

# Almirall and Athenex Announce Positive Topline Results from Two Phase III Studies of KX2-391 Ointment 1% Featured in Late Breaker Program at the 2019 American Academy of Dermatology Annual Meeting

- **Results show that 44% and 54% of patients in studies KX01-AK-003 and KX01-AK-004, respectively, achieved 100% AK lesion clearance at Day 57.**
- **Safety profile of KX2-391 ointment may be an important competitive advantage.**

Almirall, S.A. (ALM) and Athenex, Inc. (NASDAQ: ATNX), a global biopharmaceutical company dedicated to the discovery, development and commercialization of novel therapies for the treatment of cancer and related conditions, today announced that an oral presentation reporting the results from two Phase III studies of KX2-391 ointment in the treatment of actinic keratosis (AK) was featured in the Late-Breaking Research: Clinical Trials session at the 2019 American Academy of Dermatology Annual Meeting in Washington, DC on March 2, 2019. KX2-391, also known as KX-01, is a first-in-class dual Src kinase and tubulin polymerization inhibitor being developed by Athenex as a topical medicinal product (1% ointment) for the treatment of AK in adult patients.

## Topline Efficacy Results

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 (see Table 1).

Table 1: Efficacy of KX2-391 Ointment in the Field Treatment of Actinic Keratosis

Study	KX01-AK-003			KX01-AK-004		
	KX2-391	Vehicle	p-value	KX2-391	Vehicle	p-value
% of Subjects in the Intent-To-Treat Population (Number of Subjects)	N=175	N=176		N=178	N=173	
<b>100% AK Clearance on Day 57</b>	<b>44% (N=77)</b>	<b>5% (N=8)</b>	<b>&lt;0.0001<sup>a</sup></b>	<b>54% (N=97)</b>	<b>13% (N=22)</b>	<b>&lt;0.0001<sup>a</sup></b>
Face	50%	6%	<0.0001	61%	14%	<0.0001
Scalp	30%	2%	<0.0001	41%	11%	0.0003
≥75% AK Clearance on Day 57	68%	16%	<0.0001 <sup>a</sup>	76%	20%	<0.0001 <sup>a</sup>

Note:

a = p-value calculated based on Cochran-Mantel-Haenszel (CMH)

Statistical significant difference in 100% clearance was demonstrated for all subgroups analyzed in both studies based on treatment location (face or scalp), gender, age (<65 and >65 years old), number of baseline AK lesions (4-6 versus 7-8 lesions) and also skin type. Compliance to 5-day of self-treatment was over 99% for both studies.

## Safety Results

Safety results showed that KX2-391 ointment was well tolerated. Adverse events were few. Treatment related adverse events were mild to moderate application site symptoms, such as pruritus or pain. There were no serious adverse events or early discontinuations due to study drug related adverse events. Local skin reactions (LSR: erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation, erosion/ulceration) were mostly mild to moderate.

**Dr. Rudolf Kwan, Chief Medical Officer of Athenex**, said: *“We are very pleased with the results of these Phase III pivotal trials, which showed that KX2-391 ointment demonstrated excellent activity in the treatment of AK on the face or scalp and was very well tolerated. We believe that this product, if approved by the regulatory authorities, could have a major impact in the medical treatment of AK. We look forward to discussing the results with the U.S. FDA. We are grateful to all the patients, investigators and site personnel who participated in the study, and also delighted with the support from our partners”.*

**Dr. Edward Lain, MD, of Austin Institute for Clinical Research in Pflugerville, Texas**, also stated: *“The results of the pivotal trials for KX2-391 ointment 1% are impressive and exciting for our patients with actinic keratosis. The excellent clearance rate, short treatment duration, and low incidence of severe local skin reactions provide evidence that this novel mechanism of action may indeed be an important development in the AK treatment landscape”.*

## **Trial Design**

These two double-blind, randomized, vehicle-controlled, randomized, parallel group, multi-center studies (KX-AK-003 and KX-AK-004) were designed to support the registration of KX2-391 ointment as field therapy for AK of the face or scalp. The studies enrolled a total of 702 patients across 62 sites in the US. KX2-391 ointment 1% or vehicle (randomized 1:1) was self-administered to 25 cm<sup>2</sup> of the face or scalp encompassing 4-8 typical AK lesions, once daily for 5 consecutive days. Patients in both studies were predominantly white elderly male with fair skin type and median baseline AK lesions of 6 on the face or scalp.

The one year follow up of patients who had complete responses is ongoing and is expected to be complete in the second quarter 2019. Athenex plans to submit a request to the U.S. FDA for a pre-NDA meeting to discuss the data and regulatory submission timelines.

**Bhushan Hardas, M.D., MBA, Chief Scientific Officer of Almirall**, said: *“We are extremely pleased with the topline results from the phase III studies. It is important for AK patients to seek treatment and physicians need additional treatment options. Based on the encouraging efficacy and safety results on day 57, we believe this product, if approved, could change the way physicians treat AK”.*

As announced on December 11, 2017, Athenex and Almirall, S.A., a leading skin-health focused global pharmaceutical company and one of the leaders in the field of actinic keratosis treatment, entered into a license agreement in which Athenex granted Almirall an exclusive license to research, develop and commercialize KX2-391 in the U.S. and European countries, including Russia. Almirall will employ its expertise to support the development in Europe and also to commercialize the product in the defined territories. Athenex received an upfront payment, and is also entitled to milestone and royalty payments.

## **About Actinic Keratosis**

Actinic Keratosis is a common skin condition that is induced through ultra-violet light damage, resulting in patches of thick, scaly or crusty skin. Left untreated, the lesions have risk of progression to squamous cell carcinoma and consequently treatment by a dermatologist is recommended. AK is the most common pre-cancerous condition in dermatology and affects more than 55 million Americans, and account for between 14-29% of dermatologist visits in the U.S.<sup>1</sup>

## **About Almirall**

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

The company, founded almost 75 years ago with headquarters in Barcelona, is listed on the Spanish Stock Exchange (ticker: ALM). Almirall has been key in value creation to society according to its commitment with to major shareholders and through its decision to help others, to understand their challenges and to use Science to provide solutions for real life. Total revenues in 2018 were 811 million euros. More than 1,830 employees are devoted to Science.

For more information, please visit [almirall.us](http://almirall.us).

## **About Athenex**

Founded in 2003, Athenex, Inc. is a global clinical stage biopharmaceutical company dedicated to becoming a leader in the discovery and development of next generation drugs for the treatment of cancer. Athenex is organized around three platforms, including an Oncology Innovation Platform, a Commercial Platform and a Global Supply Chain Platform. The Company's current clinical pipeline is derived from four different platform technologies: (1) Orascovery, based on non-absorbed P-glycoprotein inhibitor, (2) Src kinase inhibition, (3) T-cell receptor-engineered T-cells (TCR-T), and (4) Arginine deprivation therapy. Athenex's employees worldwide are dedicated to improving the lives of cancer patients by creating more active and tolerable treatments. Athenex has offices in Buffalo and Clarence, New York; Cranford, New Jersey; Houston, Texas; Chicago, Illinois; Hong Kong; Taipei, Taiwan; and multiple locations in Chongqing, China. For more information, please visit [www.athenex.com](http://www.athenex.com).

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**References**

1. E. Stockfleth et al. Physician perceptions and experience of current treatment in actinic keratosis. JEADV 2015, 29, 298–306