

Almirall: Lebrikizumab Combined with Topical Corticosteroids Showed Significant Improvements in Disease Severity for Atopic Dermatitis

- **Skin clearance and itch, key signs and symptoms of atopic dermatitis, were significantly improved with lebrikizumab treatment in combination with TCS**

BARCELONA (SPAIN), April 11, 2022 – 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, as [announced today](#) by **Almirall S.A. (BME: ALM)** and presented 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.

“Dermatologists and patients with atopic dermatitis call for effective treatment options that achieve skin clearance and control the debilitating symptoms of the disease, such as itch, as well as improving quality of life,” stated Dr. med. **Andreas Pinter, Director of Clinical Research at the University Hospital in Frankfurt/Main (Germany) and one of the investigators of the ADhere trial.** *“Data from ADhere, one of the five global studies in the lebrikizumab Phase 3 program, together with the exciting data reported in March from the two monotherapy studies ADvocate 1 and ADvocate 2, reinforce the potential of this new treatment to become a valuable treatment for patients with atopic dermatitis.”*

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-13R α 1/IL-4R α (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

At 16 weeks, 70 percent of patients taking lebrikizumab plus TCS achieved an EASI-75 response compared to 42 percent taking placebo plus TCS. 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. 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%).

“We are pleased to announce the latest data from the lebrikizumab study combined with topical corticosteroids that support its potential in atopic dermatitis. These data suggest that lebrikizumab can be combined with topical

corticosteroid treatment, and are a further step in our commitment to deliver innovative therapies that make a meaningful difference to patients. We look forward to continuing to announce exciting new milestones leading up to potential approval in the EU,” commented **Karl Ziegelbauer, Ph.D., Almirall S.A.’s Chief Scientific Officer**.

Almirall 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.

“We look forward to seeing the full results from our broader Phase 3 program and continuing to advance lebrikizumab for people with atopic dermatitis worldwide,” said **Lotus Mallbris, M.D., Ph.D., vice president of global immunology development and medical affairs at Eli Lilly and Company**.

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 United States and the rest of world outside 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 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 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.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-13R α 1/IL-4R α 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 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 in need.

The company, founded in 1943 and headquartered in Barcelona, is publicly traded on the Spanish Stock Exchange and is a member of the IBEX35 (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 2021 were 836.5 million euros.

For more information, please visit almirall.com

Media contact:

Tinkle
Laura Blázquez
lblazquez@tinkle.es
Phone: (+34) 600 430 581

Investors' Relations contact

Almirall
Pablo Divasson del Fraile
pablo.divasson@almirall.com
Phone: (+34) 93 291 3087

Corporate Communications contact:

Almirall
Mar Ramírez
Mar.ramirez@almirall.com
659 614 173

Legal warning

This document includes only summary information and is not intended to be exhaustive. The facts, figures and opinions contained in this document, in addition to the historical ones, are "forward-looking statements". These statements are based on the information currently available and the best estimates and assumptions that the Company considers reasonable. These statements involve risks and uncertainties beyond the control of the Company. Therefore, actual results may differ materially from those declared by such forward-looking statements. The Company expressly waives any obligation to revise or update any forward-looking statements, goals or estimates contained in this document to reflect any changes in the assumptions, events or circumstances on which such forward-looking statements are based, unless required by the applicable law.

¹ Moyle M, et al. *Exp Dermatol*. 2019;28(7):756-768.

² Ultsch M, et al. *J Mol Biol*. 2013;425(8):1330-1339.

³ Zhu R, et al. *Pulm Pharmacol Ther*. 2017;46:88-98.

⁴ Simpson EL, et al. *J Am Acad Dermatol*. 2018;78(5):863-871.e11.

⁵ 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.

⁶ Tsoi L, et al. *Journal of Investigative Dermatology*. 2019;139(7):1480-1489.

⁷ Ratnarajah K, et al. *Journal of Cutaneous Medicine and Surgery*. 2021;25(3):315-328.

⁸ Bieber T. *Allergy*. 2020;75(1):54-62.

⁹ Weidinger S, Novak N. *Lancet*. 2016;387:1109-1122.

¹⁰ Langan SM, et al. *Arch Dermatol*. 2008;142:1109.

¹¹ Yosipovitch G, et al. *Curr Allergy Rep*. 2008;8:306-311.