Further macitentan (Opsumit®) data in pulmonary arterial hypertension presented at key congresses

ALLSCHWIL/BASEL, SWITZERLAND – 31 August 2013 - Actelion Ltd (SIX: ATLN) today announced that further data on its investigational drug macitentan (Opsumit®) from the SERAPHIN study will be presented at the European Society of Cardiology (ESC) Congress 2013 in Amsterdam, the Netherlands (31st August–4th September 2013) and the European Respiratory Society (ERS) Annual Congress in Barcelona, Spain (7th–11th September 2013).

Data to be presented at ESC Congress 2013
Dr Nazzareno Galiè from the Institute of Cardiology, University of Bologna, Bologna, Italy, will give an oral presentation entitled ‘Sustained effect of macitentan, a novel oral endothelin receptor antagonist, on exercise capacity and the association of its measure with long-term outcomes in pulmonary arterial hypertension’ at 11:00 on September 1st during the session ‘Advances in Drug Therapy for PAH’.

Dr Adam Torbicki of the Department of Pulmonary Circulation and Thromboembolic Diseases, Center of Postgraduate Medical Education, ECZ-Otwock, Poland, will also make an oral presentation ‘Effect of macitentan on haemodynamics in patients with pulmonary arterial hypertension: results from the long-term, randomised, placebo-controlled SERAPHIN trial’ at 11:15 on September 1st in the same session.

Data to be presented at ERS Congress 2013
Professor Hossein-Ardeschir Ghofrani from the University Hospital Giessen, Giessen, Germany, will give an oral presentation entitled ‘Effect of macitentan on morbidity and mortality in pulmonary arterial hypertension: a randomised controlled trial’ during the ‘Pulmonary circulation: treatment’ session at 10:00 on September 9th.

Professor Marion Delcroix of Gasthuisberg University Hospital, Leuven, Belgium will present a poster entitled ‘Is 6-minute walk distance (6MWD) associated with long-term outcomes in pulmonary arterial hypertension (PAH)? Results from SERAPHIN’ during the ‘Pulmonary circulation: clinical science and treatment’ session at 08:30 on September 10th.
Further macitentan data at key congresses

Professor Olivier Sitbon of the Hôpital Universitaire de Bicêtre, Université Paris-Sud, Paris, France will present a poster on the ‘Effect of macitentan on haemodynamics in SERAPHIN, a randomised controlled trial in pulmonary arterial hypertension (PAH)’ during the Pulmonary circulation: clinical treatment poster session at 12:50 on September 10th.

Professor Pavel Jansa of Charles University, Prague, Czech Republic will present the poster ‘Impact of macitentan on the health-related quality of life (HRQoL) in pulmonary arterial hypertension (PAH): results from a long-term randomised controlled trial’ during the Pulmonary circulation: clinical treatment poster session at 12:50 on September 10th.

NOTES TO THE EDITOR

ESC ABSTRACTS

Oral Presentations

Sustained effect of macitentan, a novel oral endothelin receptor antagonist, on exercise capacity and the association of its measure with long-term outcomes in pulmonary arterial hypertension.
N Galiè, R Channick, M Delcroix, H-A Ghofrani, P Jansa, F-O Le Brun, G Simmoneau, LJ Rubin
Oral abstract presentation: September 01, 11.00–11.15
Abstract Number: 1061

Effect of macitentan on haemodynamics in patients with pulmonary arterial hypertension: results from the long-term, randomised, placebo-controlled SERAPHIN trial
A Torbicki, S Mehta, L Perchenet, T Pulido, BKS Sastry, O Sitbon, R Souza, LJ Rubin, G Simmoneau
Oral abstract presentation: September 01, 11.15–11.30
Abstract Number: 1062

ERS CONGRESS 2013 ABSTRACTS

Oral Presentations

Effect of macitentan on morbidity and mortality in pulmonary arterial hypertension: a randomised controlled trial
Oral presentation: September 09, 10.00–10.15
Abstract Number: 850897

Is 6-minute walk distance (6MWD) associated with long-term outcomes in pulmonary arterial hypertension (PAH)? Results from SERAPHIN
Poster discussion: September 10, 08.30–10.00
Abstract Number: 851571

Poster Presentations

Impact of macitentan on the health-related quality of life (HRQoL) in pulmonary arterial hypertension (PAH): results from a long-term randomised controlled trial
Poster: September 10, 12:50–14:40
Abstract Number: 850697

Effect of macitentan on haemodynamics in SERAPHIN, a randomised controlled trial in pulmonary arterial hypertension (PAH)
Poster: September 10, 12:50–14:40
Abstract Number: 854762

- Further macitentan data at key congresses -
ABOUT THE SERAPHIN STUDY

SERAPHIN (Study with an Endothelin Receptor Antagonist in Pulmonary arterial Hypertension to Improve clinical outcome) was the largest and longest randomized, controlled study in PAH patients to include a clearly defined morbidity/mortality primary endpoint [2]. The pivotal Phase III study was designed to evaluate the efficacy and safety of macitentan (Opsumit®) - a novel dual endothelin receptor antagonist that resulted from a tailored drug discovery process - through the primary endpoint of time to first morbidity and all-cause mortality event in patients with symptomatic PAH.

Global enrollment was completed in December 2009 with a total of 742 patients. Patients were randomized 1:1:1 to receive two different doses of macitentan (3 mg and 10 mg once daily) or placebo. Patients were allowed to receive PAH background therapy throughout the study, either PDE-5 inhibitors or oral/inhaled prostanoids. This event-driven study was conducted in 151 centers from almost 40 countries in North America, Latin America, Europe, Asia-Pacific and Africa and was completed in the first half of 2012, with 287 patients having an adjudicated event.

ABOUT SERAPHIN STUDY DATA

Patients were randomized to placebo (n=250), macitentan 3 mg (n=250), or macitentan 10 mg (n=242). The primary end point occurred in 46.4%, 38.0%, and 31.4% of the patients in these groups, respectively. The hazard ratio for macitentan 3 mg versus placebo was 0.70 (97.5% CI, 0.52 to 0.96; p=0.0108) and the hazard ratio for macitentan 10 mg versus placebo was 0.55 (97.5% CI, 0.39 to 0.76; p<0.0001). Worsening of pulmonary arterial hypertension was the most frequent primary end point event. The effect of macitentan on this end point was observed irrespective of background therapy for pulmonary arterial hypertension. [1]

ABOUT THE SAFETY AND TOLERABILITY PROFILE

Macitentan was well tolerated in the SERAPHIN study. The overall incidence of adverse events reported and treatment discontinuations due to adverse events in patients was similar across all groups. The incidence of serious adverse events was lower in patients treated with macitentan compared to placebo, with 52% and 45% of patients in the macitentan 3 mg and 10 mg groups respectively, and 55% of patients in the placebo group experiencing serious adverse events.

Compared with placebo, a higher proportion of macitentan-treated patients had nasopharyngitis, headache, and anemia. One patient in each treatment group discontinued due to anemia.

Elevations of liver alanine or aspartate aminotransferases greater than three times the upper limit of normal were observed in 4.5 percent of patients receiving placebo, 3.4 percent of patients on 10 mg of macitentan and in 3.6 percent of patients on 3 mg of macitentan. In addition, no difference in fluid retention (edema) was observed between macitentan and placebo. [1]

ABOUT MACITENTAN (OPSUMIT®)

Macitentan (Opsumit®) is a novel dual endothelin receptor antagonist (ERA) that resulted from a tailored drug discovery process with the target of developing an ERA optimized for efficacy and safety [3]. Macitentan has a number of potentially key beneficial characteristics including increased in vivo preclinical efficacy versus existing ERAs resulting from sustained receptor binding [4] and physicochemical properties that allow enhanced tissue penetration [5]. The clinical pharmacology program also indicated a low propensity of macitentan for drug-drug interactions [6,7,8].

- Further macitentan data at key congresses -
ABOUT MACITENTAN (OPSUMIT®) SUBMISSIONS TO HEALTHCARE AUTHORITIES

On 22nd October 2012 Actelion announced that it had submitted a new drug application to the US Food and Drug Administration (FDA) seeking approval for macitentan (Opsumit®) in patients with pulmonary arterial hypertension.

On 22nd November 2012 Actelion announced that it had successfully submitted the Market Authorisation Application to the European Medicines Agency (EMA) and a validation letter had been received.

Regulatory review is also ongoing in Canada, Switzerland, Australia, Taiwan and Mexico.

ABOUT PULMONARY ARTERIAL HYPERTENSION [9, 10]

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), prostacyclins 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.

Despite these advances in PAH, survival rates are unacceptably low and PAH remains incurable.

References
2. For a general discussion of a clinically meaningful outcome end-point, please see: Proceedings of the 4th world symposium on pulmonary hypertension. J Am Coll Cardiol 2009;54(1 Suppl).
Actelion Ltd

Actelion Ltd is a biopharmaceutical company with its corporate headquarters in Allschwil/Basel, Switzerland. Actelion's first drug Tracleer® (bosentan), an orally available dual endothelin receptor antagonist, has been approved as a therapy for pulmonary arterial hypertension. Actelion markets Tracleer through its own subsidiaries in key markets worldwide, including the United States (based in South San Francisco), the European Union, Japan, Canada, Australia and Switzerland. Actelion, founded in late 1997, is a leading player in innovative science related to the endothelium - the single layer of cells separating every blood vessel from the blood stream. Actelion's over 2,300 employees focus on the discovery, development and marketing of innovative drugs for significant unmet medical needs. 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®).

For further information please contact:

Roland Haefeli
Senior Vice President, Head of Investor Relations & Public Affairs
Actelion Pharmaceuticals Ltd, Gewerbestrasse 16, CH-4123 Allschwil
+41 61 565 62 62
+1 650 624 69 36
www.actelion.com

The above information contains certain “forward-looking statements”, relating to the company’s business, which can be identified by the use of forward-looking terminology such as “estimates”, “believes”, “expects”, “may”, “are expected to”, “will”, “will continue”, “should”, “would be”, “seeks”, “pending” or “anticipates” or similar expressions, or by discussions of strategy, plans or intentions. Such statements include descriptions of the company’s investment and research and development programs and anticipated expenditures in connection therewith, descriptions of new products expected to be introduced by the company and anticipated customer demand for such products and products in the company’s existing portfolio. Such statements reflect the current views of the company with respect to future events and are subject to certain risks, uncertainties and assumptions. Many factors could cause the actual results, performance or achievements of the company to be materially different from any future results, performances or achievements that may be expressed or implied by such forward-looking statements. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected.