Press release

Exton, PA
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Almirall U.S. Launches Klisyri® (tirbanibulin), a New, Innovative Topical Treatment for Actinic Keratosis

- **Actinic keratosis (AK), the second most common diagnosis made by dermatologists in the United States[1], affects more than 40 million Americans each year[2]**
- **Klisyri® (tirbanibulin) met the primary endpoint of complete (100%) clearance of AK lesions at day 57 in treated face or scalp areas[3]**
- **Klisyri® (tirbanibulin) is a novel microtubule inhibitor, indicated for the topical treatment of actinic keratosis (AK) on the face or scalp**
- **Klisyri® has a demonstrated safety profile and a convenient 5-day application period, the shortest of any topical treatment for AK**
- **Klisyri® is available now in pharmacies across the U.S.**

EXTON, Pa., Feb. 18, 2021. Almirall, S.A. (BME:ALM), a global biopharmaceutical company focused on skin health, announced today the U.S. commercial launch of Klisyri® (tirbanibulin), developed for the topical treatment of actinic keratosis (AK) of the face and scalp. Klisyri® was approved by the **U.S. Food and Drug Administration (FDA)** in December 2020 and is now commercially available.

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. AK is the second most common diagnosis made by dermatologists in the United States.[1] It is estimated that more than 40 million Americans develop actinic keratoses (AKs) each year.[2]

"Klisyri® will help address unmet needs for many AK patients," said **George Martin, MD**, a world-renowned expert in actinic keratosis and skin cancer. "*Early diagnosis and a safe and highly effective topical for treatment of actinic keratosis is critical. Patients with actinic keratoses are at higher risk for developing non-melanoma skin cancer. Actinic keratosis can progress into squamous cell carcinoma (SCC), a common and sometimes invasive and deadly form of skin cancer."*[4]

The FDA approved Klisyri® based on the data from one of the largest Phase III clinical study programs ever conducted for a topical AK treatment,[3] consisting of 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 AKs on the face or scalp.

Klisyri® met the primary endpoint and achieved a significantly higher number of patients with complete (100%) clearance of AK lesions at day 57 in the treated area compared to vehicle (44% vs. 5% in study 1 and 54% vs. 13% in study 2; $p<0.0001$ for both studies). It also met the secondary endpoint of partial (≥75%) clearance of lesions at day 57 compared to vehicle. The most common adverse events were application-site pruritus and pain seen in 9% and 10% of patients treated with Klisyri®.

Ayman Grada, MD, Head of R&D and Medical Affairs at Almirall U.S. added, *"The incidence of actinic keratosis has been increasing,[5,6] including in younger adults. Patients may prefer a treatment option with a short duration*

and proven safety and tolerability profile.[7] *The data for Klisyri offers this, as well as demonstrating efficacy for both face and scalp actinic keratoses."*[4]

"The U.S. launch of Klisyri marks another important milestone for Almirall toward our goal to be a leader in the field of dermatology and deliver new, innovative and effective treatment options," said **Pablo Alvarez**, President and General Manager of Almirall U.S. *"We are committed to providing patients with affordable access to our medications, and we have a copay card and a network of pharmacies covering the country to support this. We are excited to be able to offer this novel treatment option for dermatologists and their patients."*

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 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, multi-center, 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 U.S. 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.

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. AK is the second most common diagnosis made by dermatologists in the United States.[1] The reported prevalence of AK is between 11% and 25%.[2]

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.

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 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. For learn more about the Almirall Advantage copay program and network pharmacy options please visit almiralladvantage.com.

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