

A productive dynamo of scientific excellence

Actelion's Drug Discovery team is one of the most productive on a per capita basis in the biopharmaceutical industry. The discoveries of the 240 in-house scientists, who filed 40 patent applications in 2006 alone, include a number of potential breakthroughs now in the pipeline: an S1P₁ agonist for autoimmune disease, orally available renin inhibitors for cardiovascular indications, Actelion-1, a highly potent successor to bosentan for pulmonary hypertension and other cardiovascular indications, and an orexin receptor antagonist as a first-in-class sleep-enhancing agent.

As these compounds are promoted to Clinical Development candidates, Drug Discovery focuses on a new set of targets that address further unmet medical needs. The 25 ongoing research projects cover indications in the cardiovascular field, oncology, central nervous system disorders, bacterial infections, immunology and allergies.

Since the company's inception, Actelion's researchers have concentrated on two platforms of molecular targets, G-protein-coupled receptors and aspartyl proteases. Today, additional platforms are being added, for example, to find novel approaches in the battle against antibiotic-resistant bacteria. While these parameters provide the framework for scientific research, Actelion's researchers remain flexible enough to follow innovation wherever it leads.

State-of-the-art Research Center built with future growth in mind

In February 2006, Actelion completed its state-of-the-art Research Center at headquarters in Allschwil. This custom-built facility, designed to facilitate communication and cross-fertilization of ideas, underlines Actelion's philosophy of concentrating research at one site. Built with continued expansion in mind, the Research Center is accommodating a steady increase in the number of employees in Pharmacology and Preclinical Development, Molecular Biology, Biochemistry and Chemistry.

In 2006, Actelion researchers continued to make new scientific advances. Structural biologists used advanced photon-beam technology to solve more than 30 structures of different enzymes. Most of these were within the scope of the joint renin inhibitor project with Merck, helping to fine tune the most promising compounds for clinical trials. A process research chemistry group, newly formed in 2006, will help to eliminate potential bottlenecks in scaling up from small amounts of compounds in the laboratory to much larger amounts needed for toxicology studies and later on for clinical trials. In coping with the increasing amount of scientific data generated by experiments, in-house information technology experts and proprietary software played a vital role. With the property prediction software, for example, Actelion's scientists can create chemical structures for new compounds on screen and obtain information such as molecular weight, toxicity, water solubility and drug-like properties.

A novel anti-bacterial agent and an anti-allergic agent to enter clinical trials

In researching a new generation of anti-bacterial agents, Actelion benefits from its evidence-based experience on the usefulness of dual blockade approaches. Addressing the increasingly alarming problem of bacterial resistance to current antibiotics, Actelion's sci-

"Compared to 2005, we have more than doubled the number of research projects. Our task is now to prioritize and promote the most promising ones for future development."

Thomas Weller

Head of Drug Discovery, Chemistry

“The steadily increasing number of compounds discovered in house that enter into pre-clinical trials every year demonstrates not only the productivity of Actelion’s scientists but also the quality of the work.”

Walter Fischli
Head of Drug Discovery,
Molecular Biology & Biochemistry

“As our research projects enter accelerated programs of clinical development, we continue to offer pre-clinical support, including further pharmacological characterization and selection of potential follow-up compounds.”

Martine Clozel
Head of Drug Discovery,
Pharmacology & Preclinical Development

entists have developed novel modes of action that kill bacteria with “double-warheads” – increasing efficacy and lowering the chance of cross-resistance. Actelion expects an antibacterial agent from Drug Discovery to begin Phase I trials in 2007: Actelion-9 (injectable), which has shown promising pre-clinical results against a broad spectrum of bacteria, is intended primarily for hospital use as a rescue therapy.

Expertise on G-protein-coupled receptors has also helped Actelion’s researchers to discover an anti-allergic agent designed to address the huge unmet medical need in treating allergic rhinitis and allergic asthma. This orally available compound, about to enter Phase I clinical trials, targets the amplification process in allergic reactions and probably also the onset of the inflammation cascade. If successful, it could be used as a replacement for or in conjunction with conventional therapies.

Actelion’s Drug Discovery Projects

Project Proposal	Project Initiated	High Through-Put Screening	Lead Identification	Lead Optimization	Preclinical Development
	Antibacterial CNS CV Immunology Immunology	Antibacterial Antibacterial Antibacterial CNS CNS CNS CNS Immunology Immunology	CNS CNS CV CV	Antibacterial CNS CV CV CV Immunology Immunology	Anti-Allergic Antibacterial

Anti-Allergic / Antibacterial / Cardiovascular (CV) / Central Nervous System (CNS) / Immunology