patients with AD, including early onset in skin clearance and itch relief, improvement in interference of itch on sleep and quality of life. Key secondary endpoints were measured by the IGA, EASI, the Pruritus Numeric Rating Scale, Sleep-Loss due to Pruritus and the Dermatology Life Quality Index.

In the initial 16-week placebo-controlled period of ADvocate 1 and ADvocate 2, the incidence of treatment-emergent adverse events (AEs) and serious AEs among patients treated with lebrikizumab was consistent with that of the previous Phase 2 lebrikizumab study in AD. The most common AEs included conjunctivitis, nasopharyngitis and headache for lebrikizumab-treated patients. Discontinuations due to AEs were similar in the lebrikizumab group (1.4%) compared to placebo (1.7%).

"We understand the needs of people in the AD community worldwide and are aware that many are still in need of new treatment options despite available medicines," said Lotus Mallbris, M.D., Ph.D., vice president of immunology development at Lilly. "Lebrikizumab is a specific inhibitor of IL-13 that offers robust binding affinity and high bioavailability. Today's results show that the inhibition of IL-13 cytokine plays a main role in AD treatment, as demonstrated by more than half of the patients achieving at least 75% clearance to total clearance on lebrikizumab monotherapy."

The full study results from ADvocate 1 and ADvocate 2 will be disclosed at future congresses in 2022. Data from a Phase 3 combination study (ADhere) of lebrikizumab with topical corticosteroids in patients with AD will be available later this year. These studies are part of the lebrikizumab Phase 3 program, which consists of five key ongoing, global studies including two monotherapy studies and a combination study as well as long-term extension (ADjoin) and adolescent open label (ADore) trials.

"We are excited about the data received from the studies that support lebrikizumab's potential efficacy in AD and by the prospect of delivering this promising therapy to people living with moderate-to-severe AD in Europe," 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 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.[7] 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.[8]

Moderate-to-severe AD is characterized by intense itching, which leads to an itch-scratch cycle that further damages the skin.[9] Like other chronic inflammatory diseases, AD is immune-mediated and involves a complex interplay of immune cells and inflammatory cytokines.[7]

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 believed to be 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.

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 planning or ongoing studies will be completed as planned, that future study results will be consistent with the results to date, 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.

1Moyle M, et al. *Exp Dermatol.* 2019;28(7):756-768.
2Ultsch M, et al. *J Mol Biol.* 2013;425(8):1330-1339.
3Zhu R, et al. *Pulm Pharmacol Ther*. 2017;46:88-98.
4Simpson EL, et al. *J Am Acad Dermatol*. 2018;78(5):863-871.e11.
5Bieber T. *Allergy*. 2020;75(1):54-62.
6Ungar B, et al. *J Invest Dermatol*. 2017;137(3):603-613.
7Weidinger S, Novak N. *Lancet*. 2016;387:1109-1122.
8Langan SM, et al. *Arch Dermatol*. 2008;142:1109.
9Yosipovitch G, et al. *Curr Allergy Rep*. 2008;8:306-311.

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