

Almirall: Majority of Patients Treated with Lebrikizumab Achieved Skin Clearance in Pivotal Phase 3 Atopic Dermatitis Studies

- **Lebrikizumab rapidly improved skin and itch symptoms in four weeks**

BARCELONA, Spain, March 26th, 2022 – More than 50 percent of patients with moderate-to-severe atopic dermatitis (AD) experienced at least 75 percent reduction in disease severity (EASI-75*) at 16 weeks when receiving lebrikizumab monotherapy in the ADvocate program, **Almirall S.A. (BME: ALM)** announced today at the American Academy of Dermatology (AAD) Annual Meeting. Lebrikizumab, an investigational IL-13 inhibitor, also led to clinically meaningful improvements in itch and other important patient-reported outcomes compared to placebo.

“Atopic dermatitis symptoms such as itch, dry skin, severe pain and inflammation take a heavy burden on patients’ lives as well as on their wellbeing. Patients seek medicines that provide effective and well tolerated treatment options that can address those symptoms and improve their quality of life. Lebrikizumab is an innovative treatment with specific inhibition of IL-13, the central pathogenic mediator in AD. The observed efficacy of lebrikizumab in these studies confirms the potential of this novel treatment, which would be a well-received addition to the atopic dermatitis armamentarium,” said **Prof. Dr. med. Diamant Thaçi**, Director at the Comprehensive Centre for Inflammation Medicine at the University of Lübeck in Germany, and principal investigator of the ADvocate 2 trial.

Lebrikizumab is a 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.⁶ In AD, IL-13 underlies the signs and symptoms including skin barrier dysfunction, itch, infection and hard, thickened areas of skin.⁷

In ADvocate 1, 43 percent of patients receiving lebrikizumab achieved clear or almost clear skin (IGA) at 16 weeks compared to 13 percent of patients taking placebo. Among those receiving lebrikizumab, 59 percent achieved an EASI-75 response, compared to 16 percent with placebo.

In ADvocate 2, 33 percent of patients taking lebrikizumab achieved clear or almost clear skin (IGA) at 16 weeks, compared to 11 percent of patients on placebo. Among those receiving lebrikizumab, 51 percent achieved an EASI-75 response, compared to 18 percent taking placebo.

Within four weeks, patients receiving lebrikizumab experienced statistically significant improvements in skin clearance and itching, as well as improvements in interference of itch on sleep, and quality of life, as measured by key secondary endpoints.

The safety profile of the 16-week period was consistent with prior lebrikizumab studies in AD. Patients taking lebrikizumab, compared to placebo, reported a lower frequency of adverse events in ADvocate 1 (lebrikizumab: 45%, placebo: 52%) and ADvocate 2 (lebrikizumab: 53%, placebo: 66%). Most adverse events across the two studies were mild or moderate in severity and nonserious and did not lead to treatment discontinuation. The most common adverse events in ADvocate 1 and 2 for those on lebrikizumab were conjunctivitis (7% and 8%, respectively), common cold (nasopharyngitis) (4% and 5%, respectively) and headache (3% and 5%, respectively).

“New positive data from the Phase 3 monotherapy studies ADvocate 1 and ADvocate 2 presented at the American Academy of Dermatology Annual Meeting demonstrate that lebrikizumab has the potential to be a leading treatment for a new generation of biologics. Patients need new treatment options that provide high efficacy and better tolerability. This milestone further drives us to continue to focus our efforts on one of the key products in our late-stage pipeline and to progress our commitment to improving the quality of patients’ lives through innovative treatments,” said **Karl Ziegelbauer, Ph.D., Almirall S.A.’s Chief Scientific Officer.**

Detailed 52-week results from ADvocate 1 and 2, as well as 16-week data from ADhere, the Phase 3 AD study of lebrikizumab with topical steroids, will be disclosed in coming months. Almirall and Eli Lilly and Company plan to submit filings to regulatory authorities around the world by the end of 2022 following completion of the ADvocate studies.

“We look forward to sharing longer term results from ADvocate 1 and 2 this year, which we believe will further highlight that lebrikizumab can provide much needed relief for people who struggle from this chronic, and many times, life-long disease,” said **Lotus Mallbris, M.D., Ph.D., 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 United States and the rest of the world outside Europe.

[†]EASI=Eczema Area and Severity Index, EASI75=75 percent reduction in EASI from baseline to Week 16

About ADvocate 1 and ADvocate 2 and the Phase 3 Program

[ADvocate 1](#) and [ADvocate 2](#) are ongoing 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 period, patients received lebrikizumab 500-mg initially and at two weeks, followed by lebrikizumab 250-mg or placebo every two 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.

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, 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.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-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.^{6,7}

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](https://www.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

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

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

⁸ Weidinger S, Novak N. *Lancet*. 2016;387:1109-1122.

⁹ Langan SM, et al. *Arch Dermatol*. 2008;142:1109.

¹⁰ Yosipovitch G, et al. *Curr Allergy Rep*. 2008;8:306-311.