

BIOTECHNOLOGY

## Receptos Inc.

*Rapid-fire reception for a GPCR platform*

The mere thought of a novel G protein-coupled receptor (GPCR)-targeting molecule can make pharma execs salivate like hungry beasts at mealtime. GPCR drugs provide as much as half of all marketed pharmaceutical products. The industry is ravenous for more. Given the rapid-fire willingness of two pharma giants to ink unspecified but apparently high-value and largely nonexclusive deals with Receptos Inc., the GPCR discovery platform and drug development venture may have the right recipe for many tasty meals to come.

GPCRs are nearly ubiquitous transmembrane proteins that send signals into the cell regulating a host of fundamental mechanisms. When those signals go awry, they can underlie a plague of medical conditions. Drugs modulating the signal transducers may benefit patients with GI conditions, cancer, hypertension, asthma, psychiatric disorders, pain, inflammation, and more. Many of the cell membrane proteins have been well characterized, and their low-hanging pharmaceutical fruit has long been plucked. Yet more fruitful harvests may await: only around 10% (40–50) of known GPCRs have proved druggable. Most pharmaceutical companies continue to invest in GPCR programs looking for untapped targets and ways to improve on existing GPCR drugs. But most of them lack the in-house expertise to tease out the exquisitely complex GPCR structures, which resist traditional crystallography methods that might enable rational drug design against those as-yet undruggable targets.

Recent years have seen significant academic advances in GPCR biology. Several young biotechs possessing emerging technologies have drawn strong investor and industry interest. (See “Building the Next Generation of GPCR-Targeting Drugs,” START-UP, February 2009.) With some of the more prominent GPCR scientific tal-

ent among its founders, Receptos found a hearty industry welcome when it arrived on the scene.

“Arguably lots of companies can prosecute GPCR targets,” Receptos President and CEO Faheem Hasnain says. “Few can prosecute the more intractable ones. If our company succeeds, a new world of targets will open.”

Receptos was spun out of the Scripps Research Institute, around the GPCR work of Hugh Rosen and Raymond C. Stevens. “Ray Stevens,” Hasnain unabashedly proclaims, “is a rock star in the GPCR world.” Stevens’ fame rests on his advances in structural biology techniques to create stable human GPCR proteins amenable to medicinal chemistry study. He has also characterized several previously poorly understood receptors. The findings have potential application in designing and optimizing molecules to modulate several as-yet undruggable targets. These include disease targets that have been shown to respond to peptide therapeutics but are so far lacking orally administered compound candidates.

Stevens teamed up with his colleague Rosen, a molecular chemist and immunobiologist expert in lymphocyte trafficking, particularly across the subfamily of GPCRs known as the Edg receptors. Rosen is adept at generating valuable information on ligand-binding interactions within the Edg subfamily for designing and developing therapeutic molecules. He identified a number of promising modulators of an essential lipid-signaling molecule, the sphingosine-1-phosphate-1 (S1P1) receptor, a member of the Edg receptor subfamily that regulates essential cellular processes such as proliferation, migration, cytoskeletal organization, and differentiation. S1P1 also plays a validated, important role in immune cell trafficking in autoimmune disorders including multiple sclerosis (MS). Rosen and Stevens exclusively

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**Contact:** Chrysa Mineo, VP of Corporate Development

**Business:** GPCR discovery platform and autoimmune drug development

**Founded:** May 2009

**Founders:** Marcus F. Boehm, PhD, VP, Chemistry; Robert J. Peach, PhD, VP, Biology; William H. Rastetter, PhD, Chairman of the Board (Venrock); Hugh Rosen, MD, PhD (Scripps Research Institute); Raymond C. Stevens, PhD (Scripps Research Institute)

**Employees:** 22

**Financing:** \$25 million

**Investors:** ARCH Venture Partners; Flagship Ventures; Lilly Ventures; Venrock; Undisclosed others

**Board of Directors:** William H. Rastetter, Chairman (Venrock); Faheem Hasnain, President & CEO; Fred Aslan, MD (Venrock); Kristina Burow (ARCH Venture Partners); Doug Cole, MD (Flagship Ventures); Raymond C. Stevens (Scripps Research Institute); S. Edward Torres (Lilly Ventures)

**Scientific Advisors:** Dale L. Boger, PhD (Scripps Research Institute); So Iwata, PhD (Imperial College London and Kyoto University); Donald S. Karanewsky, PhD (Senomyx Inc.); Edward P. Roberts, PhD (Scripps Research Institute); Hugh Rosen (Scripps Research Institute); Edgar H. Ulm, PhD (Discovery to Drug Consulting LLC)

**Clinical Advisory Board:** David M. Essayan, MD, FACP (ONCORD Inc.); Stephen L. Hauser, MD (University of California San Francisco); Alan S. Nies, MD (Nies Consulting); Hugh Rosen (Scripps Research Institute); Lawrence Steinman, MD (Stanford University)

out-licensed their combined Scripps intellectual property to create Receptos. The

Receptos team swiftly determined the protein crystal structure of S1P1 and selected a promising S1P1 agonist from among the Rosen patents.

Kristina Burow, a partner at ARCH Venture Partners, recognized the potential value in Receptos. She brought in William H. Rastetter, a Venrock partner. He had previously led development of *Rituxan* (rituximab) while serving as founding president and CEO of Idec Pharmaceuticals. Rastetter went on to become executive chairman of the merged **Biogen Idec Inc.**

Receptos opened its doors in May 2009 and in November 2009 settled in with the first of two tranches of a \$25 million Series A round. Rastetter served as interim CEO while the company used its initial funds to build out its platform, generate technology alliances with Big Pharma partners, and push its S1P1 agonist toward an IND in multiple sclerosis while developing potential follow-on opportunities targeting S1P1 in other autoimmune disorders. The company also initiated a structural biology program focused on generating a novel oral glucagon-like peptide-1 (GLP1) agonist.

The promising package of proprietary technology and preclinical compounds may have been compelling but, Hasnain says, “It was the people around the table” that convinced him to jump swiftly back into the start-up game. He came to the company late this past November, only seven months after Abbott Laboratories paid \$722 million to acquire Facet Biotech Corp., where he had served as president and CEO. Prior to that he had been president and CEO of PDL BioPharma, from which Facet spun out in 2008. Hasnain knew a number of the people involved in the Receptos launch, including Rastetter.

The two worked together during the four years when Hasnain was EVP in charge of the oncology/rheumatology strategic business unit at Biogen Idec. Rastetter also brought two other Biogen Idec veterans into the Receptos leadership: Marcus F. Boehm, the new company’s VP, chemistry, and Robert J. Peach, as VP, biology. “Receptos has a team with the ability to execute its business plan,” Hasnain believes.

The company operated quietly until it burst into public notice with the simultaneous early January announcements of two technology partnerships: **Ortho-McNeil-Janssen Pharmaceuticals Inc.** took full license of the company’s GPCR technology to deploy against its GPCR discovery pipeline, and **Eli Lilly & Co.** will work together with Receptos to identify potential orally administered candidates for an undisclosed target and advance them into preclinical development. According to Hasnain, for the latter partnership each firm will have freedom to operate after the deal period ends.

That’s unlikely to end the dealmaking. The company’s VP of biology Peach says, “There are still major problems remaining in GPCR drug discovery. High-fidelity structural information can get you the information you need to proceed.”

The initial deals, says Hasnain, generated enough non-dilutive cash by themselves that “raising capital is not the thing that’s keeping me awake at night.” In fact, he has yet to draw the last \$8 million tranche of the first financing. The company has enough money, he says, to move its S1P1 agonist through a Phase I study that commenced in late January.

Receptos hopes that molecule will improve on **Novartis AG’s** first-in-class S1P1 modulator, *Gilenya* (fingolimod).

The once-daily, oral treatment for relapsing forms of multiple sclerosis has rapidly gained a share of the \$10 billion MS drug market. However, the relatively blunt fingolimod is non-selective, hitting four of the five S1P1 receptor subtypes, leading to concerns about possible side effects. The drug also has a half-life of six to nine days, resulting in a lengthy sequestration of lymphocytes after discontinuation of therapy that can put patients at high risk for infection. The Receptos molecule binds selectively to S1P1 and has a predicted human half-life of approximately one day, potentially improving the safety profile and reducing complications for MS patients. Results from the compound’s initial study should come out in the first half of 2012.

The company is also in the process of reviewing other autoimmune disease applications for its S1P1 agonist program. Assuming positive outcomes for the Phase I study, the company could move the compound immediately into Phase II studies in a number of other indications alongside MS, and might also draw on its remaining available capital to augment the pipeline or build out its platform further.

The platform tech alliances with Big Pharma likely have just begun. Chrysa Mineo, VP of corporate development, points out that every major pharmaceutical company is now looking to bolster its in-house GPCR structural expertise. “We can make their efforts more efficient and rapid,” she says. With an industry hungry for more GPCR products, watch for Receptos to find new ways to feed the beast.

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— MARC WORTMAN