# LEO Pharma - LEO Pharma completes FIELD Study 1

Ballerup, Denmark, 26 September 2013 - LEO Pharma today announced the completion of the Phase III FIELD Study 1 – the largest1-3 ever, one year evaluation of field treatment with ingenol mebutate gel for actinic keratosis (AK) after initial cryosurgery of individual AK lesions, compared to cryosurgery followed by a vehicle gel.

The study involved more than 300 patients across 35 trial sites and is also the first to evaluate field treatment with ingenol mebutate gel subsequent to cryosurgery.

LEO Pharma reported that the study met its efficacy and safety endpoints at 11 weeks and 12 months. The 11 week results are expected to be published by the end of 2013, with publication of the one year data expected in the first half of 2014.

AKs are rough skin lesions caused by cumulative UV exposure from the sun,[4] which can lead to non-melanoma skin cancer (NMSC) if not treated early and effectively.[5] Some treatments such as cryosurgery target single visible lesions (lesion-directed therapy), whilst others, such as novel topical treatment ingenol mebutat gel, target an area or field, where visble and sub-clinical (invisible) lesions are located (field-directed therapy).

AK can be characterised as a phenomenon known as field cancerization (also known as actinic field damage) which describes both the visible and sub-clinical changes in skin cells caused by long-term UV sun exposure.[6]

A high sustained clearance of AK lesions in an area of field UV damage is generally not fully achieved with lesion-directed therapies such as cryosurgery, which target only visible AKs.[7] AK treatment strategies that include both lesion-specific and field-directed therapies to treat visible as well as sub-clinical AK lesions have demonstrated imprved clearance and lower recurrence rates.[3]

Brian Berman, MD, PhD, Voluntary Professor of Dermatology and Cutaneous Surgery at the University of Miami Miller School of Medicine in the US, and lead investigator in the FIELD Study 1, commented:

*"The results of this study are very promising. The 12 month data show sustained patient benefits beyond those the 11 week results indicated. These data provide important evidence for the beneficial role of Picato® field-directed treatment in combination with cryosurgery, in achieving clearance of sub-clinical lesions in the field and preventing further AK lesion recurrence."*

Dr Kim Kjøller, Senior Vice President of Global Development at LEO Pharma, added: *"The completion of this study represents a significant milestone; the positive results provide further clinical evidence for the role of Picato® in the management of AK in conjunction with cryosurgery."*

## NOTES TO EDITORS

About Picato® (ingenol mebutate gel) Picato® is a topical, field-directed therapy which is self-administered by the patient to the affected areas of the skin once a day for two or three consecutive days, depending on the treatment location.8 Picato® has demonstrated efficacy in clearing actinic keratosis lesions on the face and scalp, as well as on the trunk and extremities, in a large clinical trial programme.8 Picato® was approved by the US Food and Drug Administration (FDA) in

January 2012; by the Agência Nacional de Vigilância Sanitária (ANVISA) in Brazil in July 2012; by the Therapeutic Goods Administration (TGA) in Australia and the European Commission (EC) in Europe in November 2012, by Health Canada in January 2013 and by the Swiss Agency of Therapeutic Products (Swissmedic) in June 2013.

Important product information
Contact with the eyes should be avoided. Eye disorders such as eye pain, eyelid oedema and periorbital oedema should be expected to occur after accidental eye exposure of Picato®. Picato® must not be ingested. Administration of Picato® is not recommended until the skin is healed from treatment with any previous medicinal product or surgical treatment and should not be applied to open wounds or damaged skin where the skin barrier is compromised. Picato® should not be used near the eyes, on the inside of the nostrils, on the inside of the ears or on the lips. Local skin responses such as erythema, flaking/scaling, and crusting should be expected to occur after cutaneous application of Picato®. Due to the nature of the disease, excessive exposure to sunlight (including sunlamps and tanning beds) should be avoided or minimised. Lesions clinically atypical for actinic keratosis or suspicious for malignancy should be biopsied to determine appropriate treatment. There are no data from the use of ingenol mebutate gel in pregnant women. Risks to humans receiving cutaneous treatment with ingenol mebutate gel are considered unlikely as Picato® is not absorbed systemically. As a precautionary measure, it is preferable to avoid the use of Picato® during pregnancy. Actinic keratosis is not a condition generally seen within the pediatric population. The safety and efficacy of Picato® for actinic keratosis in patients less than 18 years of age have not been established.

About the FIELD Study 1[3]
FIELD Study 1 is a phase III, multicenter, randomized, 2-arm, double-blind, vehicle controlled 12-month study investigating the efficacy and safety profile of sequential treatment of AK on the face or scalp with cryosurgery followed by Picato®, 0.015% treatment compared with cryosurgery followed by vehicle gel. In Arm A of the study, patients received cryosurgery and after three weeks of healing time, were then treated with Picato®. In Arm B of the study, patients received cryosurgery and after three weeks of healing time, were then treated with vehicle gel. The selected treatment area was a 25 $cm^2$ contiguous area on the face or scalp that contained four to eight visible and discrete AK lesions. The primary efficacy endpoint in the FIELD Study 1 post-treatment initiation was complete clearance of AKs in the treatment area, measured at 11 weeks. Secondary efficacy endpoints in the FIELD Study 1 post-treatment initiation measured at 11 weeks and 12 months comprise: percentage reduction from baseline in the number of AKs and partial clearance (75% reduction from baseline) of clinically visible AKs in the treatment area. Safety endpoints in the FIELD Study 1 were comprised of the incidence of adverse events (AEs); the incidence and severity of local skin responses (LSRs) following treatments; and the incidence of AEs and LSRs leading to the discontinuation of treatment with Picato®.

ClinicalTrials.gov Identifier: NCT01541553.

About actinic keratosis (AK)
Actinic keratoses are common skin lesions which are often red and scaly.[4] The majority of lesions are caused by cumulative sun exposure in fair-skinned people.[9] AK is a precursor to NMSC.[10] The number of patients with actinic keratosis is rapidly growing, especially in Europe, the US and Australia.[11]

References
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