



## Media Release

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### **Dose-finding Phase IIb study started in patients with multiple sclerosis - Actelion/Roche S1P<sub>1</sub> alliance achieves clinical milestone**

**ALLSCHWIL, SWITZERLAND – 09 October 2009 – Actelion Ltd (SIX: ATLN)** announced today that the selective S1P<sub>1</sub> receptor agonist ACT-128800/ RG3477 has achieved an important clinical milestone. Actelion's first-in-class selective S1P<sub>1</sub> (*Sphingosine-1-phosphate*) receptor agonist has entered into a Phase IIb dose-finding study in patients suffering from multiple sclerosis. This triggers a milestone payment by Roche to Actelion of USD 20 million.

Guy Braunstein, M.D., Ph.D. and Head of Clinical Development at Actelion, commented: "Together with our partner Roche, we are committed to the rapid development of our selective S1P<sub>1</sub> receptor agonist for patients suffering from autoimmune disorders. With the start of this dose-finding study in patients with multiple sclerosis, we have made an important step forward."

#### **About the Actelion / Roche alliance**

Actelion and Roche entered into an exclusive worldwide collaboration in July 2006 to jointly develop and commercialize Actelion's selective S1P<sub>1</sub> receptor agonist, an immunomodulator with the potential for once-a-day oral dosing. The two companies plan to jointly develop and commercialize this novel compound for multiple autoimmune disorders. For the current selective S1P<sub>1</sub> receptor agonist, Actelion will fully fund all development activities up to the end of Phase II for the first two indications. All subsequent development and commercialization costs will be shared equally between Roche and Actelion. Both companies will co-promote any product resulting from this collaboration and will equally share profit.

This S1P<sub>1</sub> collaboration covers both the current selective S1P<sub>1</sub> receptor agonist in clinical development, as well as any other selective S1P<sub>1</sub> receptor agonists resulting from Actelion's research efforts in the field. Actelion received an upfront payment of USD 75 million in July 2006. In the case of future development and approval milestones being achieved, Actelion will be eligible to receive further payments of up to USD 535 million for

the first compound for all targeted indications. Further development and approval milestone payments are due for additional compounds. Roche will pay Actelion undisclosed royalties on all product sales.

### **Selective S1P<sub>1</sub> receptor agonists**

Sphingosine-1-phosphate (S1P) is a phospholipid released by platelets, mast cells and other cells. It is currently established [1,2] that S1P stimulates at least five different G-protein coupled receptors (GPCRs): S1P<sub>1,2,3,4</sub>, and 5. Activation of these GPCRs mediates a complex variety of biological responses, such as lymphocyte migration, endothelial cell proliferation, blood vessel constriction and heart rate modulation.

Actelion's efforts in the field of selective S1P<sub>1</sub> receptor agonists started in 1999 by focusing on GPCRs found on the endothelium, the inner lining of blood vessels. The result of these research efforts is Actelion's orally active selective S1P<sub>1</sub> receptor agonist.

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### **Notes to the editor**

#### **About autoimmune disorders**

Autoimmune disorders are diseases caused by the body producing an immune response against its own tissues. The cause of autoimmune disorders is unknown. Some of the most common types of autoimmune disorders include psoriasis, rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease and rejection of transplanted organs. These disorders affect millions of people worldwide.

#### **About multiple sclerosis**

Multiple sclerosis (MS) is an inflammatory autoimmune disorder of the central nervous system (CNS) and is the most common cause of progressive neurological disability in young adults [3,4]. This chronic demyelinating disease is characterized by heterogeneous clinical expression, an unpredictable course and a variable prognosis. MS results from a cascade of events involving an activation of the immune system, acute focal inflammatory demyelination, and axonal loss with limited remyelination, culminating in chronic multifocal sclerotic plaques in brain and spinal cord. The large variety of symptoms and signs of MS result from axonal demyelination which leads to the slowing or blockade of axonal conduction at diverse affected sites of the brain and spinal cord. Repeated episodes of disease activity may lead to progressive loss of neurological function.

The incidence of MS is about 7 cases per 100,000 persons per year and although the etiology of MS is still unknown, the prevalence rate varies between races and geographical latitudes, ranging from 50–120 per 100,000 [3]. It is widely accepted that it is an immune-mediated, demyelinating disease precipitated by unknown environmental factors in genetically susceptible people.

## References

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2. Rivera J, Proia RL, Olivera A. Nat Rev Immunol. 2008 Oct;8(10):753-63. Review.
3. Compston A, Coles A. Multiple sclerosis. Lancet 2002;359:1221-31.
4. Compston A, Coles A. Multiple sclerosis. Lancet 2008;372:1502-18.

## Actelion Ltd

Actelion Ltd is a biopharmaceutical company with its corporate headquarters in Allschwil/Basel, Switzerland. Actelion's first drug Tracleer®, 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 2000 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).

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