Selexipag (Uptravi) data in pulmonary arterial hypertension to be presented at American College of Cardiology (ACC) 2015

ALLSCHWIL, SWITZERLAND – 02 March 2015 – Actelion Ltd (SIX: ATLN) today announced that key data from the pivotal Phase III selexipag (Uptravi®) study will be shared during an oral presentation at the American College of Cardiology (ACC) Congress in San Diego, US. The abstract is now available on-line at the following link: http://www.abstractsonline.com/pp8/#/3658/presentation/29719

The oral presentation, entitled ‘Effect of selexipag on morbidity/mortality in pulmonary arterial hypertension: results of the GRIPHON study’ will be given by Professor Vallerie McLaughlin of the University of Michigan Health System Division of Cardiovascular Medicine in Ann Arbor, Michigan, US at 12:00pm on March 15th.

The data presentation will be followed by an invitation-only investor relations event at 6pm on March 15th, where the same presentation will be given for the investor community.

Notes to Editor:

SELEXIPAG AT ACC-15

Oral presentation


Poster presentations

‘The non-prostanoid prostacyclin receptor agonist ACT-333679, the active metabolite of selexipag, is characterized by low beta-arrestin recruitment and receptor internalization activity’. John Gatfield, Katalin Menyhart, Keith Morrison, Oliver Nayler. Presented by Martine Clozel. March 14, 2015, 10:00–10:45am.

REGULATORY STATUS OF SELEXIPAG
In December 2014, Actelion submitted the registration dossier for selexipag to both Europe's EMA and the US FDA for the treatment of patients with pulmonary arterial hypertension. Submission of the registration dossier to other Health Authorities is ongoing with regulatory review underway in New Zealand, Canada and Switzerland.

ABOUT SELEXIPAG
Selexipag, originally discovered and synthesized by Nippon Shinyaku, is a potent, orally available, selective IP prostacyclin receptor agonist.

Selexipag selectively targets the prostacyclin receptor (also called IP-receptor). The IP receptor is one of 5 types of prostanooid receptor. Prostacyclin activates the IP receptor inducing vasodilation and inhibiting proliferation of vascular smooth muscle cells. Selexipag, unlike prostacyclin analogs, is selective for the IP receptor over other prostanooid receptors. In preclinical models selective IP receptor agonism has shown to maintain efficacy and reduce the risk of side effects mediated by activation of other prostanooid receptors, such as EP₁ and EP₃ receptors. [1,2,3]

Selexipag was previously evaluated in a Phase II, 43-patient, placebo-controlled, double-blind study, where patients were randomized in a 3:1 ratio receiving selexipag or placebo on top of PDE-5 inhibitor and/or ERA. [4]

ABOUT GRIPHON
GRIPHON, (Prostacyclin (PGI₂) Receptor agonist In Pulmonary arterial HypertensiON) was a randomized, multicenter, double-blind, placebo-controlled trial evaluating the long term efficacy and safety of oral selexipag in patients with pulmonary arterial hypertension.

The GRIPHON study was the largest outcome trial ever conducted in PAH, enrolling patients in 181 centers from 39 countries in North and Latin America, Europe, Asia-Pacific and Africa.

GRIPHON enrollment was completed in May 2013 with 1,156 patients and represents the largest randomized, controlled study in PAH patients. Patients received twice daily administration of selexipag or placebo and were also permitted to receive background therapy of endothelin receptor antagonist and/or a phosphodiesterase-5 inhibitor when on a stable dose for at least 3 months prior to enrollment. At baseline, 80% of patients were receiving oral medication specific for PAH: either an ERA, a PDE-5 inhibitor, or a combination of the two.

This pivotal, event-driven study was designed to demonstrate a prolongation of time to the first morbidity/mortality event for selexipag compared to placebo and to evaluate the safety of the selexipag in PAH patients. All morbidity and mortality events reported by the investigators were adjudicated by an independent Critical Event Committee blinded to the study treatment.

DOSEING IN GRIPHON
Uptitration of selexipag allows each patient's maintenance dose to be individualized based on tolerability. Dosing in GRIPHON was initiated at 200 micrograms (mcg) bid and increased in steps of 200 mcg twice daily up to a maximum of 1600 mcg twice daily.

ABOUT SAFETY AND TOLERABILITY IN GRIPHON
The most common adverse events in GRIPHON that occurred with higher frequency on selexipag than placebo were in-line with those known in prostacyclin therapies; headache, diarrhea, nausea, jaw pain, vomiting, pain in extremity, myalgia, nasopharyngitis and flushing.
The proportion of patients discontinuing treatment due to adverse events was 14 percent on selexipag and 7 percent on placebo.

THE ROLE OF THE PROSTACYCLIN PATHWAY
The prostacyclin pathway is one of the 3 essential pathways involved in the pathophysiology and treatment of PAH. Prostacyclin is a prostanoid and serves as a signaling molecule in the human body. It is produced, like other vasoactive substances, by endothelial cells. Prostacyclin induces vasodilation, is anti-proliferative, has anti-inflammatory effects and inhibits platelet aggregation. In certain disease conditions, the production of prostacyclin by the endothelium is impaired, allowing for example, the deleterious effects of excessive levels of endothelin to predominate.

PULMONARY ARTERIAL HYPERTENSION (PAH)
Pulmonary arterial hypertension (PAH) is a chronic, life-threatening disorder characterized by abnormally high blood pressure in the arteries between the heart and lungs of an affected individual. The symptoms of PAH are non-specific and can range from mild breathlessness and fatigue during normal daily activity to symptoms of right heart failure and severe restrictions on exercise capacity and ultimately reduced life expectancy.

PAH is one group within the classification of pulmonary hypertension (PH). This group includes idiopathic PAH, heritable PAH and PAH caused by factors which include connective tissue disease, HIV infection and congenital heart disease.

The last decade has seen significant advances in the understanding of the pathophysiology of PAH, which has been paralleled with developments of treatment guidelines and new therapies. Drugs targeting the three pathways that have been established in the pathogenesis of PAH are endothelin receptor antagonists (ERAs), prostacyclin analogs and phosphodiesterase-5 inhibitors. PAH treatments have transformed the prognosis for PAH patients from symptomatic improvements in exercise tolerance 10 years ago to delayed disease progression today. Improved disease awareness and evidence-based guidelines developed from randomized controlled clinical trial data have highlighted the need for early intervention, goal-oriented treatment and combination therapy.

In PAH, survival rates are unacceptably low and PAH remains incurable.

ABOUT THE ACTELION / NIPPON SHINYAKU ALLIANCE
Actelion and Nippon Shinyaku entered into an exclusive worldwide alliance in April 2008 to collaborate on selexipag, a first orally-available, selective prostacyclin IP receptor agonist for patients suffering from pulmonary arterial hypertension (PAH). This compound was originally discovered and synthesized by Nippon Shinyaku. Actelion is responsible for global development and commercialization of selexipag outside Japan, while the two companies will co-develop and co-commercialize in Japan. Nippon Shinyaku will receive milestone payments based on development stage and sales milestones as well as royalties on any sales of selexipag.

References

NIPPON SHINYAKU
For further information on Nippon Shinyaku please visit:
http://www.nippon-shinyaku.co.jp/english/index.html

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 2,400 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®). All trademarks are legally protected.

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