

# Company Milestones

<b>2009</b>	<b>July</b>	<b>Tracleer® receives EU approval of pediatric formulation for the treatment of PAH</b> Actelion announces that the pediatric dispersible formulation of Tracleer® (bosentan) for the treatment of PAH in children has been approved in the European Union.
	<b>February</b>	<b>Actelion acquires a new formulation of i.v. epoprostenol with improved thermal stability</b> Actelion announces that it entered into a definitive agreement to acquire an improved, thermostable formulation of epoprostenol sodium for the intravenous treatment of pulmonary arterial hypertension (PAH) from privately-held GeneraMedix Inc.
	<b>February</b>	<b>Positive proof-of-mechanism study in asthma with Actelion's CRTH2 receptor antagonist</b> Actelion announces that positive data have been obtained in a proof-of-mechanism study with its orally active CRTH2 receptor antagonist in mild asthma. In the 18 patient-crossover double-blind placebo-controlled study, the primary endpoint (FEV1) was met, and the compound was well tolerated.
	<b>January</b>	<b>Zavesca® (Miglustat) receives EU approval for Niemann-Pick type C disease</b> Actelion announces that Zavesca® has been approved in the European Union for the treatment of progressive neurological manifestations in adult patients and pediatric patients with Niemann-Pick type C disease (NP-C).
<b>2008</b>	<b>November</b>	<b>Actelion's first-in-class selective S1P1 receptor agonist to enter Phase II clinical development</b> Actelion announces that the Actelion/Roche Alliance jointly agreed that preclinical and clinical data support progressing Actelion's S1P1 receptor agonist into Phase II clinical development.
	<b>September</b>	<b>Actelion included in the Swiss Market Index SMI®</b> Actelion announces that, as of Monday 22 September 2008, its shares are trading as part of the Swiss Market Index SMI®, the Swiss blue-chip index.
	<b>August</b>	<b>Tracleer® (bosentan) receives EU approval for treatment of patients with mildly symptomatic WHO FC II PAH</b> Actelion announces that Tracleer® (bosentan), a dual endothelin receptor antagonist, has been approved in the European Union for the treatment of patients with mildly symptomatic pulmonary arterial hypertension.

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	<b>July</b>	<b>Actelion and GlaxoSmithKline enter into exclusive collaboration to realise the full potential of almorexant</b> Actelion and GSK announce that they have entered into an exclusive worldwide collaboration (excluding Japan) for Actelion's almorexant, an orexin receptor antagonist in phase III development with first-in-class potential as a treatment for primary insomnia.
	<b>June</b>	<b>Bosentan (Tracleer®) receives positive EU opinion for treatment of patients with mildly symptomatic WHO FC II PAH</b> Actelion announces that the Committee for Medicinal Products for Human Use, the scientific committee of the European Medicines Agency, issued a positive opinion for bosentan (Tracleer®) to extend its use in Pulmonary Arterial Hypertension.
	<b>June</b>	<b>Pivotal PAH study EARLY published in The Lancet</b> Actelion announces that the EARLY study published in The Lancet concludes that bosentan (Tracleer®) demonstrates benefits in patients with mildly symptomatic WHO Functional Class II disease.
	<b>April</b>	<b>Actelion and Nippon Shinyaku enter into license agreement on novel PAH compound.</b> Actelion and Nippon Shinyaku announce the two companies have signed a license agreement on a novel orally-available PGI2 receptor.
	<b>February</b>	<b>Zavesca® approved and launched in Turkey</b> Actelion announces the availability of Zavesca® (miglustat) capsules in Turkey. Zavesca® is the first oral treatment option for mild to moderate type I Gaucher disease.
<b>2007</b>	<b>December</b>	<b>Phase III study initiated with novel orexin receptor antagonist almorexant</b> Actelion announces the initiation of the comprehensive Phase III clinical trial program RESTORA (REstore physiological Sleep with The Orexin Receptor Antagonist Almorexant) with its first-in-class orexin receptor antagonist.
	<b>December</b>	<b>Phase III study initiated with potent tissue-targeting ERA Actelion-1</b> Actelion announces the initiation of the Phase III clinical study with its tissue-targeting endothelin receptor antagonist Actelion-1. The study is designed to evaluate the safety and efficacy of Actelion-1 in delaying disease progression and mortality in patients with symptomatic PAH.
	<b>December</b>	<b>Actelion becomes full member of Interpharma on its 10th anniversary</b> Actelion announces that on the occasion of its 10-year anniversary the company is becoming a full member of Interpharma, the association of Swiss pharmaceutical research companies.
	<b>December</b>	<b>Actelion provides update on bosentan in metastatic melanoma</b>

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Actelion announces that preliminary efficacy data generated in the proof-of-concept study evaluating bosentan in metastatic melanoma did not support the initiation of a full clinical development program in this indication.

- December**     **Actelion/Merck & Co., Inc. Renin alliance achieves 4th milestone upon Phase II initiation**  
Actelion announces that the renin alliance with Merck & Co., Inc. has achieved its fourth milestone. The alliance has started dosing in the Phase II program for its first compound, a new renin inhibitor.
- November**     **Phase III study initiated with clazosentan an intravenous ERA**  
Actelion announces the initiation of the Phase III clinical study CONSCIOUS-2, for the endothelin receptor antagonist clazosentan. The study will evaluate safety and efficacy in reducing vasospasm-related morbidity and all-cause mortality following aneurysmal subarachnoid hemorrhage (aSAH).
- September**     **Phase IIa study initiated with miglustat in cystic fibrosis**  
Actelion announces that it has initiated a Phase IIa proof-of-concept clinical study with miglustat in cystic fibrosis (CF). It is the first time that miglustat is being tested in a clinical setting involving CF patients.
- September**     **EARLY: First PAH functional class II population study results presented**  
Actelion presents full results from a Phase IIIb trial which showed that 6 months of treatment with bosentan in patients with mildly symptomatic WHO functional class II (FCII) PAH significantly delayed time to clinical worsening and reduced the number of patients worsening to WHO functional class III/IV.
- September**     **Data on orexin receptor antagonist almorexant presented at World Sleep Congress**  
Preclinical and clinical data presented at the WSC 2007 provide preliminary evidence for key role of orexin receptor antagonist almorexant to significantly restore relevant clinical parameters of sleep in a dose-dependent manner.
- July**     **Zavesca® approved and launched in Australia**  
Actelion announces the availability of Zavesca® (miglustat) capsules in Australia. Zavesca® is the first oral treatment option for type I Gaucher disease.
- June**     **Tracleer® receives EU approval for reduction of number of new digital ulcers in systemic sclerosis patients**  
Actelion announces that the European Commission has granted marketing approval for Tracleer® for the reduction of the number of new digital ulcers in patients with systemic sclerosis and ongoing digital ulcer disease.

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	<b>June</b>	<b>Stock split 1:5 effective Wednesday, 6 June 2007</b> Actelion announces that the one-to-five split in shares of Actelion (SWX: ATLN) would take effect on Wednesday, 6 June 2007.
	<b>March</b>	<b>Positive study with bosentan in inoperable CTEPH</b> First ever placebo-controlled study with bosentan in inoperable chronic thromboembolic pulmonary hypertension - primary endpoint of reduction in pulmonary vascular resistance met.
	<b>January</b>	<b>Zavesca® approved and launched in Brazil</b> Actelion announces the approval of Zavesca® (miglustat) capsules in Brazil. Zavesca® is the first oral treatment option for type I Gaucher disease.
	<b>January</b>	<b>Successful completion of its cash tender offer for shares of CoTherix, Inc.</b> Strengthening Actelion's strong role in advancing PAH therapy - Strengthening the reach of Ventavis® in the United States.
<b>2006</b>	<b>December</b>	<b>Successful study with bosentan in patients with mildly symptomatic PAH</b> Significant reduction in pulmonary vascular resistance – Strong trend towards improvement in exercise capacity – Significant delay in time to clinical worsening.
	<b>October</b>	<b>Actelion presents detailed analysis of Clazosentan in CONSCIOUS-1 study</b> Significant reduction of cerebral vasospasm in patients with aneurysmal subarachnoid hemorrhage.
	<b>September</b>	<b>Opening ceremony of the Actelion Research Center in Allschwil</b> Opening ceremony of Actelion's research facility takes place.
	<b>July</b>	<b>Actelion and Roche enter into autoimmune disorder collaboration</b> Co-development for Actelion's selective S1P1 receptor agonist in multiple indications with co-promotion and profit share - undisclosed royalties to Actelion on all product sales.
	<b>July</b>	<b>Actelion/Merck &amp; Co., Inc. Renin alliance achieves 3rd milestone upon entry into man</b> Actelion announces that the renin alliance with Merck & Co., Inc., has achieved its third milestone. The alliance has its first compound, a new renin inhibitor, entered into man.
	<b>June</b>	<b>Preliminary results of CONSCIOUS-1</b> Actelion announces that preliminary analysis of the dose-finding study CONSCIOUS-1 indicates that all three doses of i.v clazosentan tested

have reached statistical significance versus placebo for the primary endpoint.

2005

- May**      **Data highlights strong rationale for a morbidity/mortality study with bosentan in IPF**  
Data presented from the BUILD program at the American Thoracic Society (ATS) provide a strong rationale to further evaluate the safety and efficacy of bosentan in a morbidity/mortality-driven Phase III study in patients suffering from idiopathic pulmonary fibrosis (IPF).
- November**      **Bosentan studies in pulmonary fibrosis do not meet primary endpoint. Strong rationale for new IPF study provided**  
Clinical studies with bosentan in patients suffering from either idiopathic pulmonary fibrosis (BUILD-1) or pulmonary fibrosis related to Systemic Sclerosis (BUILD-2), did not reach their primary endpoints.
- November**      **Actelion and UCB enter into assignment and license agreement for Zavesca®**  
Actelion and UCB announce that the two companies have, with immediate effect, replaced their existing license agreement covering Zavesca® (miglustat).
- August**      **Second statistically significant study with bosentan in digital ulcers related to systemic sclerosis**  
Actelion announces the preliminary result of its Phase III study, RAPIDS-2, with the dual endothelin receptor antagonist bosentan in systemic sclerosis patients suffering from digital ulcers.
- July**      **Tracleer® study first ever to show benefits in patients with Eisenmenger's syndrome**  
The BREATHE -5 trial provides preliminary information that Tracleer® decreases pulmonary vascular resistance and improves exercise capacity in those patients not amenable to any other therapy including surgery.
- June**      **Actelion Japan launches Tracleer® in PAH**  
The Japanese Ministry of Health, Labor and Welfare grants formal approval of Tracleer® for the treatment of all forms of pulmonary arterial hypertension PAH (WHO class III and IV) and granted full reimbursement status.
- May**      **Palosuran development stopped for lack of efficacy**  
Actelion announces that preliminary efficacy data generated in the proof-of-concept program do not support the initiation of a full-fledged clinical development program.

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2004

- March**      **Actelion/Merck & Co., Inc. Renin alliance achieves 2nd milestone upon preclinical candidate selection**  
Actelion announces that the renin alliance with Merck & Co., Inc., has achieved its second milestone with the selection of the first compound for full preclinical development.
- December**      **Phase IIb/III program initiated with clazosentan in vasospasm following subarachnoid hemorrhage**  
Actelion announces it has initiated the comprehensive global Phase IIb/III development program for clazosentan, an intravenous endothelin receptor antagonist.
- November**      **Study with tezosentan in acute heart failure stopped for futility**  
Actelion announces that the VERITAS study evaluating efficacy and safety of tezosentan in acute heart failure (AHF) is being stopped for futility.
- October**      **Zavesca® approved and launched in Switzerland**  
Actelion announces the availability of Zavesca® (miglustat) capsules in Switzerland. Zavesca® is the first oral treatment option for type I Gaucher disease.
- June**      **Actelion wins French Prix Galien for Tracleer®**  
Considered as the highest accolade for pharmaceutical research and development.
- March**      **Zavesca® approved in Canada**  
Actelion announces the availability of Zavesca® (miglustat) capsules in Canada. Zavesca® is the first oral treatment option for type I Gaucher disease.
- March**      **Actelion/Merck & Co., Inc. Renin alliance achieves first milestone upon completion of technology transfer**  
Actelion announces that the renin alliance with Merck & Co., Inc., has achieved its first milestone. Actelion has completed the technology transfer to Merck and the two companies have combined their research teams and efforts in this field.
- February**      **Actelion wins James D. Watson Helix Award**  
Actelion is recognized by its biotechnology peers for its outstanding leadership, significant scientific and product advancements, economic development and solid corporate citizenship exhibited throughout the year.
- January**      **Zavesca® available for prescription in the US**  
Actelion announces the availability of Zavesca® (miglustat) capsules in the United States. Zavesca® is the first oral treatment option for type I Gaucher disease and is also already approved and available in the European Union.
- January**      **Actelion sells its stake in Hesperion to Cerep SA**

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Actelion and Cerep announce that Cerep will acquire the clinical development service organization Hesperion.

**January**      **Start of Tracleer® commercialization in Australia**  
Australian launch of Tracleer® a break-through treatment for patients suffering from pulmonary arterial hypertension.

### 2003

**December**      **Actelion/Merck & Co., Inc. form Renin inhibitor alliance**  
Actelion to advance the development of its breakthrough discoveries of new classes of renin inhibitors with high oral absorption - Actelion and Merck alliance to optimize all aspects of bringing several products to market.

**September**      **Actelion acquires Axovan**  
Actelion to further develop intravenous endothelin receptor antagonist optimized for cerebral indications currently in Phase II at Axovan - Strengthening of drug discovery efforts within Actelion's core focus.

**August**      **US FDA approves Zavesca®**  
Actelion announces that the US Food and Drug Administration (FDA) has approved Zavesca® (miglustat) capsules, the first oral treatment option for type 1 Gaucher disease.

**March**      **Actelion starts introduction of Zavesca® in the EU**  
Actelion announces the introduction of Zavesca® in the EU. The first oral treatment for type 1 Gaucher disease is now available to patients in the UK.

**March**      **Entry-into-man of Palosuran**  
Palosuran the first urotensin II receptor antagonist enters first-in-human clinical trials.

### 2002

**June**      **Actelion starts introduction of Tracleer® in the EU**  
European Launch of Tracleer® a breakthrough treatment for patients suffering from pulmonary arterial hypertension.

**May**      **European Union Approval of Tracleer® (bosentan) for the treatment of PAH**  
European Commission grants marketing approval for Tracleer®.

### 2001

**December**      **Actelion launches the first ERA - Tracleer® - in the United States**  
Actelion announces US commercial availability of Tracleer® (bosentan) tablets - First oral treatment for pulmonary arterial hypertension.

**November**      **FDA approval of Tracleer® (bosentan) for the treatment of PAH**  
Actelion's Tracleer® (bosentan) tablets approved by the US Food and Drug Administration (FDA) - First oral treatment for pulmonary arterial hypertension.

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2000	March	<b>Initial Public Offering (IPO); Actelion shares are listed on the Swiss New Market Stock Exchange</b> Actelion goes public - Placement of up to 1 million shares - SWX New Market Listing - Record valuation of CHF 1.2 billion.
	February	<b>Actelion and Genentech sign licensing agreement for tezosentan in the US</b> Actelion and Genentech sign licensing agreement for tezosentan in the US.
	February	<b>Actelion subsidiaries are opened in US and Europe</b> Actelion establishes its first subsidiaries expanding its global reach.
1999	September	<b>Bosentan (Tracleer®) PAH clinical development program at Actelion is initiated</b> Recognizing the potential of an Endothelin Receptor Antagonist (ERA) - a new mechanism of action - Actelion initiates its development program for bosentan.
1998	June	<b>Actelion research laboratories established</b> Actelion establishes its facilities and recruits its first scientists.
1997	December	<b>Foundation of Actelion December 17, 1997</b> Actelion is the first company dedicated to using innovative science for the discovery, development and marketing of breakthrough pharmaceutical products for endothelium-related conditions.