

# START-UP



## Windhover's Review of Emerging Medical Ventures

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### VasoGenix Pharmaceuticals Inc. Comprehensive cardioprotection for myocardial infarction

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**Contact:** G. Lee Southard, PhD, President, CEO & Chairman

**Industry Segment:** Pharmaceuticals

**Business:** Drugs for MI and other cardiovascular diseases

**Founded:** January 2001

**Founders:** Jeffrey Southard, VP Drug Development; Sunil Wimalawansa, MD, PhD, Director

**Employees:** 3

**Financing to Date:** \$2.2 million

**Investors:** Kansas Technology Enterprise Corp.; Bi-State Investment Group; Precede Fund; PharmaVest; Prairie Investors; Wichita Technology Ventures; Brookstone Capital

**Board of Directors:** Lee Southard; Jere Goyan, PhD (former commissioner FDA); Richard Dunn, PhD (formerly Atrix Laboratories Inc.); Donald Braun, PhD (MCO Cancer Institute); Thomas Noffsinger, PhD (University of Kansas Medical Center Research Institute); Sunil Wimalawansa, MD, PhD (Robert Wood Johnson Medical School)

**Scientific Advisory Board:** Patrick Delafontaine, MD (Tulane University); Mark Creager, MD (Brigham and Women's Hospital); Lloyd Stahl, MD (Menorah Medical Center); Edgar Staren, MD, PhD (Medical College of Ohio)

Current drugs for myocardial infarction (MI) are designed to restore blood flow in coronary vessels that have been occluded by a clot. While the existing thrombolytics, antithrombotics, and vasodilators do that job effectively, none of them are able to prevent or reverse the heart muscle damage that results from the sudden and acute reduction of blood supply during a heart attack.

**VasoGenix Pharmaceuticals Inc.** is developing a naturally occurring cardioprotectant to minimize ischemic damage from MI. Calcitonin gene related peptide (CGRP) is widely distributed in neural tissue throughout the body. In the heart, nerves secrete it following a heart attack in an apparent attempt to reduce the infarct size and keep heart cells alive. But the body produces an insufficient amount to have a meaningful effect, says VasoGenix's president and CEO G. Lee Southard. VasoGenix's CGRP drug is designed not only to restore blood flow, but also to actively protect cardiac tissue. The company hopes to position its product as a front-line treatment for MI.

Jeff Southard, VasoGenix's VP of drug development, and endocrinologist Sunil Wimalawansa founded VasoGenix in 2001 around Wimalawansa's patent for CGRP. Their original goal was to create a drug to treat arterial vasospasms that occur during angioplasty. The 2003 arrival of Lee Southard, Jeff Southard's father, signaled a change in direction to the much larger opportunity of myocardial infarction—there are 1.4 million nonfatal heart attacks in the US alone each year.

Lee Southard started his career at Big Pharma, and then was founder of two successful start-ups: Vipont Pharmaceutical and Atrix Laboratories.

While current drugs for MI have a single mechanism of action, VasoGenix's candidate works on many levels, says

Southard. It acts as a vasodilator to increase blood flow to the heart and kidney and to decrease cardiac workload. It reduces levels of angiotensin II, which plays a significant role in myocardial cell death. It also boosts anti-inflammatory cytokine expression while suppressing pro-inflammatory cytokines that are associated with increased mortality from MI. Because CGRP is a naturally occurring peptide, it should not have some of the toxicity or side effects new synthetic drugs would have to be screened for, he believes.

In animal studies conducted by Dongmei Wu, MD, PhD at the **Mount Sinai Medical Center & Miami Heart Institute**, the natural release of CGRP during heart attack did not result in measurable reduction in infarct size. However, supplementing the body's natural CGRP response one hour after the infarction reduced infarct size by 40%. Although not practicable for clinical use, pre-infarction infusion of CGRP in animals resulted in an 89% reduction in infarct size. (See Exhibit 1.)

VasoGenix believes that its drug's multi-pronged action will reduce overall damage to the heart and that it will lead to faster recoveries. It may also help prevent or delay development of congestive heart failure (CHF); among heart attack survivors, 46% of women and 22% of men will develop CHF within six years.

The company believes that the drug may be effective if administered within four hours post-infarct, but the earliest possible intervention is desirable. Southard envisions IV infusion of CGRP starting in the ER (perhaps eventually in pre-hospital transport), with continuous delivery throughout angioplasty all the way into the recovery room. Southard says that a four to eight hour course of treatment should be sufficient in most patients, but VasoGenix is designing its clinical trial protocols out to 20 hours. CGRP

could also be used in conjunction with tpA, heparin, and other thrombolytics and anti-thrombotics.

VasoGenix is unusual for a preclinical-stage biopharmaceutical in that it has some human data to support the expected safety and dosing regime. In the 1990s, a number of researchers conducted a total of 27 different pharmacology studies of CGRP in 338 patients. Seven studies were of cardiovascular patients—all with CHF. There were five studies of patients with non-cardiovascular diseases, and 15 studies in healthy subjects. "That early work has enabled us to zero in on the effective clinical dose and duration of treatment for CGRP," Southard says.

He hopes to start a combined Phase I/II trial in 2006 and use this data to expedite approval for the next two big-market indications that VasoGenix plans to pursue with CGRP: CHF and renal insufficiency.

As in MI, CGRP for CHF would act on multiple fronts. It would reduce cardiac workload like ACE inhibitors and beta-blockers; increase cardiac output like inotropics; and increase urine output like diuretics. Southard believes that as a stand-alone therapy, CGRP could replace some of the drugs currently used to treat CHF, or it could be used to augment current therapies. Preclinical work on a CHF candidate is underway, and in April 2005, VasoGenix signed a deal with **QLT Inc.**'s **QLT USA** to create a sustained-release formulation of its CGRP with QLT's *Atrigel* biodegradable drug delivery platform.

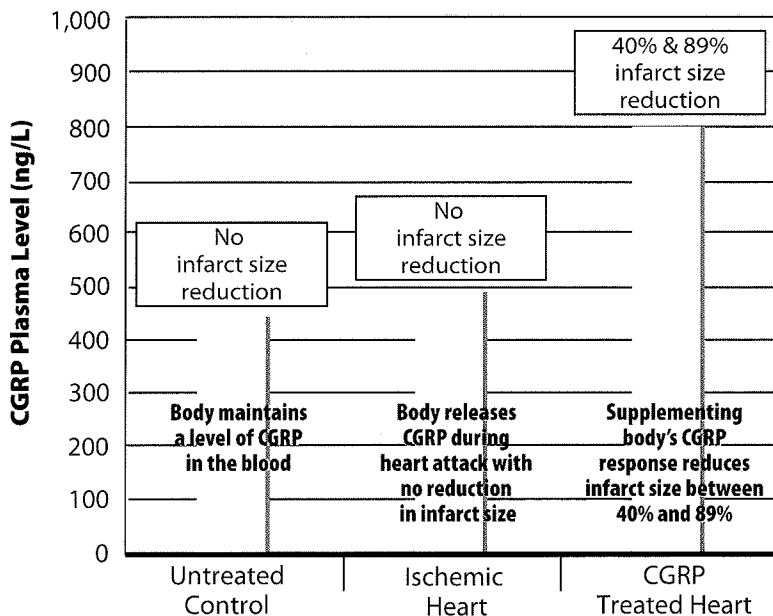
The third indication in VasoGenix's pipeline, still in early preclinical development, is a candidate for treating renal insufficiency. The company is amassing IP protection for its programs: in addition to the issued patent it in-licensed at its inception, VasoGenix has filed for three additional patents to support its current pipeline and has initiated international filings.

All told, Southard estimates the annual markets that VasoGenix hopes to address at between \$8-10 billion. He and his team have carefully managed the \$2.2 million they have raised in two rounds to date. VasoGenix operates as a semi-virtual company—preclinical work is outsourced to various contract research organizations, and the company plans to conduct its clinical trials at the **Cleveland Clinic Foundation**. It will also outsource all development including manufacturing; Southard notes that CGRP is easily synthesized using standard solid-base methods.

Now the primary challenge facing VasoGenix is to raise money to move CGRP into the clinic. Southard is looking for a \$10 million Series C round to complete preclinical work on its lead candidate, to file an IND and to complete Phase I/II trials, at which point the company will decide whether to partner the product or take it through Phase III on its own.—NTD

## Enzyme Levels Correlate with Infarct Size Reduction

EXHIBIT 1



SOURCE: VasoGenix Pharmaceuticals Inc.