Press Release

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

BARCELONA (SPAIN), May 1, 2023 – Almirall S.A. (ALM) today announced results from a new secondary analysis from the Phase 3 clinical development program which 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. Almirall and partner Eli Lilly and Company expect regulatory decisions in the European Union and U.S. later this year.

"*Atopic dermatitis is a chronic skin condition that can be challenging to manage and can have a significant impact on the person's quality of life. It is characterized by unpredictable periods of flare-ups and remissions and can cause a wide range of symptoms that vary in severity and location on the body. While there are many treatment options available to alleviate symptoms and improve outcomes, there are unfortunately few effective treatment options that offer long-term disease control*," explains **Andreas Wollenberg,** Professor of Dermatology, Ludwig-Maximilian University, Munich. "*Lebrikizumab shows promise as a new treatment option for patients with moderate-to-severe atopic dermatitis. The clinical data suggest that this new biologic can also provide improvements in hard-to-treat areas and offer long-term disease control. The recent data presented demonstrate the potential benefits that lebrikizumab may offer to patients with atopic dermatitis*."

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.

"*Based on the lasting response seen in patients, including those with traditionally challenging areas like the face and hands, we anticipate that lebrikizumab may become a first-line treatment option for people living with atopic dermatitis and their healthcare professionals*," said **Karl Ziegelbauer, Ph.D., Almirall Chief Scientific Officer**. "*These findings contribute to the growing body of evidence supporting the effectiveness of lebrikizumab and demonstrate our unwavering commitment to improving the standard of care for individuals living with atopic dermatitis. We are eagerly awaiting regulatory decisions later this year that could make this treatment available in Europe*."

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 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*," said **Lotus Mallbris, M.D., Ph.D., senior vice president of global immunology development and medical affairs at Lilly.**

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

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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.

About Almirall

Almirall is a global biopharmaceutical company focused on skin health. We collaborate with scientists and healthcare professionals to address patient's needs through science to improve their lives. Our Noble Purpose is at the core of our work: "Transform the patients' world by helping them realize their hopes and dreams for a healthy life". We invest in differentiated and ground-breaking medical dermatology products to bring our innovative solutions to patients' needs.

The company, founded in 1943 and headquartered in Barcelona, is publicly traded on the Spanish Stock Exchange (ticker: ALM). Throughout its 79-year history, Almirall has retained a strong focus on the needs of patients. Currently, Almirall has a direct presence in 21 countries and strategic agreements in over 70, with about 1,800 employees. Total revenues in 2022 were 878.5 million euros.

For more information, please visit almirall.com

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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.
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[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.
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