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## Emerging Company Profile

# Receptos: Designs against GPCRs

By Chris Cain  
Staff Writer

Up to 40% of approved drugs target GPCRs, but many of these drugs have undesirable side effects because they also bind to closely related receptors. **Receptos Inc.** believes it has overcome the barriers to structure-based drug design against GPCRs, which could enable the company to discover more specific, safer compounds.

Using its structure-guided drug discovery technology, Receptos has identified a sphingosine-1-phosphate receptor 1 (S1PR1; SIP1; EDG1) agonist it expects will have all the efficacy of more advanced compounds, without their side effects. The candidate, RPC1063, entered Phase I testing for multiple sclerosis in January. Data are expected in 2012.

The problem with studying GPCRs has been that the receptors quickly lose their conformation when removed from their natural membrane environment. Soluble, stabilized protein is needed to form crystals for structural analysis.

Receptos has exclusive rights to nanomimetic membrane materials to stabilize the receptors for crystallization, as well as crystal imaging, detection and data collection technologies developed by scientific co-founder Raymond Stevens.

### Receptos Inc.

San Diego, Calif.

Technology: Structure-guided drug discovery against GPCRs

Disease focus: Autoimmune, inflammation

Clinical status: Phase I

Founded: 2009 by William Rastetter, Marcus Boehm, Robert Peach, Hugh Rosen and Raymond Stevens

University collaborators: The Scripps Research Institute

Corporate partners: Johnson & Johnson and Eli Lilly and Co.

Number of employees: 22

Funds raised: \$25 million

Investors: Arch Venture Partners, Flagship Ventures, Lilly Ventures and Venrock

CEO: Faheem Hasnain

Patents: None issued

Stevens, professor of molecular biology and chemistry at **The Scripps Research Institute**, was the first to solve the structure of a human GPCR in 2007 and has solved structures of the four human GPCRs

that have been crystallized to date.

The company's other scientific co-founder, Hugh Rosen, led a team that discovered the mechanism of Gilenya fingolimod, a sphingosine 1-phosphate (S1P) receptor agonist marketed by **Novartis AG** to treat MS.

Rosen is professor of chemical physiology and immunology at Scripps.

While Gilenya reduces the annual relapse rate in MS patients, it also can cause cardiovascular abnormalities, elevated liver enzymes, macular edema and pulmonary toxicity.

According to Receptos President and CEO Faheem Hasnain, Gilenya agonizes four of the five S1P receptor family members. Published studies suggest agonizing S1PR1 leads to the clinical benefit of Gilenya, while agonizing S1PR3 can cause cardiovascular toxicity.

Receptos thus used Stevens' technologies to determine the structure of S1PR1. The company then in-licensed S1PR1 agonists Rosen identified through traditional chemical screening and optimized candidates based on the structure of S1PR1.

Two other S1PR1 agonists are in Phase II testing. Novartis' BAF312, a second-generation S1PR1 and S1PR5 agonist, is in Phase II trials for MS, polymyositis and

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dermatomyositis. **Actelion Ltd.**'s ACT-128800, an S1PR1 agonist, is in Phase II trials for MS and psoriasis.

Receptos also intends to use its technology to discover small molecules that can target GPCRs that are currently only amenable to peptides, such as glucagon-like peptide-1 receptor (GLP-1R) for diabetes.

The company also is making its technology available through non-exclusive licenses and R&D collaborations. In January, the company announced separate deals with **Johnson & Johnson** and **Eli Lilly and Co.**

Under a non-exclusive technology transfer agreement, J&J will use the Receptos GPCR structure determination technology to optimize molecules in its own pipeline.

The deal with Lilly is "a much more collaborative agreement to identify small molecule candidates against an undisclosed metabolic target and advance them into preclinical development," Hasnain said. The partners will jointly own the compounds.

Further terms of the deals haven't been disclosed.

At least one other company is doing structure-guided GPCR drug design. **Heptares Therapeutics Ltd.** uses its StaR technology to stabilize GPCRs in their functional forms, allowing for isolation and purification outside the native cell membrane (see *BioCentury*, Sept. 15, 2008).

Heptares' lead program targets adenosine A2A receptor (ADORA2A) to treat Parkinson's disease (PD); it is in lead optimization.

Chrysa Mineo, Receptos' VP of corporate development, suggested there is plenty of room for both companies, noting there are hundreds of potential GPCR targets to work on.

#### COMPANIES AND INSTITUTIONS MENTIONED

**Actelion Ltd.** (SIX:ATLN), Allschwil, Switzerland

**Eli Lilly and Co.** (NYSE:LLY), Indianapolis, Ind.

**Johnson & Johnson** (NYSE:JNJ), New Brunswick, N.J.

**Heptares Therapeutics Ltd.**, Welwyn Garden City, U.K.

**Novartis AG** (NYSE:NVS; SIX:NOVN), Basel, Switzerland

**Receptos Inc.**, San Diego, Calif.

**The Scripps Research Institute**, La Jolla, Calif.