Media Release

27 February 2014

Actelion's novel antibiotic cadazolid receives US FDA Qualified Infectious Disease Product designation for the treatment of *Clostridium difficile*-associated diarrhea

ALLSCHWIL/BASEL, SWITZERLAND – 27 February 2014 – Actelion Ltd (SIX: ATLN) today announced that the US Food and Drug Administration (FDA) has designated cadazolid as both a Qualified Infectious Disease Product (QIDP) and a Fast Track development program for the treatment of *Clostridium difficile*-associated diarrhea (CDAD).

The QIDP designation for cadazolid means that - among other incentives - cadazolid would receive a nine-month priority review upon successful completion of the ongoing global Phase III IMPACT program. The Fast Track designation is intended to promote communication and collaboration between the FDA and the Company on the development of the drug.

The designations are based on the 2012 US Generating Antibiotic Incentives Now (GAIN) Act. The GAIN act is a legislative effort to incentivize the development of new antibiotic agents that target serious life-threatening infections.

Guy Braunstein, M.D. and Head of Clinical Development commented: "*Clostridium difficile*-associated diarrhea is a very serious and potentially life-threatening infection. There is a great need for an antibiotic that allows effective treatment of CDAD with low recurrence rates, particularly in infections caused by hypervirulent strains. The GAIN act highlights the importance of research in this area and we are very happy to receive the advantages that this designation for cadazolid will afford us."

ABOUT THE IMPACT PROGRAM

IMPACT is an **I**nternational **M**ulti-center **P**rogram **A**ssessing **C**adazolid **T**reatment in patients suffering from *Clostridium difficile*-associated diarrhea (CDAD). The program comprises two Phase III studies comparing the efficacy and safety of cadazolid (250 mg administered orally twice daily for 10 days) versus vancomycin (125 mg administered orally four times daily for 10 days).

The IMPACT studies are designed to determine whether the clinical response after administration of cadazolid is non-inferior to vancomycin in subjects with CDAD, and whether administration of cadazolid is superior to vancomycin in the sustained clinical response. The program is expected to enroll approximately 1'280 subjects worldwide, and commenced enrollment in the fourth quarter of 2013.

ABOUT CADAZOLID

The novel antibiotic cadazolid is a strong inhibitor of *Clostridium difficile* protein synthesis leading to strong suppression of toxin and spore formation. In preclinical studies cadazolid showed potent in vitro activity against *Clostridium difficile* clinical isolates and a low propensity for resistance development. In a human gut model of CDAD, cadazolid had a very limited impact on the normal gut microflora.

Cadazolid absorption is negligible resulting in high gut lumen concentrations and low systemic exposure, even in severe cases of CDAD where the gut wall can be severely damaged and permeability to drugs potentially increased.

ABOUT CADAZOLID IN THE PHASE II STUDY

Cadazolid was studied in a Phase II multi-center, double-blind, randomized, active reference, parallel group, therapeutic exploratory study. The study evaluated the efficacy, safety and tolerability of a 10-day, twice daily oral administration of 3 doses (250 mg, 500 mg or 1,000 mg b.i.d.) of cadazolid in subjects with *Clostridium difficile*-associated diarrhea (CDAD). As the current standard of care for CDAD, oral vancomycin (125 mg qid for 10 days) was used as the active reference. The study was completed in December of 2012, after having enrolled 84 subjects with CDAD.

The results of the Phase II study indicate that the effect of all doses of cadazolid were numerically similar to, or better than vancomycin on key endpoints including CDAD clinical cure rates as well as sustained cure rates. Clinical cure rate was defined as the resolution of diarrhea and no further need for CDAD therapy at test-of-cure 24 to 72 hours after the last dose of treatment, while sustained cure rate was defined as clinical cure with no recurrence of CDAD up to 4 weeks post-treatment. Recurrence rates were numerically lower for all doses of cadazolid as compared to vancomycin. Cadazolid was safe and well tolerated.

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NOTES TO THE EDITOR

ABOUT THE GAIN ACT (INCLUDING FAST TRACK DESIGNATION)

The Food and Drug Administration Safety and Innovation Act (FDASIA) was signed into law in July 2012. The GAIN Act is Title VIII to FDASIA. The purpose of the GAIN Act is to encourage pharmaceutical research of certain antibiotics by designation of products as QIDPs. These products are intended to treat serious or life-threatening infections and include those to treat certain specifically identified pathogens, which are listed in the

GAIN Act. *C. difficile* is one such specifically identified pathogen and drugs to treat CDAD would be eligible for designation as a QIDP.

The GAIN Act also provides that qualifying drugs (QIDPs) are eligible for inclusion in the FDA's Fast Track program. This program is intended to facilitate development and expedite review of new drugs and includes close early communication between the FDA and a drug's sponsor.

ABOUT FAST TRACK DRUG DEVELOPMENT PROGRAMS

For further information regarding Fast Track Drug Development Programs, please refer to the

FDA document "Guidance for Industry on Fast Track Drug Development Programs: Designation, Development, and Application Review". This document is available on the Internet at:

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079736.pdf

ABOUT *CLOSTRIDIUM DIFFICILE*-ASSOCIATED DIARRHEA

Clostridium difficile is a Gram-positive, anaerobic, spore-forming bacterium that is the leading cause of nosocomial diarrhea. *Clostridium difficile*-associated diarrhea (CDAD or CDI for *Clostridium difficile* infection) can be a severe and life-threatening disease and results from the overgrowth in the colon of toxigenic strains of *Clostridium difficile*, generally during or after therapy with broad-spectrum antibiotics. CDAD is a major healthcare problem and a leading cause of morbidity in elderly hospitalized patients. The frequency and severity of CDAD in the western world has increased in recent years, and new hypervirulent and epidemic strains of *Clostridium difficile* have been discovered that are characterized by overproduction of toxins and other virulence factors, and by acquired resistance to fluoroquinolones such as moxifloxacin.

Current antibiotic therapy for CDAD includes vancomycin and metronidazole. While clinical cure rates are generally 85-90%, recurrences rates of 15-30 % with either drug are problematic as *Clostridium difficile* produces spores that are resistant to antibiotic treatment and routine disinfection. Spores surviving in the gut of patients and/or in the hospital environment may play a major role in re−infection and recurrence of CDAD after antibiotic treatment. Vancomycin and metronidazole are reported to promote spore formation *in vitro* at sub-inhibitory concentrations.

Only one new antibiotic, fidaxomicin, has been approved over the last 30 years for this indication, and there remains a need for new drugs with improved properties, in particular, antibiotics that allow effective treatment of infections caused by hypervirulent strains, with low recurrence rates.

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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 in patients with cutaneous T-cell lymphoma.

Founded in late 1997, with now over 2,400 dedicated professionals covering all key markets around the world including 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®). All trademarks are legally protected.

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