

Several startups flirt with success

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In the realm of biotechnology, the odds invariably are stacked against survival.

But for the few hundred privately held biotech startups that exist in San Diego County at any given time, those odds, and the chances of gaining venture-capital funding, improve greatly if a company can offer a truly novel drug or technology, coupled with a seasoned management team.

Periodically, *The San Diego Union-Tribune* conducts an informal survey of local venture capitalists to come up with a list of new biotech startups that have the ingredients for success. But with only one out of 10 experimental drugs making it to market, there are still no guarantees that even the most innovative of startups will beat the odds.

The scorecard on past venture-capital candidates offered in 2002, and again in 2005, has been mixed. Companies such as Favrilite and Senomyx went on to go public. Others, such as Idun Pharmaceuticals and CryoGen, were acquired by bigger companies. Many, such as TargeGen, CardioNet, Ceregene and Ambit Biosciences, continue to thrive but remain private. And some, such as Quorex Pharmaceuticals, quietly went out of business.

Another crop of early-stage biotechs is emerging and, according to a survey of about 10 venture-capital firms, these biotechs may have what it takes to become the next regional success story:

■ **Ascenta Therapeutics, founded in 2003, is focused on discovering drugs that shut down cancer cell growth and proliferation. It already has its first experimental drug in Phase 2 testing for treatment of chronic lymphocytic leukemia, small-cell lung cancer, prostate cancer and other cancers.**



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John Zacharia, an engineer at biotech startup Oculir, demonstrated the company's experimental device for monitoring diabetic patients' glucose levels.

Along with a novel experimental drug, some venture capitalists also like the startup's lean business model. That includes doing work that would be costly to perform in the United States at its China research subsidiary, which employs 16 of Ascenta's 53 employees.

“We're attractive because of the intersection of a unique approach to cancer therapeutics, a business model that allows us to leverage the excellent R&D work done in China, and a seasoned team with a significant body of experience in drug development,” said Mark Benedyk, vice president of business development for Ascenta.

The biotech has other experimental drugs lined up for human testing, most of them licensed from the National Institutes of Health or the laboratory of Dr. Shaomeng Wang at the University of Michigan.

■Oculir is developing a device for diabetic patients that measures glucose by shining an infrared light at the tiny blood vessels in the white of the eye. The point-and-click sensor, which is expected to be about the size of a cell phone, could reach the market as early as 2009.

John Burd, chief executive officer of the San Diego startup, said the device would offer a painless and more convenient alternative for diabetic patients who traditionally monitor blood-sugar levels with diagnostic tests that require a drop of blood from the prick of a finger.

Oculir, which employs 10, has raised about \$7.3 million from venture capitalists since it was founded in 2003.

This is the third diabetes-related company that Burd, a scientist and former venture capitalist, has been involved with – and his run has been impressive. His first company, LXN Corp., was sold to Inverness Medical in 2000, and a second company, San Diego's Dexcom, went public in 2005.

■CovX has an impressive scientific pedigree, the brainchild of leading researchers Carlos Barbas and Richard Lerner of The Scripps Research Institute.

The startup, founded in 2002, is developing CovX-Bodies, a hoped-for new class of drugs that would combine the therapeutic benefit of peptides with certain performance characteristics of antibodies.

Independently, peptides and antibodies have limitations: Peptides break down rapidly in the body, and therefore require frequent doses; antibodies have more staying power in the body, but are difficult and costly to produce.



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DR. WILLIAM RICE,
Cylene Pharmaceuticals chief executive

Using technology developed by Barbas and Lerner, CovX has created a chemical “tether” to link peptides to specially designed antibodies, according to the company. The startup filed an application in December to begin testing its first drug candidate.

■Cylene Pharmaceuticals raised \$44 million from venture capitalists early this year to fund tests of its lead drug candidate, CX-3543. The drug's potential attributes and broad applications are promising, according to local venture capitalists.

The drug, which begins Phase 2 testing this year against several cancers, aims to disrupt a DNA structure that is needed for the production of ribosomal RNA, which is required in turn for production of ribosomes and proteins.

To grow and proliferate excessively, cancer cells need to produce excessive levels of ribosomal RNA, said Cylene's chief executive, Dr. William Rice. CX-3543 is designed to turn off production of ribosomal RNA in a selective way that will trip up cancer cells.

“Various pathways that control cell growth (altered in cancer cells) converge on to one unifying pathway where ribosomal RNA is produced, and we are able to target that unifying pathway with new drugs,” said Rice, whose company employs 30. “Think of it as several different pipelines leading into one big pipe. We are trying to hit the big pipe downstream, where other companies are developing drugs to hit the little smaller pipelines upstream.”

■Anaptys Biosciences began operations early last year in the burgeoning field of monoclonal antibodies. Co-founded by Bill Boyle, a key protein expert out of biotech giant Amgen, and using key technology licensed from Cambridge University and the Albert Einstein College of Medicine in New York, the startup is isolating leads for new therapies and hopes to test its first antibody in humans in 2008.

Boyle said Anaptys' technology involves somatic hypermutation, a natural process of mutation that occurs during B-cell development when the body produces antibodies. The technology should allow Anaptys to develop therapies that bind tighter and more specifically to the desired disease target, making it more potent and less toxic, Boyle said.

Drug companies have been snatching up biotechs in the monoclonal antibody field – including Amgen's \$2.2 billion cash buyout last year of Fremont-based Abgenix, which developed Vectibix, a monoclonal antibody for treatment of colorectal cancer.

Boyle said venture capitalists find Anaptys a compelling company because it is involved “in a hot area where there are diminishing providers of monoclonal antibodies with a novel technology that is free and clear of other companies' proprietary technologies.”

■Syndax Pharmaceuticals, with its first venture financing – about \$40 million – raised this month, is one of the newer biotechs.

The startup was formed around a discovery by Salk Institute researcher Ronald Evans that a new class of drugs called HDAC inhibitors can be combined with older drugs, known as nuclear-receptor ligands, to provide a potentially significant added therapeutic benefit.

It was only last year that the first HDAC inhibitor, a drug called Zolinza developed by Merck to treat a slow-growing lymphoma, was approved in the United States. Several other HDAC – short for histone deacetylase – inhibitors are now in clinical trials.

Syndax, which has licensed Evans' patents and an experimental HDAC inhibitor from another drug company, plans to create a combination drug and test it against several cancers this year.

“Our company believes, as most people do in oncology, that the way forward is combined agents rather than broad-based therapies,” said Joanna Horobin, chief executive officer of Syndax. “Evans' work was prophetic, given that he was combining HDAC inhibitors when the class of drugs didn't exist in the clinic, and showing it had potential to re-sensitize cells to drugs already on the market.”
