Press Release

Almirall: Lebrikizumab Dosed Every Four Weeks Maintained Durable Skin Clearance in Phase 3 Monotherapy Atopic Dermatitis Trials

- **New, late-breaking data show lebrikizumab responders reported long-lasting results at one year of treatment across measures of improvement in skin clearance, itch and disease extent and severity**
- **Results suggest less frequent, every four week dosing of lebrikizumab provided similar improvements to every two week dosing**
- **Regulatory submissions for EU and U.S. planned for this year**

BARCELONA, Spain. September 8th, 2022 – Almirall, S.A. (ALM), a global biopharmaceutical company focused on skin health, today announced **new detailed results from Phase 3 monotherapy studies in atopic dermatitis (AD)** which showed investigational lebrikizumab provided robust and durable improvements in skin clearance and itch for patients who achieved a clinical response* at Week 16 through one year of treatment. Lebrikizumab, a high-affinity and potent IL-13 inhibitor, delivered similar results when dosed once every four weeks or once every two weeks after Week 16. These data were featured in a late-breaking, oral presentation at the 31st European Academy of Dermatology and Venerology (EADV) Congress. The company previously announced topline results of these one-year analyses of ADvocate 1 and ADvocate 2 in June 2022.

"*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 demonstrate how lebrikizumab maintained response in skin clearance, disease severity and symptoms such as itch independent of the dosing scheme tested after the induction period. Lebrikizumab, which acts directly on the IL-13 key cytokine, opens the door to a new, well-tolerated treatment option that can provide long-term disease control,"* said **Jacob Thyssen, MD PhD DmSci, Professor at University of Copenhagen, dermatologist at Bispebjerg Hospital and senior author of the ADvocate analyses.**

Efficacy with every four week dosing, after a 16-week induction period with lebrikizumab every two weeks, was similar to that of every two week dosing.

In ADvocate 1, lebrikizumab demonstrated the following results:

- 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.
- 79% of patients dosed every four weeks and 79% of patients dosed every two weeks maintained 75% or greater skin improvement (EASI-75) at one year of treatment.
- 80% of patients dosed every four weeks and 81% of patients dosed every two weeks maintained clinically meaningful reductions in itch at one year of treatment, as measured by a four-point or larger reduction in itch severity on the Pruritus Numerical Rating Scale (NRS).

In ADvocate 2, lebrikizumab demonstrated the following results:

- 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.
- 85% of patients dosed every four weeks and 77% of patients dosed every two weeks maintained EASI-75 response at one year of treatment.
- 88% of patients dosed every four weeks and 90% of patients dosed every two weeks maintained clinically meaningful reductions in itch at one year of treatment, as measured by a four-point or larger reduction in itch severity on the Pruritus NRS.

Safety among patients at 52 weeks was consistent with the induction phase of the trials and prior lebrikizumab studies in AD. The incidence rate of treatment-emergent adverse events remained stable over time in patients with lebrikizumab. The proportion of lebrikizumab-treated patients who reported an adverse event in ADvocate 1 and ADvocate 2 through Week 52 was 58% and 68%, respectively. Most adverse events across the two studies were mild or moderate in severity, nonserious and did not lead to treatment discontinuation. The most commonly reported adverse events were conjunctivitis, common cold and headache.

"*The detailed data that were presented today at EADV demonstrate the potential benefit that lebrikizumab could bring to HCPs and patients. Living with atopic dermatitis means facing a complex condition that impacts quality of life and overall wellbeing. At Almirall, we are determined to find life-changing treatments for every patient, and we are convinced that, once approved, we will be bringing to market a promising first-line advanced systemic treatment for moderate-to-severe AD that offers robust and durable efficacy with less frequent dosing,"* said **Karl Ziegelbauer, Ph.D., Almirall's Chief Scientific Officer.**

Full results from the Phase 3 studies will be published in a peer-reviewed journal. Almirall and Eli Lilly and Company plan to submit regulatory applications to European Medicines Agency (EMA) and U.S. Food and Drug Administration (FDA) respectively for lebrikizumab in AD this year. The FDA granted lebrikizumab Fast Track designation in AD in December 2019.

"*Based on the robust and clinically meaningful results from our clinical trial program in atopic dermatitis, we believe lebrikizumab, if approved, could become an important treatment for dermatologists and many of their patients with moderate-to-severe disease who suffer from debilitating symptoms and seek new options*," 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.

[*]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.

About ADvocate 1 and ADvocate 2 and the Phase 3 Program

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 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 every 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.

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 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 signaling, thereby inhibiting the biological effects of IL-13 in a targeted and efficient fashion. AD is an IL-13 dominant disease in which IL-13 drives skin barrier dysfunction, itch, skin thickening, and susceptibility to infection.[1-5]

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 (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

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