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**Press Release**

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**NEW DATA PRESENTED AT THE EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY (EADV) CONGRESS IN MADRID**

# Tildrakizumab confirms its long-term efficacy and safety with the longest IL23p19 data available

- **The results of two extension studies confirm the long-term safety of tildrakizumab and show high and durable PASI and PGA response rates**
- **The extension study from reSURFACE 1 shows that over up to 4 years of treatment with tildrakizumab 100 mg, PASI and PGA response rates were high and durable[1]**
- **A post hoc analysis from reSURFACE 1 and reSURFACE 2 suggests there is no dose-dependent effect on safety up to 5 years of follow-up[2]**
- **Tildrakizumab is a high-affinity humanized monoclonal antibody that inhibits the p19 subunit of IL-23, fundamental in the pathogenesis of psoriasis[3]**

**Almirall, S.A. (ALM)** announces the presentation of the results of 14 abstracts about efficacy and safety of long-term tildrakizumab treatment at the 28th EADV Congress by Almirall and SUN Pharma to bring the newest data about psoriasis biological therapies. One of the studies, an open-label extension from baseline reSURFACE 1 a phase III clinical trial and shows that, following up to 4 years of treatment with tildrakizumab 100 mg, PASI and PGA response rates are high and durable.[1] An extension study from reSURFACE 1 and reSURFACE 2 phase III clinical trials has also been presented showing that there is no dose-dependent tildrakizumab effect on the incidence of malignancy.[2] This is the longest data available on an IL23p19 inhibitor, the most innovative class of drugs for the treatment of moderate-to-severe psoriasis. The third study is a pooled analysis through 3 years also from reSURFACE 1 and 2 phase III clinical trials showing that tildrakizumab was well tolerated with low SAEs and adverse effects of a subpopulation of patients 65 years of age or older.[4]

Tildrakizumab is a humanized high-affinity anti-IL23p19 monoclonal antibody approved in Europe under the brand name ILUMETRI® for the treatment of moderate-to-severe plaque psoriasis.[3] Due to its specific mechanism of action, it selectively blocks interleukin-23 (IL-23), a key regulatory cytokine, essential in T-helper 17 cell differentiation and survival, which are the cells instrumental in the pathogenesis of psoriasis.[3]

## Long-term efficacy and safety: up to 4-year results from reSURFACE 1[1]

According to the results of the open-label extension from reSURFACE 1, at week 64, 87% of patients achieved PASI 75, 54% PASI 90 and 31% PASI 100, respectively. And at week 208, these values were 82% for PASI 75, 56% for PASI 90 and 28% for PASI 100. In addition, the proportion of patients receiving tildrakizumab 100 mg with a favorable PGA response was 65% at week 64 and 58% at week 208. Both doses were well tolerated with low rates of AEs of interest. In conclusion, these results are in line with previous tildrakizumab safety data obtained in a 148-week pooled analysis from both reSURFACE 1 and 2 phase III clinical trials that showed the sustainability

of efficacy and safety over 3 years of tildrakizumab treatment in patients with moderate-to-severe chronic plaque psoriasis who were responders to this therapy.[5]

## No dose-dependent effect on the incidence of malignancy up to 5 years of follow-up[2]

Evidence is lacking on the long-term effect of IL-23p19 monoclonal antibodies on malignancy rates. The results of an extension study from reSURFACE 1 and reSURFACE 2 Phase III clinical trials in up to 5 years of follow-up suggest there is no dose-dependent tildrakizumab effect on the incidence of malignancy.

In reSURFACE 1, 239 patients receiving tildrakizumab 100 mg and 267 receiving tildrakizumab 200 mg enrolled in the extension for a mean duration of 154.2 weeks and 165.7 weeks, respectively. In reSURFACE 2, 376 patients receiving tildrakizumab 100 mg and 347 receiving tildrakizumab 200 mg enrolled for a mean duration of 146.8 weeks and 148.5 weeks, respectively. The exposure-adjusted malignancy rate for patients who received 100 mg of tildrakizumab in reSURFACE 1 and 2 base + extension studies was 1.6 events/100 patient-years and 0.8 events/100 patient-years, respectively. The rate for patients receiving tildrakizumab 200 mg was 0.9 events/patient-years and 1.0 events/patient-years, respectively.

In reSURFACE 1, patients receiving tildrakizumab 100 mg had exposure-adjusted rates of melanoma and nonmelanoma skin cancers of 0.1/100 patient-years and 0.5/100 patient-years, and patients with 200 mg had exposure-adjusted rates of 0.1/100 patient-years and 0.4/100 patient-years, respectively.

In reSURFACE 2, patients receiving tildrakizumab 100 mg had exposure-adjusted rates of melanoma and nonmelanoma skin cancers of 0.1/100 patient-years and 0.3/100 patient-years, respectively; meanwhile, the rates in patients receiving tildrakizumab 200 mg were 1,1/100 patient-years and 0.5/100 patient-years, respectively.

When excluding nonmelanoma skin cancer, exposure-adjusted malignancy rates were 1.1/100 patient-years for patients receiving tildrakizumab 100 mg in reSURFACE 1 and 0.5/100 patient-years for those receiving tildrakizumab 200 mg in reSURFACE 1 and both doses in reSURFACE 2.

## Safety in patients 65 years of age or older[3]

Additionally, long-term data in patients 65 years of age or older was presented. In a pooled analysis after 3 years (148 weeks) of treatment from reSURFACE1, 2 clinical trials, tildrakizumab was well tolerated with low SAEs and adverse effects of special interest. No dose related increase in the rate of adverse events were observed.

## Results from a pooled analysis through 3 years from reSURFACE 1 and reSURFACE 2[5]

According to the results of 148-week pooled analysis from reSURFACE 1 and reSURFACE 2 phase III trials have shown sustained efficacy and safety over three years of tildrakizumab use in patients with moderate-to-severe chronic plaque psoriasis who were responders (≥75% improvement in PASI) or partial responders (≥50 to 75% improvement in PASI) to tildrakizumab 100 mg at week 28.

For responders to tildrakizumab 100 mg, proportions of patients (OC) achieving PASIs of <5, <3 and <1 at week 28 were 96.3%, 85.4% and 50.9%, respectively; at week 52 were 89.9%, 82.0% and 56.5%, respectively; and finally, at week 148 were 91.6%, 79.8% and 51.9%. For partial responders to tildrakizumab 100 mg, proportions of patients (OC) achieving PASIs of <5, <3 and <1 at week 52 were 58.3%, 41.7% and 19.4%, respectively; and at week 148 were 72.7%, 45.5% and 27.3%, respectively. These data confirm the robustness of the tildrakizumab data among the IL23p19 class.

The safety profile of tildrakizumab was favourable over the three years, with low rates of severe infections, malignancies, and extended MACEs (major adverse cardiovascular events) for tildrakizumab 100 and 200 mg

treatment over a 148-weeks period. Exposure-adjusted incidence rates of severe infections, malignancies, NMSC (non-melanoma skin cancer), melanoma skin cancer, and extended MACEs with tildrakizumab were low and comparable to placebo, indicating in this study no increased risk of these events with tildrakizumab treatment.[6]

## About reSURFACE 1/2[6]

ReSURFACE 1 and reSURFACE 2 included over 1,800 patients from more than 200 clinical sites worldwide. According to both studies' data, an average of 63% of patients achieved 75% of skin clearance (Psoriasis Area Sensitivity Index per PASI 75) by week 12 and an average of 78% at week 28, after only three doses. The data further showed that a higher number of patients on tildrakizumab achieved PASI 90 and 100 compared to placebo and etanercept: an average of 59% of patients achieved PASI 90 and an average of 30% reached PASI 100 at week 28. Over a year, more than 92% of patients who responded to tildrakizumab within 28 weeks maintained a PASI 75 response.

## About tildrakizumab[3]

Tildrakizumab is a humanized monoclonal antibody that targets the p19 subunit of interleukin-23 (IL-23) and inhibits the release of proinflammatory cytokines and chemokines with limited impact on the rest of the immune system. Indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy, in phase 3 studies tildrakizumab has shown to provide long-term efficacy, safety, and convenient dosing regimen.-Its lower frequency of injections -only 4 doses per year during maintenance- significantly improve the life quality of patients as well as encourage adherence.

Almirall in-licensed Tildrakizumab from Sun Pharmaceutical Industries Ltd. (Sun Pharma) in July 2016. The agreement is for development and commercialization of tildrakizumab in Europe. So far, tildrakizumab has been launched in Germany, United Kingdom, Switzerland, Austria, Denmark and Spain.

## About Psoriasis

Psoriasis is a chronic immune disease that appears on the skin. It affects an estimated 7.8 million adults in Europe and approximately 125 million people worldwide.[7] It is a non-contagious disorder that accelerates the growth cycle of skin cells and results in thick scaly areas of skin. The most common form of psoriasis, called plaque psoriasis, appears as red, raised areas of skin covered with flaky white scales, which may be itchy and painful and can crack and bleed. Despite different treatment options existing, many people with plaque psoriasis continue to struggle with the ongoing, persistent nature of this chronic disease.

## About Almirall

Almirall is a leading skin-health focused pharmaceutical company that partners with healthcare professionals, applying Science to provide medical solutions to patients and future generations. Our efforts are focused on fighting skin health diseases and helping people feel their best. We support healthcare professionals in continuous improvement, bringing our innovative solutions where they are needed.

The company, founded almost 75 years ago and with headquarters in Barcelona, is listed on the Spanish Stock Exchange (ticker: ALM). Almirall has become a key element of vale creation to society according to its commitment with its shareholders and its decision to help others by understanding their challenges and using Science to improve solutions for real life. Total revenues in 2018 were 811 million euros. Almirall has more than 1,800 employees.

For more information, please visit almirall.com linkedin.com/company/almirall

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