

CARDIOLOGY COMPANIES:

TAKING
COLORADO'S
PULSE

In 2005 publicly traded Myogen announced encouraging clinical trial results for its two most advanced candidates, ambrisentan and darusentan. The drugs treat pulmonary arterial hypertension and resistant hypertension, respectively.

If progress continues, Myogen will submit a new drug application to the FDA for ambrisentan this year. And the firm is planning to start a Phase III trial for darusentan in 2006.

“This is a pivotal year for us,” says Derek Cole, the company’s director of investor relations.

Myogen is among a handful of firms in Colorado working on treatments for heart diseases, broadly speaking. Some – such as Spectranetics – have long marketed products. Others are in the early stages of venture funding.

Myogen’s darusentan showed promising results in a Phase II trial for resistant hypertension, a condition that affects about 4 million to 12 million people in the U.S. Resistant hypertension is high blood pressure that does not respond to traditional medications; darusentan was found to significantly reduce patients’ systolic and diastolic blood pressure when used on top of three other anti-hypertensive medications. The company plans to launch a Phase III trial this year.

Myogen’s ambrisentan is intended to treat pulmonary arterial hypertension, a rare and lethal condition affecting about 200,000 people. The disease is characterized by high blood pressure in the lungs. Through a complex series of events, the heart eventually pumps less blood to the lungs, leaving patients breathless and unable to walk up a flight of stairs.

Both darusentan and ambrisentan are endothelin receptor antagonists. Endothelin is a chemical produced by endothelial cells – cells that line the insides of blood vessels.

In some cardiovascular diseases, these cells produce too much endothelin. Endothelin receptor antagonists help prevent excess endothelin from causing harm.

In December 2005, Myogen announced positive results for the first of two Phase III trials for ambrisentan. The drug improved patients’ exercise capacity and slowed the progress of their disease, one trial showed. Results from a second trial are due this year.

If the second trial confirms the first, Cole says, “We’d expect to file a new drug application by the end of the year.”

Wall Street analysts’ estimates indicate ambrisentan could achieve \$500 million a year in sales at peak.

Myogen, founded by three academic scientists including University of Colorado’s Dr. Michael Bristow, has grown quickly in recent years. If either ambrisentan or darusentan succeeds through clinical trials, Myogen promises to bring international recognition to Colorado, a significant development.

“The state has all the things you need for a world-class biotechnology and medical device presence,” Cole says. “It has a lot of great things going on, and is ready to tip over the tipping point.”

Another company working to treat pulmonary arterial hypertension is Fort Collins-based **PR Pharmaceuticals**. The 60-person firm, known as PRP, develops injectibles that marry medications with the company’s sustained delivery technologies. These formulations allow drugs to be delivered to the body over a period of time. PRP already has



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Cardiology Companies: Taking Colorado's Pulse – continued

one FDA-approved long-acting veterinary product on the market.

Capitalizing on the company's state-of-the-art manufacturing facility and expertise in sustained release technologies, PRP's scientists have turned their attention to developing human therapeutics. The company's lead candidate is PulmoLAR for pulmonary arterial hypertension. It will enter Phase I trials in early 2006.

The active ingredient in PulmoLAR is a drug that inhibits the production of endothelin, increases production of prostacyclin and reduces proliferation of vascular tissues. Unlike existing treatments for pulmonary arterial hypertension, which are delivered through a central venous catheter or multiple daily pills, PulmoLAR would be administered to patients in a subcutaneous injection that provides a treatment lasting up to 30 days.

"Our work in numerous animal models of cardiovascular injury, and in models of PAH in particular, indicates treatment with PulmoLAR has a dramatic effect in improving survival," says Principal Investigator Dr. Stevan Tofovic.

PRP other pipeline products include InsuLAR, a sustained-release once-a-week basal insulin injection for diabetics. Additionally, the firm recently struck a deal with OSI Pharmaceuticals to create a sustained release formulation of OSI's macular degeneration drug, Macugen.

One hundred and twenty miles south of PRP along the Front Range, Colorado Springs is home to **Spectranetics**, one of the state's oldest medical device firms.

The 22-year-old publicly traded company makes and markets both a proprietary laser system and related single-use medical devices that are used to attack cardiovascular disease. Since 1993, Spectranetics' excimer lasers have been FDA approved to remove arterial blockages and open clogged arteries. Like balloon angioplasty, a narrow, flexible tube is inserted into an artery in the patient's arm or leg. Inside the tube is a laser catheter – bundle of optical fibers the carry laser light. The laser catheter is advanced inside the coronary artery to the target obstruction and energized to destroy the obstruction.

The treatment is often used instead of or in conjunction with balloon angioplasty. Some 446 hospitals worldwide use the company's lasers.

In 2004 Spectranetics revenues were \$34.7 million. That year the company introduced the CliRpath laser system. CliRpath is designed to treat critical limb ischemia, a common consequence of diabetes. It occurs when plaque and blood clots build up in the arteries of the leg, inhibiting blood flow. These peripheral arteries are usually not large enough for balloon angioplasty, and without treatment can lead to foot ulcers, severe pain and amputation.

CliRpath works similarly to Spectranetics' coronary artery system using a fiber-optic catheter inserted into the patient's clogged artery. The laser delivers short bursts of ultraviolet energy through the catheter, removing the blockage.

“We’re very excited about CliRpath,” says Will McGuire, the company’s chief operating officer. “If you look at all of the opportunities in front of the company now, certainly the largest potential application of our technology is in peripheral arteries. The biggest piece of our growth in 2005, and it will be the same for 2006, is from the CliRpath line.”

He estimated the market potential for CliRpath is the 700,000 procedures currently performed each year for critical limb ischemia, “and it could be higher as more people are diagnosed and treated.”

The 200-person company is hiring 20 sales representatives this year, bringing its total sales force to 75, to keep up with demand, McGuire says.

An entirely different sort of catheter is at the center of **CardioOptics’** technology. The Wilmington, Mass. firm, which was founded in Boulder and still employs 10 research and operations employees in Boulder, is commercializing a catheter that allows doctors to see through blood.

The catheter uses infrared light, which lends see-in-the-dark abilities much like those developed in the Gulf War. In this case, the “night vision” will allow doctors to peer through blood-filled arteries and into the heart.

CardioOptics’ first product aims to help guide doctors when they are implanting pacemakers. The Coronary Sinus Access System was approved by the FDA last year, and the company recently raised \$26.5 million in a Series B financing to commercialize it.

Still in the early stages of development, five-person **Cardiac Access LLC** is developing a technology that blurs the lines of medicine, engineering and computer science.

The founders are programming an artificial neural network to detect the difference between benign and pathologic pediatric heart murmurs.

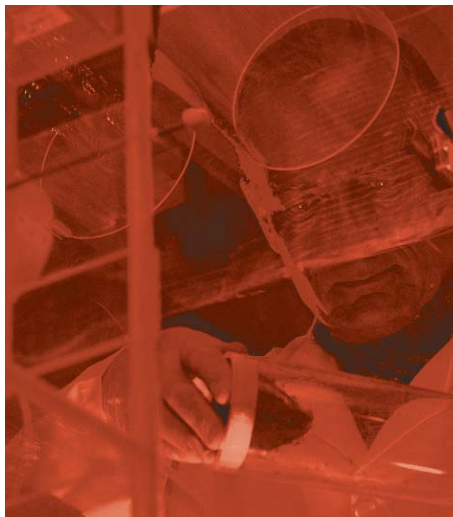
“Many children will have a heart murmur at some point in their life, but the vast majority of murmurs are benign,” explains Chip Galaty, Cardiac Access’ general manager. “Right now, if a community physician hears a heart murmur, she typically refers the patient to a pediatric cardiologist for a complete diagnostic workup.”

To save time and money, Cardiac Access is developing a proprietary software system that will be able to act as the “expert.”

An artificial neural network is being fed digital phonocardiographic signals of heart murmurs. In time, the software will learn the difference between normal and abnormal heart rhythms.

Eventually, the founders hope that the decision support system will allow community physicians to listen to a child’s heart with a digital stethoscope and get a foolproof diagnosis at the point-of-care.

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OTHER COLORADO COMPANIES developing and selling products used in cardiac care include Braun BioSystems, Genesee BioMedical, ARCA Discovery and COBE Cardiovascular.