Company Milestones

2012  Sept  Macitentan Phase III PAH outcome study results to be presented at CHEST 2012

The results from the first ever Phase III long-term outcome study with macitentan in patients with Pulmonary Arterial Hypertension (PAH) were accepted for oral presentation at the annual CHEST meeting of the American College of Chest Physicians (ACCP) in Atlanta (Georgia).

2012  April  Actelion’s macitentan meets primary endpoint in pivotal Phase III SERAPHIN outcome study in patients with pulmonary arterial hypertension

Initial analysis indicated that the pivotal, long-term, event-driven study SERAPHIN with macitentan, a novel dual endothelin receptor antagonist, in 742 patients suffering from pulmonary arterial hypertension (PAH) and treated for up to three and a half years, met its primary endpoint.

2012  April  Japan’s Ministry of Health, Labour and Welfare approves miglustat for Niemann-Pick type C disease

Japan’s Ministry of Health, Labour and Welfare granted approval for miglustat for the treatment of Niemann-Pick type C disease. The approval was based on the data generated for the first approval of miglustat in this indication in the European Union, as well as data specifically generated for the submission to the Japanese Health Authorities.

2012  February  Auxilium Pharmaceuticals, Inc. and Actelion Pharmaceuticals Ltd. enter a collaboration for XIAFLEX

Auxilium Pharmaceuticals, Inc. and Actelion Ltd. entered into a long-term partnership for the development, supply and commercialization of XIAFLEX® (collagenase clostridium histolyticum), a novel, first-in-class biologic for the potential treatment of Dupuytren’s contracture and Peyronie’s disease.

2011  September  Jean-Pierre Garnier elected as Chairman of Actelion’s Board of Directors

Jean-Pierre Garnier became Chairman of the Board of Directors of the Swiss biopharmaceutical company. In order to ensure a smooth transition, Robert Cawthorn, who had been Chairman since the inception of the company, stayed on the Board as planned until the 2012 Annual General Meeting.
2011 August Results of exploratory study with macitentan shows efficacy data not supportive of Phase III in IPF

An exploratory Phase II study with macitentan in patients with idiopathic pulmonary fibrosis (IPF) showed a promising safety and tolerability profile of macitentan.

2011 August Ponesimod meets primary endpoint in Phase II dose-finding study in patients with relapsing-remitting multiple sclerosis.

The primary endpoint – reduction in the number of new active inflammatory lesions in the brain – was met with its selective S1P1 receptor agonist, ponesimod, in a Phase IIb dose-finding study in patients with relapsing-remitting multiple sclerosis.

2011 June Change in management structure - Otto Schwarz appointed Chief Operating Officer (COO)

Changes also include the membership of the Executive Committee (AEC), chaired by Jean-Paul Clozel, with regards to the needs of a growing organization and to strengthen leadership and governance. In addition, Legal, HR, Research and IR are now part of the extended AEC.

2011 May Novel CRTH2 antagonist meets primary endpoint in Phase II study in patients with seasonal allergic rhinitis

For the first time, there was proof that CRTH2 antagonists can bring clinically relevant benefit to patients suffering from allergic rhinitis. This study complemented the positive proof-of-mechanism study in asthma reported in 2009.

2011 April Jean-Pierre Garnier and Robert Bertolini nominated to join Actelion’s Board

Actelion nominated two Board Directors with outstanding pharmaceutical industry, management and financial expertise for election at the Annual General Meeting. Both candidates were elected at the AGM on May 5th, 2011

2011 January Actelion and GSK discontinued clinical development of almorexant

Actelion Ltd and GlaxoSmithKline decided to discontinue the clinical development of the Phase III investigational dual orexin receptor antagonist, almorexant. This decision was based on a review of data from additional clinical studies, which were conducted to further establish the clinical profile of almorexant, including the tolerability profile.

2011 January Change in Board of Directors

Dr. Elias Zerhouni resigned from Actelion’s Board of Director at the end of 2010. Dr. Zerhouni will focus on his new role as President, Global Research and Development at Sanofi-aventis, an executive function he is assuming as of the beginning of 2011.
2010 December Opening of new business center at Allschwil Headquarters

Actelion’s new Business Center was inaugurated in a ceremony attended by Federal President Doris Leuthard and other representatives from politics, business and science. The five-floor steel building created by the architects’ office of Herzog & de Meuron offers space for 350 employees.

2010 September CONSCIOUS-2 study with clazosentan: primary endpoint not met

Initial results of CONSCIOUS-2, a clinical study evaluating the safety and efficacy of clazosentan in reducing vasospasm-related morbidity and all-cause mortality in clipped patients following aneurysmal subarachnoid hemorrhage (aSAH), did not meet its primary endpoint.

2010 July Actelion obtains option to acquire privately-held Trophos

Actelion and privately-held Trophos SA announces that they have entered into a binding agreement whereby Actelion has, for EUR 10 million, obtained an exclusive option to acquire privately-held Trophos SA, a clinical stage pharmaceutical company.

2010 May Selexipag Phase II results are presented at the American Thoracic Society [ATS] 2010 International Conference

Actelion announces that full data from the Phase II study of selexipag, the company’s first-in-class, orally available, selective IP receptor agonist in patients with pulmonary arterial hypertension, were presented by Gerald Simonneau M.D., PhD, during the 2010 International Conference of the American Thoracic Society (ATS) in New Orleans.

2010 April Epoprostenol for Injection, Actelion’s fourth product, is launched in the United States for the treatment of PAH

Actelion announces that Epoprostenol for Injection, an improved formulation of epoprostenol which is stable at room temperature, has become available for the treatment of primary pulmonary hypertension and pulmonary hypertension associated with the scleroderma spectrum of disease in NYHA Class III and Class IV patients who do not respond adequately to conventional therapy.

2010 March Actelion receives FDA complete response letter for Zavesca® for the treatment of NP-C disease

Actelion announces that a complete response letter from the U.S. Food and Drug Administration has been received for its supplemental New Drug Application for Zavesca® (miglustat) for the treatment of progressive neurological manifestations in adult and pediatric patients with Niemann-Pick type C (NP-C) disease.
2010 March BUILD-3 study with bosentan in IPF does not meet primary endpoint

Actelion announces the initial results of BUILD-3, a clinical study evaluating the safety and efficacy of bosentan in patients suffering from idiopathic pulmonary fibrosis (IPF). While there was a trend in favor of bosentan, the primary endpoint, reduction in morbidity/mortality, was not met (p = 0.21). The well characterized safety profile of bosentan was confirmed.

2010 January Zavesca® receives positive vote from the FDA’s Advisory Committee for the treatment of NP-C disease

Actelion announces that United States Food and Drug Administration’s Endocrinologic and Metabolic Drugs Advisory Committee voted in favor of the overall risk/benefit profile supporting the approval of Zavesca® for the treatment of progressive neurological manifestations in adult patients and pediatric patients with Niemann-Pick type C (NP-C) disease.

2009 December Almorexant meets primary endpoint in phase III study in insomnia

Actelion announces that the first phase III study with almorexant (RESTORA 1) met its primary endpoint, superiority of the dual orexin receptor antagonist almorexant compared to placebo on objective and subjective wake after sleep onset. The finding was highly significant (p < 0.001). Several secondary endpoints of the study were also met with statistical significance.

2009 December Roche leaves S1P1 alliance following comprehensive portfolio review and prioritization

Actelion announces its decision to proceed with advanced clinical development with its orally available and selective S1P1 receptor agonist in psoriasis.

2009 November FDA grants priority review for Actelion’s miglustat in NP-C disease

Actelion announces that a supplemental new drug application for an extension of indication for Zavesca® [miglustat] for the treatment of progressive neurological manifestations in adult and pediatric patients with Niemann-Pick type C (NP-C) disease has been accepted by the U.S. Food and Drug Administration.

2009 October Actelion/Roche S1P1 alliance achieves clinical milestone

Actelion’s first-in-class selective S1P1 (Sphingosine-1-phosphate) receptor agonist has entered into a Phase IIb dose-finding study in patients suffering from multiple sclerosis. This triggered a milestone payment by Roche to Actelion of USD 20 million.
Dose-finding Phase IIb study started in patients with multiple sclerosis

Actelion announces that the selective S1P1 receptor agonist has achieved an important clinical milestone. Actelion’s first-in-class selective S1P1 (Sphingosine-1-phosphate) receptor agonist entered into a Phase IIb dose-finding study in patients suffering from multiple sclerosis.

Ventavis (Iloprost) in PAH receives US approval for increased 20 mcg/ml strength formulation

Actelion announces that the US Food and Drug Administration (FDA) has approved a new 20 microgram per milliliter (mcg/ml) dose strength of Ventavis® as a therapy for New York Heart Association Class III and IV pulmonary arterial hypertension.

Tracleer® receives label extension in the US for the treatment of patients with mildly symptomatic WHO FC II PAH

Actelion announces that the U.S. Food and Drug Administration has approved the company’s supplemental New Drug Application for Tracleer® (bosentan) to treat patients with mildly symptomatic WHO Functional Class II pulmonary arterial hypertension.

Tracleer® receives EU approval of pediatric formulation for the treatment of PAH

Actelion announces that the pediatric dispersible formulation of Tracleer® (bosentan) for the treatment of pulmonary arterial hypertension in children has been approved in the European Union.

Actelion acquires a new formulation of i.v. epoprostenol with improved thermal stability

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 from privately-held GeneraMedix Inc.

Positive proof-of-mechanism study in asthma with Actelion’s CRTH2 receptor antagonist

Actelion announces that positive data was 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.

Zavesca® (Miglustat) receives EU approval for NP-C disease

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 (NP-C) disease.
2008 November  Actelion’s first-in-class selective S1P1 receptor agonist to enter Phase II clinical development

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.

2008 September  Actelion included in the Swiss Market Index SMI®

Actelion announces that, as of Monday 22 September 2008, its shares are trading as part of the Swiss Market Index SMI®, the Swiss bluechip index.

2008 August  Tracleer® (bosentan) receives EU approval for treatment of patients with mildly symptomatic WHO FC II PAH

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.

2008 July  Actelion and GlaxoSmithKline enter into exclusive collaboration to realise the full potential of almorexant

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.

2008 June  Bosentan (Tracleer®) receives positive EU opinion for treatment of patients with mildly symptomatic WHO FC II PAH

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.

2008 June  Pivotal PAH study EARLY published in The Lancet

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.

2008 April  Actelion and Nippon Shinyaku enter into license agreement on novel PAH compound

Actelion and Nippon Shinyaku announce the two companies have signed a license agreement on a novel orally-available PGI2 receptor.

2008 February  Zavesca® approved and launched in Turkey

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.
2007 December Phase III study initiated with novel orexin receptor antagonist almorexant
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.

2007 December Phase III study initiated with potent tissue-targeting ERA Actelion-1
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.

2007 December Actelion becomes full member of Interpharma on its 10th anniversary
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.

2007 December Actelion provides update on bosentan in metastatic melanoma
Company Milestones
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.

2007 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.

2007 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).

2007 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.

2007 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.
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.

Actelion announces the availability of Zavesca® (miglustat) capsules in Australia. Zavesca® is the first oral treatment option for type I Gaucher disease.

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.

Actelion announces that the one-to-five split in shares of Actelion (SWX: ATLN) would take effect on Wednesday, 6 June 2007.

First ever placebo-controlled study with bosentan in inoperable chronic thromboembolic pulmonary hypertension - primary endpoint of reduction in pulmonary vascular resistance met.

Actelion announces the approval of Zavesca® (miglustat) capsules in Brazil. Zavesca® is the first oral treatment option for type I Gaucher disease.

Strengthening Actelion’s strong role in advancing PAH therapy - Strengthening the reach of Ventavis® in the United States.

Significant reduction in pulmonary vascular resistance – Strong trend towards improvement in exercise capacity – Significant delay in time to clinical worsening.

Significant reduction of cerebral vasospasm in patients with aneurysmal subarachnoid hemorrhage.
2006  September  Opening ceremony of the Actelion Research Center in Allschwil
Opening ceremony of Actelion’s research facility takes place.

2006  July  Actelion and Roche enter into autoimmune disorder Collaboration
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.

2006  July  Actelion/Merck & Co., Inc. Renin alliance achieves 3rd milestone upon entry into man
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.

2006  June  Preliminary results of CONSCIOUS-1
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  November  Bosentan studies in pulmonary fibrosis do not meet primary endpoint. Strong rational 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.

2005  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].

2005  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.
2005 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.

2005 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.

2005 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.

2005 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.

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2004 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.

2004 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.

2004 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.

2004 June  
**Actelion wins French Prix Galien for Tracleer®**

Considered as the highest accolade for pharmaceutical research and development.

2004 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.
2004 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.

2004 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.

2004 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.

2004 January  Actelion sells its stake in Hesperion to Cerep SA

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

2004 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.

2003 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.

2003 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.

2003 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.
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<tr>
<th>Year</th>
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<th>Event</th>
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<tr>
<td>2003</td>
<td>March</td>
<td>Entry-into-man of Palosuran</td>
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<td>Palosuran the first urotensin II receptor antagonist enters first-</td>
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<td>inhuman clinical trials.</td>
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<td>2002</td>
<td>June</td>
<td>Actelion starts introduction of Tracleer® in the EU</td>
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<td>European Launch of Tracleer® a breakthrough treatment for patients</td>
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<td>suffering from pulmonary arterial hypertension.</td>
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<td>2002</td>
<td>May</td>
<td>European Union Approval of Tracleer® (bosentan) for the treatment of</td>
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<td>European Commission grants marketing approval for Tracleer®.</td>
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<td>2001</td>
<td>December</td>
<td>Actelion launches the first ERA - Tracleer® - in the United States</td>
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<td>Actelion announces US commercial availability of Tracleer® (bosentan)</td>
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<td>tablets - First oral treatment for pulmonary arterial hypertension.</td>
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<td>2001</td>
<td>November</td>
<td>FDA approval of Tracleer® (bosentan) for the treatment of PAH</td>
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<td>Actelion's Tracleer® (bosentan) tablets approved by the US Food and</td>
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<td>Drug Administration (FDA) - First oral treatment for pulmonary</td>
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<td>arterial hypertension.</td>
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<td>2000</td>
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<td>Initial Public Offering (IPO); Actelion shares are listed on the</td>
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<td>Swiss New Market Stock Exchange</td>
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<td>Actelion goes public - Placement of up to 1 million shares - SWX New</td>
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<td>Market Listing - Record valuation of CHF 1.2 billion.</td>
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<td>2000</td>
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<td>Actelion and Genentech sign licensing agreement for tezosentan in the</td>
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<td>2000</td>
<td>February</td>
<td>Actelion subsidiaries are opened in US and Europe</td>
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<td>Actelion establishes its first subsidiaries expanding its global reach</td>
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</table>
1999  September  Bosentan (Tracleer®) PAH clinical development program at Actelion is initiated
Recognizing the potential of an Endothelin Receptor Antagonist (ERA) - a new mechanism of action - Actelion initiates its development program for bosentan.

1998  June  Actelion research laboratories established
Actelion establishes its facilities and recruits its first scientists.

1997  December  Foundation of Actelion December 17, 1997
Actelion is the first company dedicated to using innovative science for the discovery, development and marketing of breakthrough pharmaceutical products for endothelium-related conditions.

Updated: Sept. 2012