Up to 73% of Atopic Dermatitis Patients Taking Lilly's Lebrikizumab Had Improved or Cleared Skin on Face or Hands in New Analysis

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INDIANAPOLIS, May 1, 2023 /PRNewswire/ -- New secondary analysis from Eli Lilly and Company's (NYSE: LLY) Phase 3 clinical development program showed patients receiving lebrikizumab who were assessed at 16 weeks experienced improved or cleared face or hand dermatitis, which can be particularly burdensome and stigmatizing because these areas are highly visible parts of the body. An additional secondary analysis further demonstrated lebrikizumab's stable and long-lasting results at one year of treatment in patients with moderate-to-severe atopic dermatitis (AD), commonly called eczema. These results from the ADvocate and ADhere studies were presented at the 5th annual Revolutionizing Atopic Dermatitis (RAD) Congress.

Lebrikizumab is an investigational high-affinity and potent IL-13 inhibitor being studied in adult and adolescent patients 12 years of age and older with moderate-to-severe AD. Lilly and partner Almirall S.A. expect regulatory decisions in the U.S. and European Union later this year.

"The fluctuating symptoms and unpredictable nature of atopic dermatitis, along with limited medicines that can adequately manage long-term uncontrolled symptoms, represent major challenges in the treatment of this chronic disease," said Jenny Murase, M.D., Associate Clinical Professor of Dermatology at the University of California San Francisco (UCSF), Director of Medical Dermatology Consultative Services and Patch Testing for the Palo Alto Foundation Medical Group and lead author on the face and hand analysis. "These data provide valuable insights into how lebrikizumab may help improve clinical outcomes by providing improvements in dermatitis on the face or hands, which can be difficult to treat, and offer long-term disease control for patients."

Lebrikizumab Improved or Cleared Face or Hand Dermatitis at 16 Weeks

A post-hoc analysis based on data from the 16-week induction periods of the ADvocate 1 and ADvocate 2 studies and the ADhere study showed 58 to 73 percent of adult and adolescent patients treated with lebrikizumab experienced improvement or clearance of face or hand dermatitis (Abstract #381).[1] Improved or cleared skin was seen with and without the use of topical corticosteroids (TCS).

	ADvocate 1		ADvocate 2		ADhere	
	Placebo Week 16 (N=141)	LEB Week 16 (N=283)	Placebo Week 16 (N=146)	LEB Week 16 (N=281)	Placebo + TCS Week 16 (N=66)	LEB + TCS Week 16 (N=145)
Face Dermatitis: Improved or Cleared	32 %	62 %	22 %	58 %	46 %	69 %
Hand Dermatitis: Improved or Cleared	29 %	67 %	19 %	62 %	43 %	73 %

N = number of ITT population

Sample size (n) for patients with face dermatitis at baseline: ADvocate 1: Placebo (n=114), LEB (n=202); ADvocate 2: Placebo (n=115), LEB (n=207); ADhere: Placebo+TCS (n=39), LEB +TCS (n=105)

Sample size (n) for patients with hand dermatitis at baseline: ADvocate 1: Placebo (n=103), LEB (n=204); ADvocate 2: Placebo (n=106), LEB (n=206); ADhere: Placebo+TCS (n=44), LEB +TCS (n=103)

Lebrikizumab Dosed Every Four Weeks Maintained Stable Response with No or Minimal Fluctuations through One Year of Treatment

Eighty percent of patients treated with lebrikizumab (either every four weeks or every two weeks) in ADvocate 1 and ADvocate 2 maintained EASI-75 response at one year (52 weeks) after achieving EASI-75 response with lebrikizumab treatment at 16 weeks, with more than 70 percent maintaining EASI-75 response with no or minimal fluctuations across 10 study visits through one year of treatment (Abstract #380).[2] Patients treated with the four-week dosing regimen saw similar improvements compared to patients treated with two-week dosing. This post-hoc analysis is based on individual patient trajectory data from two double-blind, placebo-controlled, monotherapy Phase 3 studies of lebrikizumab in adult and adolescent patients with moderate-to-severe AD.

No safety analysis was conducted as part of these post-hoc analyses. Safety among patients in ADvocate 1 and ADvocate 2 at one year was consistent with the induction phase of the trials and other lebrikizumab studies in AD, including ADhere. The proportion of lebrikizumab-treated patients who reported an adverse event (AE) in ADvocate 1 and ADvocate 2 at one year was 58 percent and 68 percent, respectively. Most AEs across the two studies were mild or moderate in severity, nonserious, and did not lead to treatment discontinuation. The most commonly reported AEs were conjunctivitis, common cold (nasopharyngitis) and headache.

"We believe lebrikizumab, if approved, has the potential to be the preferred first-line treatment option for people suffering with atopic dermatitis given

the durability of response and the consistency of results even among patients with more difficult-to-treat regions like the face and hands," said Lotus Mallbris, M.D., Ph.D., senior vice president of global immunology development and medical affairs at Lilly. "These novel data add to the robust body of evidence on lebrikizumab to date and further represent our commitment to setting new expectations for people living with atopic dermatitis. We look forward to regulatory decisions later this year."

Additional lebrikizumab data will be shared at RAD including results from an integrated safety analysis from eight trials and response in patients previously treated with dupilumab. Data from the Phase 3 ADvocate 1 and ADvocate 2 studies were recently published in the *New England Journal of Medicine* (NEJM) and *British Journal of Dermatology* (BJD). In addition, *JAMA Dermatology* published detailed results from the ADhere TCS combination study of lebrikizumab.

"These data suggest lebrikizumab may improve the signs and symptoms that many patients with atopic dermatitis experience and are particularly meaningful for those who are in urgent need of new approaches to treating this disease," said Karl Ziegelbauer, Ph.D., Almirall's Chief Scientific Officer. "We're excited lebrikizumab may be a promising new medicine if approved this year."

Lilly has exclusive rights for development and commercialization of lebrikizumab in the U.S. 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.

About ADvocate 1 and ADvocate 2

ADvocate 1 and ADvocate 2 are 52-week randomized, double-blind, placebo-controlled, parallel-group, global, 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.

During the 16-week treatment induction period, patients received lebrikizumab 500-mg initially and at two weeks, followed by lebrikizumab 250-mg or placebo every two weeks. In the maintenance period, patients with moderate-to-severe AD who achieved a clinical response after 16 weeks of lebrikizumab treatment were re-randomized to receive lebrikizumab every two weeks or four weeks or placebo for an additional 36 weeks. Patients who required rescue treatment during the induction period or who did not meet protocol-defined response criteria at 16 weeks received lebrikizumab every two weeks for an additional 36 weeks.

The primary endpoints 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 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 IGA, EASI, the Pruritus Numeric Rating Scale, Sleep-Loss due to Pruritus and the Dermatology Life Quality Index.

About ADhere

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' baseline 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.

About Lebrikizumab and Clinical Development Program

Lebrikizumab is a novel, investigational, monoclonal antibody designed to bind IL-13 with high affinity, slow disassociation rate and high potency 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.[3,4] AD is an IL-13 dominant disease in which IL-13 drives skin barrier dysfunction, itch, skin thickening, and susceptibility to infection.[5,6]

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 evaluating more than 2,000 patients, including two monotherapy studies (ADvocate 1 and 2), a combination study with topical corticosteroids (ADhere), as well as long-term extension (ADjoin) and adolescent open label (ADore) studies. Lilly has also initiated a first-of-its-kind clinical study dedicated to people of color living with AD. The study will further evaluate the efficacy and safety of lebrikizumab in people of color to generate additional data and disease information to help investigators and clinicians provide better diagnoses and treatment options.

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 51 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. P-LLY

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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[1] Murase J., et al. Improved and Cleared Facial and Hand Dermatitis With Lebrikizumab in Patients With Moderate-to-Severe Atopic Dermatitis. 2023 Revolutionizing Atopic Dermatitis. April 30, 2023.

[2] Silverberg J., et al. Patients Maintain Stable Response With No or Minimal Fluctuations During Treatment With Lebrikizumab. 2023 Prevolutionizing Atopic Dermatitis. April 29 – May 1, 2023.

[3] Simpson EL, et al. *J Am Acad Dermatol*. 2018;78(5):863-871.e11.

[4] Okragly A, et al. *Comparison of the Affinity and in vitro Activity of Lebrikizumab, Tralokinumab, and Cendakimab*. Presented at the Inflammatory Skin Disease Summit, New York, November 3-6, 2021.

[5] Tsoi LC, et al. Atopic Dermatitis Is an IL-13-Dominant Disease with Greater Molecular Heterogeneity Compared to Psoriasis. *J Invest Dermatol.* 2019;139(7):1480-1489.

[6] Bieber T. Interleukin–13: Targeting an underestimated cytokine in atopic dermatitis. *Allergy*. 2020;75:54–62.

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