Media Release

16 December 2016

Actelion receives positive CHMP opinion for chlormethine gel (Ledaga) for the treatment of MF-CTCL

ALLSCHWIL/BASEL, SWITZERLAND – 16 December 2016 – Actelion Ltd (SIX: ATLN) announced today that the Committee for Medicinal Products for Human Use (CHMP), the scientific committee of the European Medicines Agency (EMA), issued a positive opinion for the use of chlormethine gel 160 micrograms/g (Ledaga®) for the treatment of mycosis fungoides-type cutaneous T-cell lymphoma (MF-CTCL) in adult patients and recommended that the European Commission approves the product.

The CHMP opinion is based on the results of the pivotal 201 study, the largest randomized controlled study ever conducted in MF-CTCL involving 260 patients. In this study 77% of patients who were treated for at least 6 months with chlormethine gel achieved a clinical response, in the Composite Assessment of Index Lesion Severity (CAILS) score, while 59% of those treated with the compounded control had a clinical response. A response was defined as an at least 50% improvement in the baseline CAILS score. Complete response was achieved in 19% of patients versus 15% of patients treated with the compounded control. Reductions in mean lesion severity were seen as early as four weeks into the study, with further reductions observed with continuing therapy. The time to first confirmed response favored chlormethine gel (Ledaga) compared to the compounded control.

MF-CTCL is a rare, potentially life-threatening immune system cancer that appears in the skin. MF-CTCL is usually a chronic disease and the course of disease in individual patients is unpredictable. In around 10% of cases, MF-CTCL cells can metastasize to other body tissues, including the liver, spleen and lungs.

In the 201 study, the most frequent adverse reactions reported with chlormethine gel were skin related: dermatitis (54.7%; e.g., skin irritation, erythema, rash, urticaria, skin-burning sensation, pain of the skin), pruritus (20.3%), skin infections (11.7%), skin ulceration and blistering (6.3%), and skin hyperpigmentation (5.5%). No systemic absorption of chlormethine was detected with treatment.

A CHMP positive opinion is one of the final steps before marketing authorization is granted by the European Commission. The European Commission is expected to issue a final decision by the end of February 2017.

Actelion has agreed to a list of recommendations from the CHMP (post-authorization measures) with regards to release of the product in Europe. Subject to the agreed recommendations and achieving market access in different countries, a potential first launch of Ledaga could occur at the end of 2017 at the earliest.

ABOUT CHLORMETHINE GEL (LEDAGA)

Chlormethine is an alkylating drug indicated for the treatment of mycosis fungoides-type cutaneous T-Cell lymphoma (MF-CTCL) formulated as a topical, once-daily, colorless gel (Ledaga).

Chlormethine gel, under the brand name Valchlor® (mechlorethamine) is commercially available in the US (since 2013) and in Israel through special import authorization procedure (since 2016).

In France, patients benefit from the drug under a temporary authorization for use ("ATU") program initiated during the second half of 2014.

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Notes to Editor:

ABOUT MF-CTCL

Mycosis fungoides-type cutaneous T-Cell lymphoma (MF-CTCL) is a rare, but serious and life-threatening, immune system cancer that appears in the skin. MF-CTCL is the most common form of cutaneous T-cell lymphoma.

MF-CTLC typically appears in patients over 50 years of age (median age is 54), and is more common in men. It presents first as dry skin and a red rash, with or without itching. As a result, MF-CTLC is often mistaken for eczema or psoriasis, delaying diagnosis.
MF-CTLC goes on to form scaly plaques on the skin, which can cover small or large areas of the skin. Large bumps or tumor nodules may also develop, and lymph nodes may be involved.

While MF-CTCL is usually a chronic disease, the course of disease in individual patients is unpredictable with some patient progressing into advanced stages. In around 10% of cases, MF-CTCL cells can metastasize into other body tissues, including the liver, spleen and lungs.

Current research suggests that patients who are diagnosed in early stages of MF-CTCL have a normal life expectancy, however the average time to diagnosis ranges from two to seven years. An important therapeutic objective in treating MF-CTLC is prevention of disease progression. Failure to maintain MF-CTLC in its early stages results in a drastically reduced median survival.

ABOUT STUDY 201

Study 201 was a multicenter, randomized, observer-blinded, active-controlled, 12-month study of Stage I and IIA MF-type CTCL patients, conducted in 13 centers in the US to evaluate the efficacy and safety of

chlormethine gel compared with chlormethine HCl 0.02% compounded in Aquaphor® ointment. In total, 260 patients were randomized 1:1 to topical treatment with chlormethine gel or chlormethine HCl 0.02% compounded in Aquaphor® ointment once daily for up to 12 months.

In the study, 77% of patients treated with chlormethine gel had a clinical response at 12 months, in the Composite Assessment of Index Lesion Severity (CAILS*) score, while 59% of those treated with the compounded control achieved a confirmed response. (*A response was defined as an at least 50% improvement in the baseline CAILS score).

Complete response was achieved in 19% of patients versus 15% of patients treated with the compounded control. Reductions in mean lesion severity (CAILS) were seen as early as four weeks, with further reductions observed with continuing therapy. The time to first confirmed response favored chlormethine gel (Ledaga) compared to the compounded control.

The most frequent adverse reactions reported with chlormethine gel were skin related: dermatitis (54.7%; e.g., skin irritation, erythema, rash, urticaria, skin-burning sensation, pain of the skin), pruritus (20.3%), skin infections (11.7%), skin ulceration and blistering (6.3%), and skin hyperpigmentation (5.5%). No systemic absorption of chlormethine was detected with treatment.

Actelion Ltd.

Actelion Ltd. is a leading biopharmaceutical company focused on the discovery, development and commercialization of innovative drugs for diseases with significant unmet medical needs.

Actelion is a leader in the field of pulmonary arterial hypertension (PAH). Our portfolio of PAH treatments covers the spectrum of disease, from WHO Functional Class (FC) II through to FC IV, with oral, inhaled and intravenous medications. Although not available in all countries, Actelion has treatments approved by health authorities for a number of specialist diseases including Type 1 Gaucher disease, Niemann-Pick type C disease, Digital Ulcers in patients suffering from systemic sclerosis, and mycosis fungoides type cutaneous T-cell lymphoma.

Founded in late 1997, with now over 2,500 dedicated professionals covering all key markets around the world including Europe, the US, Japan, China, Russia and Mexico, Actelion has its corporate headquarters in Allschwil / Basel, Switzerland.

Actelion shares are traded on the SIX Swiss Exchange (ticker symbol: ATLN) as part of the Swiss blue-chip index SMI (Swiss Market Index SMI®).

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