Relypsa Inc.

(A#2007900234)

Written By	Jim Kling (Contributor)
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Summary:	When Amgen bought Ilypsa last summer, it kept one of its non−absorbed polymer drug candidates for itself, leaving Ilypsa's other candidates in limbo. Key Ilypsa employees and investors wanted to carry out those programs, and with Amgen's blessing, they moved swiftly to form Relypsa Inc., which retains rights to Ilypsa's remaining pipeline and drug discovery platform. Relypsa management, all from Ilypsa, intends to continue Ilypsa's fast pace of pipeline development, with a NCE planned for entry into the clinic every year for the next three years.

Further Analysis:

Title	Magazine	Issue	Article ID
Amgen's Biotech Shopping Spree	*IN VIVO*	Jun. 2007	2007800108
The New Polymer Drugs−−They're Not Just for Delivery Anymore	*Start−Up*	Nov. 2005	2005900217

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Relypsa Inc.

Non−absorbed polymer drugs

5301 Patrick Henry Drive

Santa Clara, CA 95054

Phone: (408) 200−9500

Fax: (408) 215−2854

Web Site: www.relypsa.com

Contact: Jay P. Shepard, President & CEO; Gerrit Klaerner, PhD, SVP, COO

Industry Segment: Biotechnology

Business: Polymer drugs for renal and cardiovascular disease

Founded: October 2007

Founders: Scott Rocklage, PhD (5AM Ventures); Gerrit Klaerner; Jay P. Shepard; Detlef Albrecht, MD (CMO & SVP, Drug Development); Jerry M. Buysse, PhD (CSO & SVP, Research); Michael Burdick (VP, Regulatory Affairs, QA & Project Management); George Tyson (VP, Pharmaceutical Sciences); Vic Ciaravino, PhD, DABT (VP, Toxicology & EH&S)

Employees: 38

Financing to Date: $33 million

Investors: 5AM Ventures; New Leaf Venture Partners; Sprout Group; Delphi Ventures; CMEA Ventures; Mediphase Venture Partners

Board of Directors: Scott Rocklage; Vijay Lathi (New Leaf Venture Partners); Deepa Pakianathan, PhD (Delphi Ventures); Jay Shepard

Polymers have a long tradition of industrial uses−−as coatings, fillings, catalysts for manufacturing processes, and in other areas. As the director of business development at Symyx Technologies Inc., whose customers include Exxon and Dow, Gerrit Klaerner was steeped in that world. In 2003, he and a small group of Symyx scientists decided to found a company in the therapeutic space. "Most people think about polymers only as excipients, to help deliver a drug. We thought of the polymer as being the drug. That’s the highest value application," he says. (*See "The New Polymer Drugs−−They're Not Just for Delivery Anymore,"* START−UP, *November 2005 [A# 2005900217].*)

Klaerner and his co−founders recognized that the unique absorptive capabilities of polymers could make them ideal agents to lower serum levels of phosphorus, potassium, sodium, and other substances that become elevated in a variety of medical conditions or as the result of therapeutic regimens, causing a range of serious side effects. Symyx investors weren’t willing to accept the risks of the FDA approval process, so the logical move was to spin out a new company.

So Klaerner co−founded Ilypsa Inc., which licensed from Symyx a technology to develop novel polymers. The company quickly developed a pipeline of four polymer drug candidates, led by ILY 101, a phosphorus binder designed to treat high phosphorus levels that commonly occur as a result of kidney disease. That product candidate, which has completed Phase II clinical trials, did so well that it attracted the attention of biotech giant **Amgen Inc.**, which acquired Ilypsa for $420 million in July 2007. [W#200710086]

"The idea is to capture the ion in the GI tract before it enters the system," says Klaerner, now Relypsa's SVP and chief operating officer. The polymers contain negatively charged particles that bind to the positively charged ions. The physical size of the crevices within the polymer causes it to selectively bind a target ion. That selectivity can be changed to favor a different substance by altering the structure of the polymer.

Amgen wanted ILY 101 (now AMG 223) to complement its renal franchise, and the acquisition left Ilypsa's other candidate drugs−−first− and second−generation potassium binders, a sodium binder, and a Clostridium difficile (responsible for antibiotic−associated colitis) toxin binder in limbo. Key Ilypsa employees and investors wanted to carry out those programs, and with Amgen's blessing, they moved swiftly to form **Relypsa Inc.** Launched in October, it raised a $33 million Series A round led by 5AM Ventures and New Leaf Venture Partners, [W#200730746] and it is staffed by 38 former Ilypsa employees. Relypsa retains rights to Ilypsa's remaining pipeline and drug discovery platform.

Relypsa's management intends to continue Ilypsa's fast pace of pipeline development, with a new chemical entity planned for entry into the clinic every year for the next three years, starting in the first quarter of 2008. That goal was part of the reason for recruiting so many of Ilypsa's employees. "This team knows each other. We know how to work well together, and we like each other," says Jay P. Shepard, president and CEO of Relypsa, who also served as president and CEO of Ilypsa.

The non−absorbed nature of the polymers is attractive from a clinical development standpoint, Shepard says. They pass through the patient's system without ever leaving the gastrointestinal tract and are eventually excreted. That simplifies clinical development because it minimizes the need for toxicology, biodistribution, and other studies. "These kinds of products are very capital efficient, he says."

Ions that are bound in the GI tract never get absorbed into the blood stream, thus lowering serum levels. "It's a very clearly defined event. You bind a certain ion, reduce its concentration in the GI tract, reduce it in the serum, and you have a therapeutic benefit," says Klaerner.

Other therapeutic areas can be more difficult to track. Take cancer, for example. Clinical trials measure tumor response, but that doesn't necessarily correlate to survival. Results can also vary wildly from one trial to another. Ion levels are "a much more straightforward end point. You're measuring serum end points that in many cases correlate with the desired therapeutic effect. As a result, clinical trials have the potential to be much more efficient to conduct," says Shepard. "We believe that premise is playing out nicely with the product that Amgen acquired" from Ilypsa, he says.

Relypsa's lead product is RLY 105, a potassium binder. High potassium is a serious problem in renal disease because it commonly occurs in both dialysis and chronic kidney disease, according to Shepard. Drugs that control high blood pressure, such as ACE (angiotensin converting enzyme) inhibitors, are protective of renal function, but they can cause dangerous elevations in potassium levels. "These drugs are a key tool that nephrologists have to slow down progression of kidney disease, but they can have a side effect of elevating potassium levels," Shepard says.

Currently physicians manage this by scaling back drug dosage or stopping it altogether for a time. "When the potassium goes up, the physician gets nervous. There's a significant need for a drug that could independently control potassium levels," says Klaerner.

According to Klaerner, pharmaceutical companies are working to develop next−generation drugs that don't affect potassium levels, but those efforts haven't yielded much success yet. "We think a combination approach where you can continue to use high doses of the drug and independently (control) the potassium levels has a good chance to help the patient," he says.

The potassium binder, RLY 105, should begin clinical trials in the first quarter of next year. A sodium binder, RLY 102, is scheduled to enter the clinic sometime in 2010. Klaerner predicts that both a sodium binder and a potassium binder could have a billion dollar market.

Relypsa's management is keeping an open mind about potential exit strategies. "We want to focus on developing these drugs to handle unmet medical needs. If we do that right, we have lots of options in terms of deals, raising money, and partnering," says Shepard.

The company is also investigating options outside the US. Ilypsa did a deal in Japan for its phosphate binder. "Given the significant medical needs, we're going to look at our capital requirements and our ability to do very selective, specialized deals along the way," says Klaerner.

Relypsa is very much a continuation of what Ilypsa started. Both Shepard and Klaerner feel that Ilypsa's successful model can guide Relypsa into the future. "We're excited about the opportunity to do it again and take lessons learned from the past and apply them to the future," says Shepard.—***Jim Kling***