Press Release

Exton, PA

11 February, 2021

Almirall announces New England Journal of Medicine publication of Phase III data demonstrating efficacy and safety of Klisyri® (tirbanibulin)

- **Klisyri® (tirbanibulin) is a novel microtubule inhibitor, recently approved by the U.S. Food and Drug Administration (FDA) for the topical treatment of actinic keratosis (AK) of the face or scalp**
- **In one of the largest Phase III clinical study programs[i] ever conducted for a topical actinic keratosis treatment, Klisyri® (tirbanibulin) demonstrated complete clearance of AK 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 from the Phase III studies due to treatment-related adverse events, and a convenient 5-day application period**
- **Actinic keratosis is the second most common diagnosis made by dermatologists in the United States[ii]**

Almirall, S.A. (BME:ALM), a global biopharmaceutical company focused on skin health, announced today that the New England Journal of Medicine (NEJM) has published the results from the pivotal Phase III trials of Klisyri® (tirbanibulin) ointment for actinic keratosis. The two double-blind, vehicle-controlled, randomized, parallel-group, multi-center trials (KX01-AK-003 and KX01-AK-004), are one of the largest Phase III clinical study programs ever conducted for a topical AK treatment.

Volker Koscielny, MD, Chief Medical Officer of Almirall said, *"We are delighted by the publication of the Phase III data for Klisyri® in the NEJM, one of the most prestigious and rigorously peer-reviewed medical journals in the world. The clinical trial data presented not only demonstrates significant efficacy, but importantly a proven tolerability and safety profile. Added to the short 5-day application period, we believe that Klisyri® provides an important addition to the therapeutic armamentarium of US dermatologists in treating actinic keratosis."*

The Phase III studies evaluated the efficacy and safety of Klisyri® (tirbanibulin) ointment 1% (10 mg/g) in adults with actinic keratosis on the face or scalp, and included 702 patients across 62 sites in the United States. Enrollment across patients was controlled to achieve a 2:1 ratio of facial to scalp treatment areas encompassing 4-8 typical AK lesions. Patients were randomly assigned in a 1:1 ratio to receive Klisyri® (tirbanibulin) ointment or vehicle ointment which was self-administered to 25 cm^2 of the face or scalp once daily for 5 consecutive days.

Both Phase III studies, KX01-AK-003 and KX01-AK-004, met the primary endpoint, which was defined as complete (100%) clearance of AK lesions at Day 57 within the face or scalp treatment areas, each study achieving a highly statistically significant result (p<0.0001).

In the KX01-AK-003 study, complete clearance was observed in 44% of the patients treated with Klisyri (tirbanibulin) versus 5% for those treated with vehicle, and in the KX01-AK-004 study, complete clearance was observed in 54% of the patients treated with Klisyri (tirbanibulin) versus 13% for vehicle. Furthermore, tirbanibulin also achieved the secondary endpoint of partial (≥75%) clearance of lesions in each study (68% of patients receiving tirbanibulin versus 16% receiving vehicle in study KX01-AK-003, and 76% versus 20% respectively in study KX01-AK-004). Both results were again highly statistically significant (p<0.0001).

"*In addition to robust efficacy data, tirbanibulin demonstrated a favorable safety profile. The most common (≥2%) adverse events were local skin reactions, including pruritus and pain, at the application site. No patients withdrew from the study due to treatment-related adverse events,"* stated **Andrew Blauvelt, MD, MBA,** President of Oregon Medical Research Center, and one of the lead investigators of the studies.

Local skin reactions were mostly mild-to-moderate in nature and resolved without intervention. The percentages of subjects with the maximal post-baseline grades for each local skin reaction greater than baseline (>10%) by treatment group (Klisyri vs. Vehicle) were: Erythema: Mild (22%, 28%), Moderate (63%, 6%), Severe (6%, 0%); Flaking/Scaling: Mild (26%, 25%), Moderate (47%, 9%), Severe (9%, <1%); Crusting: Mild (30%, 9%), Moderate (14%, 2%), Severe (2%, 0%); Swelling: Mild (29%, 4%), Moderate (9%, <1%), Severe (<1%, 0%).

"This important publication represents a significant achievement for Athenex and all of our colleagues who have worked to discover, develop, and bring Klisyri® to market," said **Johnson Lau**, **MD,** CEO of Athenex. *"We would like to wholeheartedly thank our clinical investigators and the patients who participated in these trials, which were critical in confirming the clinical efficacy and safety profile in order to obtain FDA approval of Klisyri."*

About Klisyri®

Klisyri® is a novel, first-in-class microtubule inhibitor indicated for the topical treatment of actinic keratosis of the face or scalp. It 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.

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

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/.

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 publically 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

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References

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iii 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