Press Release

Almirall: The New England Journal of Medicine (NEJM) and the British Journal of Dermatology (BJD) publish Ph3 data evaluating lebrikizumab efficacy and safety in moderate-to-severe atopic dermatitis

- **Lebrikizumab is a novel monoclonal antibody that binds to IL-13 with high affinity and prevents its downstream signaling with high potency**
- **The NEJM manuscript reports Week 16 efficacy and safety data from ADvocate1 and ADvocate2, two identically designed Phase 3 monotherapy studies in adults and adolescents with moderate-to-severe atopic dermatitis (AD)**
- **Lebrikizumab showed statistically significant and clinically meaningful improvements vs placebo in the co-primary endpoints, IGA 0/1 and EASI 75, and improvements in itch and the interference of itch on sleep (secondary endpoints) at week 16[1]**
- **The BJD manuscript reports Week 52 efficacy and safety data from ADvocate1 and ADvocate2[2]**
- **Lebrikizumab provided robust long-lasting and durable efficacy in skin clearance and itch, in patients who achieved a clinical response at Week 16, through one year of treatment with a monthly (Q4W) maintenance dosing**
- **Recently, the medical journal JAMA Dermatology also published the results of the Phase 3 clinical trial ADhere, evaluating the efficacy and safety of lebrikizumab in combination with topical corticosteroids (TCS)**

BARCELONA, Spain. March 31, 2023 – Almirall, S.A. (ALM), a global biopharmaceutical company focused on medical dermatology, announced today the publication of Week 16 and Week 52 results of ADvocate1 and ADvocate2 by the New England Journal of Medicine (NEJM) and the British Journal of Dermatology (BJD), respectively. ADvocate1 and ADvocate2 are two identical 52-week randomized, double-blind, placebo-controlled, parallel-group, Phase 3 studies (NCT04146363 and NCT04178967), evaluating lebrikizumab as monotherapy in adult and adolescent* patients with moderate-to-severe atopic dermatitis.

"*People living with moderate to severe atopic dermatitis need more treatment options that are tailored to their unique needs and preferences,"* said **Jonathan Silverberg, M.D**., professor of Dermatology at

* Adolescents aged 12 to less than 18 years of age and weighing at least 40 kg

George Washington University School of Medicine & Health Sciences and co-investigator of the studies. "*In clinical trials, patients experienced significantly clearer skin and less interference with sleep due to itch when taking lebrikizumab compared to placebo. These results are very promising for patients with atopic dermatitis*."

"AD is a debilitating chronic disease that requires effective treatment options that, in addition to achieving skin clearance and control of symptoms, can improve the quality of life of those patients who suffer it. The encouraging data from the ADvocate trials give us confidence that lebrikizumab, which acts directly on the IL-13 key cytokine, may offer a new treatment option for moderate-to-severe AD, once approved," 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.

"We are delighted by the publication of the Phase 3 data in the NEJM and BJD respectively, highly regarded and rigorously peer-reviewed journals. The published clinical trial data support the positive results we have reported previously on the potential efficacy of lebrikizumab in moderate-to-severe AD and underscore our commitment to people living with AD," said **Karl Ziegelbauer**, Ph.D., Almirall's Chief Scientific Officer. *"Awaiting approval in Europe later this year, we are still working toward the market launch of this treatment, convinced of its potential to become a best-in-class treatment for atopic dermatitis,"* he added.

The Phase 3 studies, which included 851 patients, evaluated the efficacy and safety of monotherapy with subcutaneous lebrikizumab 250 mg (with a 500 mg loading dose given at baseline and Week 2) in adult and adolescent patients with moderate-to-severe AD. Patients were randomly assigned in a 2:1 ratio to lebrikizumab 250 mg or placebo every 2 weeks in the 16-week induction period.

Both Phase 3 studies met the co-primary endpoints, which were IGA 0/1 with a reduction of at least two points from baseline at Week 16, and the proportion of patients achieving EASI-75 or greater change from baseline at Week 16. For patients who achieved a clinical response* at Week 16 through one year of treatment, lebrikizumab maintained robust and durable efficacy in skin clearance and itch. The results delivered were similar when dosed once every four weeks or once every two weeks.

These two publications in the NEJM and BJD add to the recent recognitions of lebrikizumab's value by the scientific community. Recently, the peer-reviewed medical journal **JAMA Dermatology**[3] published the results of the Phase 3 clinical trial Adhere (ClinicalTrials.gov Identifier: NCT04250337) evaluating the efficacy and safety of lebrikizumab in combination with topical corticosteroid (TCS) therapy in adolescents and adults with moderate-to-severe AD. In this randomized Phase 3 clinical trial, lebrikizumab in combination with TCS was associated with improved outcomes compared with TCS alone, and safety was consistent with previously reported AD trials.

Almirall has licensed the rights to develop and commercialize lebrikizumab for the treatment of dermatology indications, including AD, in Europe. Eli Lilly and Company has exclusive rights for the development and commercialization of lebrikizumab in the United States and the rest of the world, not including Europe.

About Advocate1&2 studies results

In ADvocate1, the proportions of patients achieving IGA 0/1 at Week 16 were 43.1% of patients treated with lebrikizumab versus 12.7% those treated with placebo. EASI-75 responses were 58.8% vs. 16.2%, respectively. In ADvocate2, the proportions for IGA 0/1 were 33.2% in patients treated with lebrikizumab versus 10.8% treated with placebo; EASI-75 responses were 52.1% versus 18.1%, respectively. The

results were highly statistically significant (p<0.0001). Lebrikizumab also improved measures of itch and itch interference on sleep.

TEAEs were reported in 51.8% and 66.2% of placebo patients, compared with 45.7% and 53.4% of patients receiving lebrikizumab in ADvocate1 and ADvocate2, respectively. Most TEAEs were mild-to-moderate in severity and resulted in a low frequency of treatment discontinuation. The most common TEAE was conjunctivitis in 7.4% and 7.5% of lebrikizumab patients, compared with 2.8% and 2.1% of patients receiving placebo in ADvocate1 and ADvocate2 respectively. These events were non-serious and mostly mild or moderate in severity. There were no clinically meaningful differences between placebo and lebrikizumab-treated patients regarding vital signs and laboratory analyses.

Regarding the results through one year of treatment (Week 52) in responders† at Week 16 with lebrikizumab, in ADvocate 1, 74% of patients dosed every four weeks and 76% of patients dosed every two weeks maintained clear or almost clear skin (IGA 0 or 1) at one year of treatment and 79% of patients dosed every four weeks and every two weeks maintained 75% or greater skin improvement (EASI-75) at one year of treatment. In ADvocate 2, 81% of patients dosed every four weeks and 65% of patients dosed every two weeks maintained clear or almost clear skin (IGA 0 or 1) at one year of treatment and 85% of patients dosed every four weeks and 77% of patients dosed every two weeks maintained EASI-75 response at one year of treatment.

In the studies, most patients maintained clinically meaningful reductions in itch at one year of treatment (ADvocate 1: 80% of patients dosed every 4 weeks, and 81% of those dosed every 2 weeks; Advocate 2: 88% of patients dosed every 4 weeks and 90% of those dosed every 2 weeks), as measured by a four-point or larger reduction in itch severity on the Pruritus Numerical Rating Scale (NRS).

Safety among patients at 52 weeks was consistent with the induction phase of the trials and prior lebrikizumab studies in AD.

About Atopic Dermatitis

Atopic dermatitis (AD), or atopic eczema, is a non-contagious chronic, inflammatory disease of the skin characterized by recurrent inflammation of the skin associated with intense pruritus (severe itching). Apart from the evident physical effects (dry, itchy, red, and inflamed skin), this skin disease causes severe emotional effects that can have a big impact on the academic, social, and/or work life of patients with AD. Up to 4.4% of adults in EU are affected, the prevalence appears to have increased over the past decades, and approximately 30% of adult patients have moderate-to-severe disease.[4,5]

About Lebrikizumab

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 signalling, thereby inhibiting the biological effects of IL-13 in a targeted and efficient fashion[6,7]. AD is an IL-13 dominant disease in which IL-13 drives skin barrier dysfunction, itch, skin thickening, and susceptibility to infection.[8,9,]

About Almirall

Almirall is a global biopharmaceutical company focused on medical dermatology. 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.

† Responders were defined as those achieving a 75% reduction in the Eczema Area and Severity Index from baseline (EASI-75) or an IGA 0 or 1 ("clear" or "almost clear") with a 2-point improvement and without rescue medication use at Week 16. At Week 16, responders were re-randomized to lebrikizumab 250 mg every two weeks or four weeks or placebo for an additional 36 weeks.

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 Silverberg JI, Guttman-Yassky E, Thaçi D, et al. Two Phase 3 Trials of Lebrikizumab for Moderate-to-Severe Atopic Dermatitis. N Engl J Med. 2023;doi:10.1056/NEJMoa2206714 (Ahead of print)

2 Andrew Blauvelt, Jacob P Thyssen, Emma Guttman-Yassky, et al. Efficacy and safety of lebrikizumab in moderate-to-severe atopic dermatitis: 52-week results of two randomized double-blinded placebo-controlled phase III trials, British Journal of Dermatology, 2023;, ljad022, https://doi.org/10.1093/bjd/ljad022

3 *Simpson EL, Gooderham M, Wollenberg A, et al. Efficacy and safety of Lebrikizumab in combination with topical corticosteroids in adolescents and adults with moderate-to-severe atopic dermatitis: a randomized clinical trial (ADhere). JAMA Dermatol. Published online January 11, 2023. doi:10.1001/jamadermatol.2022.5534*

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7 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.

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