Press Release
BARCELONA, Spain

Almirall receives European Commission approval of Klisyri®▼ (tirbanibulin), an innovative topical treatment for actinic keratosis

- **Klisyri® (tirbanibulin) is a topical microtubule inhibitor indicated for the treatment of actinic keratosis (AK) of the face or scalp in adults and it acts through a selective antiproliferative mechanism of action**
- **The regulatory approval of Klisyri® (tirbanibulin) represents a significant step forward in the treatment of AK due to its short treatment protocol –one application daily for 5 days–, proven efficacy, and safety profile**
- **Klisyri® (tirbanibulin) met the primary endpoint of complete (100%) clearance of AK lesions at day 57 in treated areas in a significantly higher number of patients than with vehicle, together with a very acceptable tolerability profile[1]**
- **Actinic keratosis (AK) is one of the most common diagnoses made by dermatologists in Europe and its prevalence can be calculated to be around 18% of the population in Europe[2,3]**

BARCELONA, Spain. July 19th 2021 – Almirall S.A. (BME: ALM), a global biopharmaceutical company, announced today that the **European Commission (EC) has approved Klisyri®** (tirbanibulin) for the topical treatment of actinic keratosis (AK) on the face or scalp in adults.

Tirbanibulin is a novel, topical first-in-class microtubule inhibitor with a selective antiproliferative mechanism of action that represents a significant **step forward in the treatment of AK due to its short treatment protocol -one application daily for 5 days-, proven efficacy and safety profile, with very acceptable local tolerability**.

"*The approval of Klisyri® represents a breakthrough for actinic keratosis patients, who seek new treatments that could offer them better tolerability and short treatment duration. We have once again demonstrated Almirall's commitment to promoting future value through innovation and differentiated therapies with the potential to make a significant difference to patients' lives",* stated **Gianfranco Nazzi**, Almirall's Chief Executive Officer.

The reported prevalence of AK in the European population is around 18%[2,3] and its incidence is predicted to increase globally due to an aging population, increased exposure to UV radiation, and changes in UV-seeking behaviours.[4]

"AK is the most frequent pre-cancerous skin disease and it is thought to be underdiagnosed or considered just as sun-damaged skin. Treating AK is crucial since it can progress to skin cancer with its associated burden in the future. With tirbanibulin, patients could significantly improve their AK lesions, using a 5-day convenient dose regimen" explained **Susana Puig**, MD PhD, Chief Dermatology Service at the Hospital Clinic in Barcelona.

This approval is based on two pivotal **phase III studies' (KX01-AK-003 and KX01-AK-004) positive results**, published in the New England Journal of Medicine (NEJM)[1] These two double-blind, vehicle-controlled, randomised, parallel-group, multi-centre phase III clinical trials, included 702 patients from 62 clinical sites across the US, and demonstrated that once-daily application of tirbanibulin ointment 1% (10 mg/g) during 5 consecutive days in adults with AK on the face or scalp is effective and generally well tolerated.

Both phase III studies achieved their primary endpoint, which was defined as 100% clearance (Complete Clearance) of the AK lesions on Day 57 in the face or scalp treatment areas, each study achieving statistical significance (p<0.0001) versus vehicle on this endpoint. In the KX01-AK-003 study, complete clearance was observed in 44% of the patients treated with tirbanibulin versus 5% for vehicle-treated groups. In the KX01-AK-004 study, complete clearance was observed in 54% of the patients treated with tirbanibulin versus 13% for vehicle-treated groups. Local reactions were mostly mild-to-moderate erythema, flaking or scaling, application-site pruritus, and application-site pain that was resolved spontaneously[1]

In December 2020, Almirall's development partner, Athenex, Inc., received approval from the **U.S. Food and Drug Administration** (FDA) for the commercialisation of Klisyri® (tirbanibulin) in the United States for the topical treatment of AK of the face or scalp. Later, in May 2021, the **Committee for Medicinal Products for Human Use** (CHMP) of the EMA issued a positive opinion for the regulatory approval of Klisyri®.

In addition, Almirall submitted Klisyri® for a marketing authorisation in Switzerland in December 2020 and the dossier is currently under review by Swissmedic. The company has already submitted in Great Britain via the European Commission Decision Reliance Procedure.

About Klisyri® (tirbanibulin)

Klisyri® (tirbanibulin) is a microtubule inhibitor indicated for the topical treatment of actinic keratosis of the face or scalp in adults. Two phase III studies (KX01-AK-003 and KX01-AK-004) evaluated the efficacy and safety of tirbanibulin ointment 1% (10 mg/g) in adults with actinic keratosis on the face or scalp. The studies achieved their primary endpoint, which was defined as 100% clearance of the AK lesions at Day 57 within the face or scalp treatment areas, each study achieving statistical significance (p<0.0001) on this endpoint. [1]

About Actinic Keratosis

Actinic keratosis (AK) or solar keratosis is a chronic and precancerous skin disease that occurs primarily in areas that have been exposed to ultraviolet (UV) radiation for a long period of time. It is usually found on the face, ears, lips, bald scalp, forearms, the posterior part of the hands, and lower legs. It is not possible to predict which AK lesions will develop into squamous cell carcinoma. AK is the most common pre-cancerous dermatological condition[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 and is a member of the IBEX35 (ticker: ALM). Throughout its 78-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, through 13 subsidiaries, with about 1,800 employees. Total revenues in 2020 were 814.5 million euros.

For more information, please visit almirall.com

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[1] Blauvelt A, Kempers S, Lain E, et al. Phase 3 Trials of Tirbanibulin Ointment for Actinic Keratosis. N Engl J Med. 2021 Feb 11;384(6):512-520. doi: 10.1056/NEJMoa2024040

[2] Lucas R, McMichael T, Smith W, Armstrong B. Solar ultraviolet radiation: Global burden of disease from solar ultraviolet radiation: World Health Organization, 2006.

[3] Worldometer. Population of Europe. 2020. Available at: https://www.worldometers.info/world-population/europe-population/ Accessed: October 2020.

[4] Chetty P, Choi F, Mitchell T. Primary care review of actinic keratosis and its therapeutic options: a global perspective. Dermatol Ther (Heidelb) 2015; 5(1): 19-35

[5] Skin Cancer Foundation. Actinic Keratosis Overview. Available at: https://www.skincancer.org/skin-cancer-information/actinic-keratosis/#:~:text=Actinic%20keratosis%20(AK)%20is%20the,to%20ultraviolet%20(UV)%20radiation January 2021