

START-UP



Windhover's Review of Emerging Medical Ventures

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Endovalve Inc.

Pioneering percutaneous mitral valve replacement

103 Carnegie Center
Suite 100
Princeton, NJ 08540
Phone: (609) 921-1456
Fax: (609) 921-8703
Web Site: www.endovalve.com

Contact: Robert G. Wilkins, MBChB, CEO
Industry Segment: Cardiovascular Devices
Business: Minimally invasive mitral valve replacement

Founded: June 2005
Founders: Nascent Enterprises LLC;
Howard Herrmann, MD
Employees: 0 full-time
Financing to Date: \$2.5 million
Investors: Battelle Ventures LP; Innova-
tion Valley Partners LP
Board of Directors: Robert Wilkins; Tracy
Warren (Battelle Ventures)
Scientific Advisory Board: Howard
Herrmann (Hospital of the University of
Pennsylvania)

Long the exclusive province of cardiovascular surgeons, procedures for repairing or replacing damaged heart valves are starting to shift into the hands of interventionalists. Developers of new percutaneous technologies for aortic, mitral, and pulmonary valve disease hope to replicate what interventional technologies have done for other cardiovascular surgeries: eliminate or minimize time on cardiopulmonary bypass, enable faster recoveries, and improve the economics of treatment. Device companies aim to create new, minimally invasive options for patients too sick to have surgery, and to expand treatment to those at an earlier stage of the disease to halt its progression to heart failure.

Of the four million people in the US

with moderate to severe mitral valve regurgitation (MVR), about 40,000 undergo surgery for valve repair or replacement each year. This unmet opportunity has attracted major device companies such as **Edwards Lifesciences Corp.** and **St. Jude Medical Inc.**, and a number of start-ups as well. (See "In Heart Valves, a Brave, New, Non-Surgical World," *START-UP*, February 2004 and "New Frontiers in Heart Valve Disease," *Medtech Insight*, August 2005.) But all of these companies—large or small—are focused on mitral valve repair. **Endovalve Inc.** is the first to attempt to commercialize a percutaneous approach to replacing damaged mitral valves.

The start-up's technology was invented by Howard Herrmann, director

of interventional cardiology and the cardiology catheterization labs at the **Hospital of the University of Pennsylvania**, and a well known figure in the heart valve world. Indeed, says Endovalve's CEO Bob Wilkins, it was Herrmann's expertise in percutaneous valve repair—he has been an investigator in numerous studies, including **Evaluate Inc.**'s EVEREST trials—that spurred him to conceive and develop Endovalve's percutaneous replacement technology. Just as surgical valve repair is more complex than surgical valve replacement, Herrmann reasoned that percutaneous valve replacement might be preferable to percutaneous repair: complex, long procedures that require a high degree of skill.

Herrmann's own early efforts to attract local funding and spin out the technology were not successful. Medical device advisors Nascent Enterprises LLC eventually led him to Battelle Ventures in the fall of 2005. Battelle helped launch Endovalve, putting up a \$2.5 million Series A round in May 2006, and licensing exclusive rights to Herrmann's technology from UPenn, on which one US and related international patents are pending, in exchange for milestone payments.

Battelle's early involvement is noteworthy on several levels, says CEO Wilkins, who earlier in his career held executive posts at Abbott Laboratories

Inc., Baxter Healthcare Corp., Physiometrix Inc., and Datascope Corp. One, it's rare for an early-stage device company to raise capital from a VC and, two, Battelle Ventures' backing allows him to focus on product development rather than hunting for cash.

The venture firm's involvement also enables the start-up to operate in a completely virtual mode. It occupies space in Battelle Ventures' Princeton office, and it also shares human resources. When he's not focused on Endovalve, Wilkins consults for the firm on other ventures. Battelle Ventures general partner Tracy Warren is a director of the start-up, and Endovalve's acting VP of R&D is VP of medical device solutions for Battelle Memorial Institute, the venture firm's sole limited partner. Scientific founder Herrmann, a full-time clinician at UPenn, is a member of the scientific advisory board. Endovalve will remain virtual for the foreseeable future, Wilkins says, with all R&D outsourced to Foster Miller Inc. If everything succeeds as planned, there will ultimately be a need to build up staff and infrastructure, but Wilkins doesn't see this happening for at least two to three years.

First, the company must demonstrate that Herrmann's concept will fly in the tricky mitral valve anatomy. "Most people looking at any percutaneous valve approach have looked at variations on the stent theme. That's fine with aortic valves where there is a tube of tissue in which to anchor a stent. But the mitral valve ring is truly a ring—there isn't enough wall to anchor anything," Wilkins explains. Thus, Herrmann's novel design, which consists of a bistable prosthetic heart valve folded inside a small catheter. The catheter is delivered through a femoral vein, passed into the right atrium, and then transseptally crossed into the left. Once the catheter is in the left atrium, the valve is deployed. Wilkins likens deployment to opening an umbrella. The valve locks into the open position, and numerous clamps on its

rim anchor it to the heart tissue and hold it in place. Total procedure time should be in the two- to three-hour range, much shorter than the four to six hours for current percutaneous valve repair procedures. Still to be determined is the nature of the valve, whether it will be mechanical, biological, or a combination of both.

In opting to pioneer a new procedure with a novel valve, Endovalve is charting itself a challenging course. To achieve commercialization and to generate enthusiasm among interventional cardiologists, it will have to demonstrate that its percutaneously implanted valve works at least as well as surgical counterparts so the benefits of avoiding open surgery are crystal clear to doctors and patients.

But first things first. "If we can't build the system we can't build the product," Wilkins acknowledges. "If we get three years down the road and discover it's a wonderful valve but we can't deliver it, it's a waste of everybody's time and money." To avoid that fate, the company is taking a very staged, milestone-based approach from the get-go.

During the next four months, Endovalve will complete its initial feasibility review and build a prototype device to demonstrate basic deployment and fixation. That prototype will be refined in the next 10 to 12 months into a version that could be implanted into animals. During this period, the company will also perform bench-top tests to establish the device's basic hemodynamic performance.

By the end of 2007, Wilkins hopes to have sufficient prototypes to start a few informal animal studies. If survival rates are sufficient, Endovalve will make any necessary design modifications and embark on definitive animal studies in late 2008 en route to an IDE filing in 2009. It will need a new infusion of capital in the \$6- to 10-million range at that point. Tracy Warren confirms that Battelle Ventures intends to participate in that second round.

If the company succeeds in making it to market, the first patients it will target will be those who are unfit for surgical procedures and thus have no other options. As adoption increases, Wilkins sees the market for Endovalve's device growing in three major segments. First, patients who are candidates for surgical valve replacement but who would prefer to avoid the risks of open surgery. Second, patients who are today being treated with drugs for heart failure caused by mitral regurgitation because they are not well enough to undergo surgery. And third, Endovalve wants to ultimately expand out to patients who have moderate degrees of disability from mitral regurgitation but aren't yet ill enough to be considered for surgical replacement.

To get to that last group, Endovalve will need to rack up several years of successful outcomes. But it is by far its biggest opportunity: according to Wilkins, 20% percent of people over the age of 50 have mitral valve regurgitation. That number is unlikely to dwindle because MVR is a disease of aging and a common consequence of cardiac ischemia caused by now-endemic diabetes.

Despite many potential roadblocks that stand between the early-stage company and the marketplace, Wilkins is confident of Endovalve's choice to pioneer in mitral valve replacement. "Percutaneous repair procedures today, even in the most expert hands, are long and complicated," he says. "Not many patients are being enrolled in clinical trials, and the results vary from encouraging to disappointing depending on who is presenting what data at what time." Current technologies and procedures, he says, have not yet passed the point where they are suitable for the general interventionalist. "Our goal, and clearly we are a long way away from being there, is to develop a procedure that is capable of being performed by a broad range of interventional cardiologists."—**Nancy Dvorin**