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Press release

Barcelona (Spain)
15 December 2020

Almirall announces FDA approval of Klisyri® (tirbanibulin), a new innovative topical treatment for actinic keratosis

- **Klisyri® (tirbanibulin) is a novel microtubule inhibitor, indicated for the topical treatment of actinic keratosis (AK) on the face or scalp**
- **Actinic keratosis is the second most common diagnosis made by dermatologists in the United States[1]**
- **In one of the largest Phase III clinical study programs[2] ever conducted for a topical AK treatment, tirbanibulin demonstrated complete clearance of actinic keratosis lesions at day 57 in treated face or scalp areas in a significantly higher number of patients than with vehicle**
- **Klisyri has a demonstrated safety profile with no patient withdrawals due to adverse events, and a convenient 5-day application period which is the shortest of any topical treatment for AK**
- **This approval represents a key milestone in Almirall's therapeutic pipeline**

Barcelona (Spain), 15 December 2020. Almirall, S.A. (BME:ALM), a global biopharmaceutical company focused on skin health, announced today that Klisyri® (tirbanibulin) has been approved by the **U.S. Food and Drug Administration (FDA)** for the topical treatment of actinic keratosis (AK) of the face or scalp. Klisyri® (tirbanibulin) will be launched in the US during the first quarter of 2021.

Klisyri® is a novel, topical first-in-class microtubule inhibitor that represents a significant step forward in the treatment of AK due to its short treatment protocol (once daily application for 5 days), and proven efficacy and safety profile. Actinic keratosis is the second most common diagnosis made by dermatologists in the United States[1]. The reported prevalence of AK is between 11% and 25%[3].

"Early diagnosis and treatment of actinic keratosis (AK) is critical, since those who already have an AK are likely to develop more actinic keratoses (plural) in the future," said **Deborah S. Sarnoff, MD,** President of the Skin Cancer Foundation. "*Patients with AK are at higher risk for skin cancer, since AKs can progress into squamous cell carcinoma (SCC), a common and sometimes invasive form of skin cancer."*

The FDA approved Klisyri® (tirbanibulin) based on the data from one of the largest Phase III clinical study programs ever conducted for a topical AK treatment, two pivotal, randomized, double-blind, vehicle-controlled Phase III studies (KX01-AK-003 and KX01-AK-004) that evaluated the efficacy and safety of Klisyri® (tirbanibulin) ointment 1% in adults with actinic keratosis on the face or scalp.

"*These studies enrolled a total of 702 patients across 62 sites in the United States, providing robust data. Tirbanibulin achieved a significantly higher number of patients with complete (100%) clearance of AK lesions in the treated area compared to vehicle (44% vs. 5% in study 1 and 54% vs. 13% in study 2), as well as reaching the secondary endpoint of partial (≥75%) clearance of lesions*" stated **Andrew Blauvelt, MD, MBA,** President of Oregon Medical Research Center, and one of the lead investigators of the studies.

Ayman Grada, MD, head of R&D and Medical Affairs for Almirall US went on to explain, "*In addition to proven efficacy, Klisyri demonstrated safety, with the most common adverse events being application site pruritus and pain seen in 9% and 10% respectively of patients treated with it. Of note, no patients withdrew from the study due to adverse events".*

Klisyri® (tirbanibulin) is supplied in boxes of 5 single-use sachets, and is applied to the treatment area once daily for 5 days. "*The convenient dosing regimen should lead to better patient compliance*" continued Dr Grada.

Pablo Alvarez, President and General Manager of Almirall US, summarized *"The approval of Klisyri marks another important milestone for Almirall towards our goal to be a leader in the field of dermatology. We believe that this treatment, with its 5-day treatment course and proven efficacy and tolerability, make it an important therapeutic option for dermatologists and their patients. We appreciate the efforts of Athenex from discovery, to development, to approval of Klisyri, and we look forward to launching this exciting product in early 2021"*

Almirall and Athenex partnership

Almirall and Athenex, Inc. (NASDAQ: ATNX) entered into a strategic partnership in December 2017 to develop and market tirbanibulin for the treatment of actinic keratosis and other skin conditions in the United States and Europe, including Russia. Athenex has been responsible for conducting all preclinical and clinical studies in order to gain FDA approval of tirbanibulin. Almirall will leverage its expertise to support development in Europe and to market the product in all licensed territories. Global peak sales of tirbanibulin are expected to surpass €250 million.

Peter Guenter, CEO of Almirall, stated, *"Athenex is a great partner for Almirall. We very much appreciate all their efforts in gaining the FDA approval for Klisyri, which brings a new option for dermatologists and their patients with actinic keratosis. The US launch of Klisyri will be the first of many, and we look forward to continuing our excellent partnership with Athenex as we market the product in the US and EU."*

Dr. Johnson Lau, Chairman and CEO of Athenex, *"We are delighted to have Almirall as our partner for both the US and EU market. Almirall has been actively preparing to launch Klisyri in the US market in the first quarter of 2021, and we are excited to receive the US FDA approval on time to support this timeline. Almirall is leading the regulatory effort in the EU and we are excited to have this experienced dermatology-focused company as our commercial partner."*

About Klisyri®

Klisyri® (tirbanibulin) is a microtubule inhibitor indicated for the topical treatment of actinic keratosis of the face or scalp. The two double-blind, vehicle-controlled, randomized, parallel group, multicenter, 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 enrolled a total of 702 patients across 62 sites in the US. Tirbanibulin ointment 1% (10 mg/g) or vehicle (randomized 1:1) was self-administered to 25 cm^2 of the face or scalp encompassing 4-8 typical AK lesions, once daily for 5 consecutive days.

Both Phase III studies, KX01-AK-003 and KX01-AK-004, 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. 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.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Ophthalmic Adverse Reactions
KLISYRI may cause eye irritation. Avoid transfer of the drug into the eyes and to the periocular area during and after application. Wash hands immediately after application. If accidental exposure occurs, instruct patient to flush eyes with water and seek medical care as soon as possible.

Local Skin Reactions
Local skin reactions, including severe reactions (erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation and erosion/ulceration) in the treated area can occur after topical application of KLISYRI. Avoid use until skin is healed from any previous drug, procedure, or surgical treatment. Occlusion after topical application of KLISYRI is more likely to result in irritation.

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥2%) were local skin reactions, application site pruritus, and application site pain.

Please see Full Prescribing Information for Klisyri at https://www.klisyri.com/

About Actinic Keratosis

Actinic keratosis 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, so all lesions should be treated by a dermatologist. Actinic keratosis is the most common pre-cancerous dermatological condition. Actinic keratosis comprises between 14% and 29% of dermatologist visits in the United States.[1]

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 groundbreaking medical dermatology products to bring our innovative solutions to patients in need.

The company, founded in 1943 and headquartered in Barcelona, is publically traded on the Spanish Stock Exchange and is a member of the IBEX 35 (ticker: ALM). Throughout its 77-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 2019 were 908.4 million euros.

For more information, please visit almirall.com

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2 Phase III studies KX01-AK-003 (NCT03285477) and KX01-AK-004 (NCT03285490)
3 Stockfleth E, Ferrandiz C, Grob JJ, et al. Development of a treatment algorithm for actinic keratoses: a European Consensus. Eur J Dermatol. 2008;18(6):651–659