Actelion provides an update on the bosentan study - COMPASS-2

ALLSCHWIL/BASEL, SWITZERLAND – 17 March 2014 – Actelion Ltd (SIX: ATLN) today announced the results of COMPASS-2, a Phase IV, prospective, randomized, double-blind, placebo-controlled, event-driven study evaluating the effect of bosentan on the time to first morbidity or mortality event in patients with symptomatic pulmonary arterial hypertension (PAH) already treated with sildenafil.

COMPASS-2 did not meet the primary endpoint of time to first morbidity or mortality event; bosentan showed a risk reduction of 17% versus placebo (p=0.25). In an exploratory analysis, bosentan on top of sildenafil showed an improvement of 21.8 meters in 6MWD at week 16 (p=0.01). The well characterized safety profile of bosentan was confirmed and a placebo-corrected incidence of 15.4% in liver enzyme elevations (aspartate aminotransferase (AST) or alanine aminotransferase (ALT)) greater than three times the upper limit of normal was observed over a median exposure to double-blind treatment of 23 months.

Vallerie McLaughlin MD, University of Michigan, Ann Arbor, US, Chair of the COMPASS-2 Steering Committee commented; “While the observed risk reduction of 17% did not reach statistical significance, I am convinced that this study provides important information for the scientific community and we are committed to perform all the necessary analyses to fully understand the outcome of the study.”

Alessandro Maresta MD, Vice President, Head of Global Medical Affairs, Actelion commented; “The completion of the COMPASS-2 study has been a significant effort in a changing PAH environment and shows our commitment to ongoing clinical research in PAH. We acknowledge that taking part in research is one of the most important ways to advance scientific knowledge, and we thank the investigators, their staff and all the patients for their participation in this long-term study.”

Full data from this study will be made available through scientific disclosure at upcoming congresses and peer-reviewed publications.

– COMPASS-2 results –
About COMPASS-2

The primary objective of COMPASS-2 was to demonstrate that bosentan prolongs the time to first morbidity or mortality event in patients with symptomatic PAH already receiving sildenafil therapy. COMPASS-2 was a prospective, double-blind, placebo-controlled, event-driven study evaluating the progression of PAH in two groups of patients already treated with sildenafil, one group receiving placebo and the second group receiving bosentan. Sildenafil and bosentan are approved treatments for PAH but which exerts their effects through different pathological pathways of the disease. The study was designed to demonstrate a relative risk reduction of 43% in the primary endpoint.

About Pulmonary Arterial Hypertension [1,2,3]

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. Three pathways have been established in the pathogenesis of PAH, the endothelin, nitric oxide and the prostacyclin pathways.

PAH treatments targeting these pathways 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.

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Notes to the Editor

About Tracleer® in Pulmonary Arterial Hypertension (PAH)

Tracleer® (bosentan), the first oral dual endothelin receptor antagonist, is approved for the treatment of pulmonary arterial hypertension (PAH) and made available by Actelion subsidiaries in the United States, the European Union, Japan, Australia, Canada, Switzerland and other markets worldwide.

-- COMPASS-2 results --
Treatment with Tracleer requires attention to two significant safety concerns [4]: Potential for serious liver injury (including rare cases of liver failure and unexplained hepatic cirrhosis in a setting of close monitoring) - Liver monitoring of all patients is essential prior to initiation of treatment and monthly thereafter. High potential for major birth defects - Pregnancy must be excluded and prevented by two forms of birth control; monthly pregnancy tests should be obtained. Because of these risks, Tracleer® is only supplied through controlled distribution.

References
1. Proceedings of the 5th World Symposium on Pulmonary Hypertension. JACC 2013;62 Suppl D
4. Tracleer® SPC

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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