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ValveXchange, Inc. products have not been approved by the U.S. FDA or any other Regulatory Agencies. This newsletter contains forward looking statements which represent management's best judgment, but are speculative and may not occur as projected or not at all.

NEWS RELEASE

February 2009



[From the Desk of Ivan Vesely, Ph.D.](#)

Dear Colleague

February saw three more successful animal implants, a refinement to the sewing cuff and continued development of the exchange tools. This month, we were notified that ValveXchange Inc. is the recipient of the 2009 North American Frost & Sullivan Technology Innovation of the Year Award. We look forward to receiving the honor at the Frost & Sullivan awards banquet in San Francisco on March 18th.

We are also happy to report that [Dr. Joseph Sabik](#), Chair of Cardiothoracic Surgery, The Cleveland Clinic Foundation, has agreed to chair the VXi Medical Advisory Board. Dr. Sabik is a highly respected cardiothoracic surgeon, widely recognized for his critical work in outcomes-based analysis of both coronary bypass grafting and mitral valve repair procedures.

This month, the "Reality Check" column is entitled "*How to Spend a Billion Dollars in One Week*", and reports on a stunning series of valve company acquisitions by Medtronic. This month, Medtronic showed the world that when it comes to heart valves, they are back in the game!

For those new to this Newsletter, ValveXchange is a start-up company based in Colorado. We call ourselves "*The Lifetime Tissue Valve Company*" and are developing the first-of-its-kind "serviceable" bioprosthetic valve. By offering periodic, minimally invasive exchange of the worn-out leaflet set, young and physically active patients can avoid the use of a mechanical valve and the associated Coumadin® anticoagulation therapy. By adhering to the time-proven design tenets of conventional bovine pericardial valves, the ValveXchange system offers the best combination of least-invasive reoperation and greatest longevity and durability.

Press Release

ValveXchange is recipient of Frost & Sullivan Technology Innovation of the Year Award

February, 2009. Denver -

ValveXchange Inc. announced that it is the recipient of the 2009 North American Frost & Sullivan Technology Innovation of the Year Award.

According to Frost & Sullivan Research Analyst S.R. Priya, "The ValveXchange Heart Valve System represents a safe and less invasive alternative to conventional therapies.... Overall, the ValveXchange system provides the innate hemodynamic and non-

thrombogenic benefits of tissue valves to patients of all ages, thus obviating the need for expensive and potentially problematic anti-coagulation therapies and major lifestyle modifications," concludes Priya.

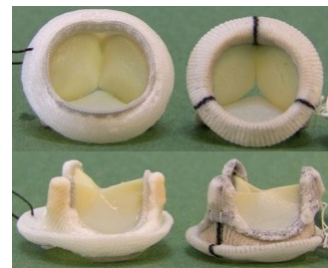


February, 2009. Denver - ValveXchange Inc. announced that of [Dr. Joseph Sabik](#), Chair of Cardiothoracic Surgery, The Cleveland Clinic Foundation, will serve as the Chair of the VXi Medical Advisory Board. Dr. Sabik is recognized for his critical work in outcomes-based analysis of coronary bypass grafting and mitral valve repair. In a recent [review article published in The Cleveland Clinic Journal of Medicine](#), Dr. Sabik writes that when it comes to comparing patient survival after coronary artery bypass grafting (CABG) and Percutaneous Coronary Intervention (PCI), "the truth is in the details." Dr. Sabik's critical review of the Clinical Trials literature makes him an ideal candidate to lead an advisory group that will shape the future of heart valve technology at VXi, focusing on treatment options that put the patient first.

Other News

Technology Update

As discussed in January's newsletter, the objectives of the ValveXchange development program are to take the best features of the off-patent, industry-leading Edwards pericardial valve and blend them with the proprietary design features that enable the leaflet set to be exchanged, when needed, by



way of a minimally invasive, off-pump approach. There are many features in a valve that may make it desirable for the surgeon. Clearly, long-term performance has always been the most significant factor. But once long-term performance of a new valve in the patient is assured, the next feature is its performance in the hands of the surgeon - How does it feel when handled? Is it bulky or elegant? How does the needle pass through the sewing cuff? Is it sufficiently low-profile? With these

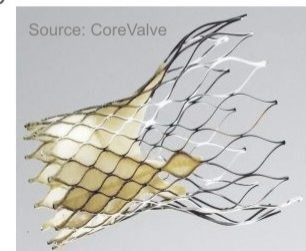
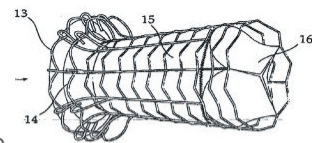
subjective features in mind, the VXi *Vitality*^(tm) valve has been designed to match the Edwards Perimount® valve. In the comparison images, the Edwards Perimount® valve is shown on the left and the VXi *Vitality*^(tm) valve is shown on the right. In the coming months, additional "surgeon preference" features will be explored in this Newsletter.

Reality Check

How to Spend a Billion Dollars in One Week?

Of the "Three Sisters" that make heart valves their business (Medtronic, Edwards and St.Jude), Edwards Lifesciences came out as the clear leader in making a bet on the Percutaneously Implantable Valve (PIV) field. In January of 2004, [Edwards Lifesciences acquired Percutaneous Valve Technologies](#) (PVT) for \$125 million, plus another \$30 million in payments upon the achievement of key milestones. At that time, it was considered a huge amount of money for a company that had little success in their first-in-man studies. In the eyes of many, however, that purchase was justified since the technology came along with some key early patents in the percutaneous valve field. After the acquisition, Edwards moved rapidly with a clinical feasibility trial of the PVT device. Unfortunately, that trial had to be [suspended in the summer of 2005](#) pending a revision to the delivery system due to some early adverse outcomes. The Edwards clinical trial was restarted in late 2007 under the name [PARTNER \(Placement of AoRTic traNscathetER valves\)](#). With regard to the PVT patents, Edwards tested their validity in 2007 with a [lawsuit against CoreValve](#) claiming infringement on its key Andersen patents. Late in 2008, a [German court found that CoreValve did not infringe on the Edwards patent](#), however, casting doubt on the strength of the Edwards PIV patent portfolio. This story is clearly not over, though. Early this year, a [British court dismissed CoreValve's claims that the Andersen patent is invalid](#) although CoreValve claimed victory also, stating that "[CoreValve Prevails in a United Kingdom Patent Infringement Action](#)". Regardless, the original Andersen patents may not be as rock-solid as initially thought, opening the door for many other PIV companies.

On the heels of a seeming patent infringement victory by CoreValve, Medtronic stunned the valve community by announcing its [acquisition of CoreValve for an initial payment of \\$700 million](#) plus two additional \$75 million milestone payments. What was even more interesting about this huge valuation for CoreValve was a that it came just a few days after Medtronic announced that it will acquire [Ventor Technologies for \\$325 million](#). Medtronic thus spent over \$1 Billion in less than a week! How could this type of valuation be justified, particularly for Ventor whose product apparently "[has not been tested on humans](#)?" Indeed, the two technologies are remarkably similar, at least according to the image in the [Ventor patent](#) (see comparison above between the Ventor valve and the CoreValve device). What is it about Ventor that gives it some edge

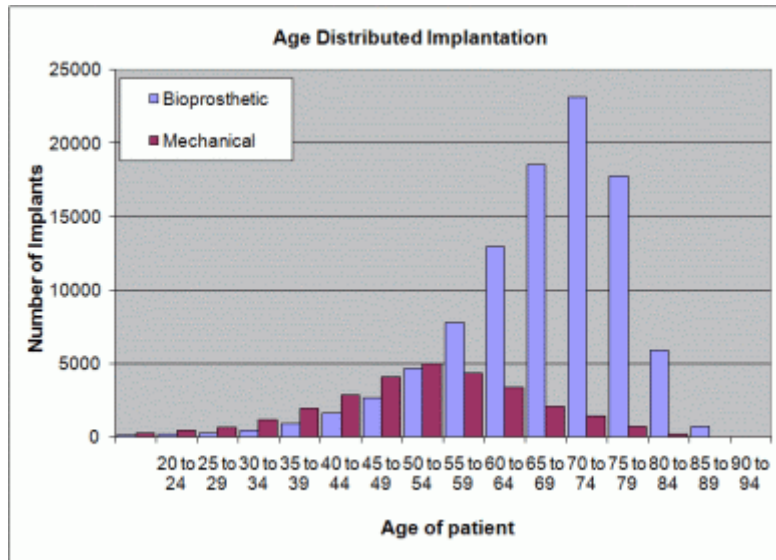


over CoreValve? Why would Medtronic buy two apparently similar companies, and why is CoreValve, which has clinical approval and has sold over 2,000 valves in Europe, worth only twice as much as Ventor which has almost no clinical history? More importantly, how can a PIV company be worth \$700 million in the first place?

The calculation is quite simple, actually. Medtronic claims in its press release that the market for calcific aortic stenosis is 300,000 per year world-wide. Actually, the market for ALL calcific aortic stenosis could be that high, but for the inoperable patient, the current indication for PIV's, the market is roughly 100,000 - an additional 1/3 of the current market. But even if we use this conservative number, a 100,000 unit yearly market for a valve that can sell for \$20,000 equates to \$2 billion/year. If Medtronic were to grab one half of this market, they would be making an additional \$1 billion in revenues per year. Given the margins typical for such devices their \$1 billion acquisition of Ventor and CoreValve could pay back after roughly two years of operations. With numbers like these, a billion dollars is not a bad investment at all. Indeed, by comparison, the \$125 million investment by Edwards in PVT seems like a steal, even with the additional work that may be necessary before this technology is fully commercialized.

For Medtronic, this acquisition of CoreValve is a clear signal that it intends to compete head on with Edwards. A year ago, Medtronic announced a deal with [Arbor Surgical Technologies for its pericardial valve](#) making it very clear that it intends to compete with Edwards in the pericardial valve space. For decades, Medtronic has touted its porcine valve based products as being superior to the Edwards bovine pericardial valve, largely from a theoretical viewpoint claiming that a porcine valve is "a real valve" and hence functionally superior. Unfortunately, convincing clinical data supporting greater durability of porcine valves has been scarce, and bovine valves have gradually done better and better in the marketplace. Now that Medtronic is "back in the game" with both bovine pericardial valves and PIV's, the heart valve field is sure to become more competitive in the coming years.

Now for the "Reality Check"! Medtronic states in their press release that "*The acquisition of CoreValve gives additional momentum to our strategies for growth and will improve the quality of care for more than 300,000 people worldwide with severe aortic stenosis*". The market for calcific aortic stenosis is 300,000 patients per year? Perhaps not. For example, a [Research and Markets study](#) available on the web lists the total world market at 350,000 heart valve procedures per year. Aortic replacement represents 57% of that, with the remainder being mitral procedures - 10% being mitral repair. Per this report, calcific aortic stenosis represents about 175,000 procedures per year, at best. Now let's take a look at the distribution of these patients. The figure below, compiled from the STS data base, shows the number of procedures tracked from 2004 to 2006, stratified by age of the patient at time of implant. Note that the bulk of the patients that receive tissue valve are between 65-75 years old.



What then is the life expectancy of these patients? Data from the [National Center for Health Statistics](#) indicates that in 2004 a white male 65 years old had a life expectancy of about 18 years. A white female had a life expectancy of 20 years. Extrapolating the life expectancy curve from 2004 to 2010, which is when the PIVs will likely come to market, the life expectancy of the average 65-75 year old patient could very well be 15-20 years. I will argue that most of these patients will NOT be candidates for PIVs. Why? In the words of Dr. Sabik "*The truth is in the details*". In this case the "*details*" are engineering factors that suggest that the average durability of PIVs is likely to be far less than that of current generation surgical valves, as discussed below.

Clearly, PIVs are a welcome alternative for inoperable patients and will no doubt appeal to some elderly surgical valve candidates. However, studying the engineering details of the highly refined, current generation bioprosthetic valves of Edwards and Medtronic, in comparison to the PIV, one cannot conclude anything else but that PIVs are remarkably immature devices. Because of the engineering compromises that are required to fit a 23 mm valve into a 6 mm (18 French) catheter, PIVs cannot incorporate many of the time-proven design features of current generation bioprostheses. Some of these features are listed in the table below.

Bioprosthetic Valve Design Feature	Importance	PIV Problem
No suture holes in the load-bearing portion of leaflet	Suture holes cause stress concentrations and lead to leaflet tearing, primarily at the commissures	Most PIV cannot use leaflet clamping because of space and thus use sutures, even at the commissures
Flexible stent posts	Cushion pericardial leaflets against shock loading during valve closure	Metal stent of PIVs is not compliant and therefore cannot cushion leaflets
Closed valve must have a central gap	Gap provides space to accommodate leaflets when closed, as stent posts deflect inward and valve leaflets	Variable distension of metal cage during deployment leads to variable central gap
Optimized leaflet thickness	Thinner leaflets have greater tensile stresses, thicker leaflets have greater bending stresses	For bundling into catheters, PIVs have very thin leaflets and thus elevated stresses
Avoid close proximity of valve leaflets to other valve materials	Leaflets that impinge on other materials, even soft sutures, eventually abrade and perforate	Leaflets of PIVs can impinge on the metal cage if not fully dilated, or on the calcific nodules that may protrude through cage
Symmetry of leaflet shape and material properties	Symmetry in shape and material properties minimizes leaflet stress	Presence of calcific nodules in native leaflets can prevent fully symmetrical dilation
Sewing cuff is soft and conforms to aortic annulus	Perivalvular leak is the most common reason for early valve reoperation. It causes regurgitation and hemolysis	PIVs have no sewing cuff and typically have 2+ or 3+ regurgitation
Refined implant technique limits damage to AV node	Any disruption to AV node will require use of a pacemaker, increase costs and limit quality of life for recipient	Up to 20% of PIV patients require pacemaker, presumably because metal cage damages conduction pathways

Given the above noted design compromises and procedural complications, it is difficult to see how PIVs can offer the same longevity as conventional bioprosthetic valves have over the past 20 years. A PIV will eliminate the sternotomy, but at the price of significant post-operative risk for strokes, [pacemakers](#), valvular insufficiency and, most likely, decreased valve durability. Based on the above noted engineering factors, it is thus unlikely that PIVs will last more than 7 years. They will most likely suffer fatigue-induced leaflet tearing and prolapse, for the design reasons noted above. Many others expert in the field have written articles expressing concern for the unproven durability of PIV's, [recommending careful clinical evaluation before widespread usage](#).

And what course of action is there for a patient with a PIV that has failed after 7 years? Placing a PIV inside another PIV has been suggested and indeed performed a few times. How much further will this reduce the effective orifice area and will this be appropriate for an otherwise healthy patient? Certainly, if the PIV needs to be completely removed, it will likely necessitate a complete aortic root reconstruction which, for the elderly patient, is dangerous! For example, complete aortic root reconstruction has been reported for redo's of stentless valves, [with operative mortality of 11%](#). These valves lasted on average 8 years, a very disappointing outcome for a technology with high expectations.

With this experience in mind, many physicians will find it difficult to recommend PIVs to otherwise healthy, active patients with a life expectancy beyond 10 years. Besides their continued use in the inoperable patient (which is the current indication), the appropriate cut-off age for PIVs may be 75-80 years. According to the STS database, that represents about 20-25% of the current aortic stenosis market of 175,000 procedures, or 45,000 procedures. However, when added to the estimated inoperable patient population (1/3 of 175,000 aortic stenosis = 58,000), the total expected market for PIVs is over 100,000 procedures per year. So coming full circle, the \$1 billion purchase that Medtronic made does address a \$2 billion market, and their investment should be recouped in 2 years. That is still a good deal! But make no mistake, surgery for heart valve disease will continue to thrive and predominate, as innovative approaches to MIS and off-pump techniques make surgery less and less invasive, and with outcomes better than with transcatheter valve implants.

In closing, I'd like to offer a personal note of opinion regarding the notion that PIVs will quickly obsolete surgically implantable valves. As a researcher in heart valve mechanics for over 25 years, I can say with confidence that making valves last 15 years or more is not straight forward. Many surgical valves, complete with flexible stents and near perfect geometry, have failed to match the proven longevity of the Edwards Perimount® valve. The scientific literature is littered with actuarial curves showing how one valve after another failed to meet its longevity expectations. So if one does depart from the time-proven engineering design of conventional valves in order to incorporate new beneficial features, there must be some assurance that such devices do not get missused. One must not forget the principal precept of medicine: "[Do no harm](#)".

Sincerely,

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Previous News Releases

January 30, 2009. Denver - ValveXchange Inc. announced that it has begun long-term animal testing of its proprietary exchangeable valve technology. [Read More.](#)

October 13, 2008. Denver - Aurora-based medical device company ValveXchange Inc. announced today that it has been awarded a European patent (EP1,671,608) entitled Cardiovascular Valve Assembly, authored by Dr. Ivan Vesely, the company's Founder and Chief Scientific Officer. [Read More.](#)

July 29, 2008. Denver - Aurora-based medical device company ValveXchange Inc. announced today that they have received a \$1.6 million grant from the National Institutes of Health (NIH) for funding under the SBIR Program related to research and development of its proprietary two-piece heart valve technology. [Read More.](#)

January 1, 2008. Denver - ValveXchange Inc. is a featured company in Start-Up magazine. [Read Article.](#)

December 7, 2007. Denver - ValveXchange Wins The Third Annual Faegre & Benson Venture Showcase Award, Presented At BioWest 2007. [Read More.](#)



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