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July/August 2001

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Percardia CEO NANCY BRIEFS on fundraising and company-building in the cardiovascular sector

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From Patent to PMA

Percardia CEO Nancy Briefs says her company has the technology, talent, and tenacity necessary to be a leader in the cardiovascular marketplace.

Interview by Stacey L. Bell

Since its inception a mere three years ago, Percardia (Merrimack, NH) has raised a total of $32 million in funding—and the company is just getting started. Under the leadership of CEO Nancy Briefs, Percardia has built a solid patent portfolio, recruited an expert scientific advisory board and a top-notch management team, demonstrated proof of concept for its new technology, and reached several key milestones. These accomplishments have not gone unnoticed; Percardia counts among its key investors cardiac giant Medtronic (Minneapolis).

Not a bad beginning for a start-up. In fact, the story of Percardia's development is just as compelling to investors as its core technology. The company was founded by a venture incubator to investigate the feasibility of developing a new approach for the treatment of coronary artery disease (CAD). Using patents licensed from a noted surgeon, Percardia developed a proprietary technology intended to provide improvement or relief of angina pectoris, which often results from preexisting ischemic conditions typically caused by blockage of the vessel that significantly restricts the flow of oxygenated blood to the heart.

The company's technology could address as much as 40% of the worldwide market for CAD treatment devices. With nearly 60 million Americans suffering from one or more types of CAD and the total CAD market estimated at more than $5 billion, Percardia has positioned itself pretty well—even if it is a start-up.

In this interview with *MX* contributing editor Stacey L. Bell, Briefs discusses the earliest stages of her company's interesting beginnings, as well as the challenges of fundraising for a premarket approval (PMA) technology.

Photo by STEWART WOODWARD courtesy VISUAL TALENT GROUP

MX: ***Percardia had an interesting start as the brainchild of a venture incubator, Itasca Ventures [Minneapolis]. How did this take place? Is it common for a venture incubator to give birth to a company in this way?***

Briefs: Itasca was an incubator funded by Medtronic, Vanguard Venture Partners [Palo Alto, CA], and Crescendo Ventures [Minneapolis]. It no longer exists as an incubator, but its focus was to look for paradigm-shifting technologies in the cardiovascular field. The president of Itasca, Scott Wolf, learned about the core technology for Percardia while looking in a patent review. The inventor of the original intellectual property is Peter Wilk, MD, a surgeon from New York.

Wolf licensed the patents from the Wilk Patent Development Corp., and then Itasca put up seed funding of $1 million in March 1998. One of the milestones attached to that funding was to find a chief executive officer, and that's when they recruited me.

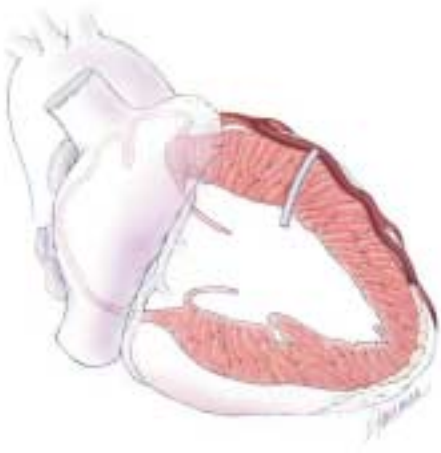
Is it common for a venture incubator to develop a new company? Don't companies usually come to them?

If you look at incubators around the country, there are a number of different models. Some conceive of the ideas, work through the feasibility testing or prototypes, and then determine whether they want to fund the company, spin it out, and find a CEO. Others—such as Itasca—look for and license technologies first and then begin the search for a CEO or president who can build the company. Still others actually start and run companies for a period of time, then spin them out.

So because it's a new way to help generate concepts and prove feasibility, there are a number of models. It's probably too early to predict which of those models will prove most efficient.

You mentioned that Itasca Ventures is no longer a venture incubator. How has it changed its business?

Itasca was very successful in starting both Percardia and CardioClasp [Somerville, NJ], but after those ventures, the original investors decided not to continue funding the company. One of the founders, Crescendo Ventures, decided last year to get out of medical technology altogether. The others, Medtronic and Vanguard Venture Partners, remain very active medtech investors, but they have chosen to do their investments independently.



Percardia's VStent implant is placed through the heart muscle, thereby establishing a channel between the left ventricle and the coronary vessel through which oxygenated blood can flow.

So Percardia was founded in March 1998. How soon after that did you come on board, and what was your first order of business?

I was recruited in summer 1998 and actually joined the company in November of that year. My first order of business was to determine the feasibility of the concept in animal trials.

At the time, we began by having contract developers make different iterations of our first design concept. I used the seed round to determine whether the concept had merit, and then started to build the team so that we could raise the first round of financing to support our research and development efforts.

Among the challenges in starting up any new medtech company is that of finding well-known and respected scientific advisors. How did you go about finding appropriate people?

When you're looking for scientific advisors, you want individuals who understand your market and your technology, and have had experience in developing innovative products with other companies.

We were fortunate, because most of my background has been in cardiovascular and medtech start-ups, and I knew a number of people in cardiology and cardiac surgery that we could turn to. I also used our investors, who were very well connected in this space—particularly our chairman, Jack Gill—to make connections with physiologists and other advisors.

I would definitely consider our scientific advisory panel a world-class group. It's been the real strength of the company in these early days, as we have been moving toward understanding the unique physiology involved in using a stent to provide coronary revascularization from the ventricle with both systolic and diastolic flow.

We wanted a stellar group to help us understand the physiology; we had to prove to ourselves that the concept would work. It was such a contrarian notion that some of the scientific advisory board members joined our team just for the opportunity to try to prove that the concept would not work. But over the past couple of years, as we've demonstrated feas-

Illustration courtesy PERCARDIA

It Takes a Lot of Heart

Though still an early-stage company, cardiac device maker Percardia (Merrimack, NH) has proven to be an investor's dream in every phase of its development thus far. Perhaps that's because the company was founded on the most basic of business principles: market opportunity. In Percardia's case, the market opportunity represents a potential $2 billion annually.

The company is currently developing a core technology that could offer a new approach to treating coronary artery disease (CAD), a narrowing of the coronary arteries caused by the progressive buildup of plaque. CAD is the most common form of heart disease, which remains the number one cause of death in the developed world. The worldwide market for CAD treatment devices is impressive—more than $5 billion annually.

Percardia's technology seeks to relieve angina pectoris, or chest pain resulting from a temporary imbalance between the demand for oxygen by the heart and the ability of the coronary arteries to supply enough blood to meet that demand. Its first-generation VStent implant is based on a balloon-deployable stainless-steel stent that is coated and covered, and is intended to deliver oxygenated blood from the left ventricle of the heart to a targeted coronary vessel. This approach enables more-flexible delivery options for patients requiring revascularization—approximately 40% of the total CAD market, or $2 billion.

The initial market for the VStent technology will target patients with degenerating saphenous-vein bypass grafts who require intervention. This market is estimated at 1.5 million patients worldwide, with a growth rate of approximately 100,000 patients per year.

Percardia expects to develop different delivery systems that allow its VStent device to be implanted in both open-surgical, less-invasive environments as well as percutaneously or through the patient's femoral artery. Currently under development is the VCab surgical delivery system, which is designed to enable a surgeon to place a VStent into the targeted coronary vessel in the operating room, as well as the VPass delivery system, a catheter-based technology designed for use by interventional cardiologists in the catheterization laboratory.

ibility, they've become our biggest supporters.

When did you first start hiring staff members, and which positions did you fill first?

We started hiring our team in spring 1999, after we had established our scientific advisory board. We knew that we had a fairly massive project ahead of us in understanding cardiac physiology and how it related to the implementation of our device. And from the beginning, our business model called for us to use contract manufacturing and some contract development services.

So the first position that I needed to fill was vice president of research, and I set out criteria that I felt would get us the best minds in the industry. We used an executive search firm and found our VP of research, Patrick Calahan. From that point, we built our research and development department and the entire company as it stands today, which has 27 employees. About 80% of the company's employees are engineering professionals.

When your executive search firm was helping to build your staff, what particular skills were you looking for? Did you expect your new staff to have developed relationships with any particular agencies or scientific boards?

It depended on the position. When the product development team was recruited, we already had our scientific advisors pretty much in place. We've added some additional people, but we had a pretty good start on that.

Instead, we were mostly looking for talented engineers who knew how to run programs, and project managers with the kinds of leadership skills that we would need in uncharted waters. Since no one had worked in this area before, we were looking for people who knew the industry and had past experiences that were successful. All of our team members have backgrounds in medical technologies, but most come with experience in less-invasive devices, particularly cardiology and cardiac surgery. They almost all have experience in stents, balloons, catheters, or wires with major cardiovascular companies.

One important hire whose past relationships were especially important for us was Jill Wollins, our vice president for regulatory and quality assurance. She holds a PhD, did postdoctoral work at the Mayo Clinic [Rochester, MN], and has worked in the cardiovascular field for a significant number of years. She also had relevant experience with PMA devices at FDA.

Developing the Technology

Percardia is focused around the VStent technology. How does this technology work, and how does it differ from what's currently on the marketplace?

The VStent technology and our extensive intellectual property portfolio—we have 11 issued patents and more than 30 additional patent

Nancy Briefs, CEO, and engineer Jianlu Ma at work in the laboratory at Percardia headquarters (Merrimack, NH). Briefs credits Percardia's success to knowledgeable staff and an expert scientific advisory board.

filings—are based on the early innovative work by Peter Wilk, MD.

In traditional cardiology, coronary stents are used as a scaffolding to hold open the arteries. But what Wilk envisioned was placing the stent in a perpendicular position, right through the muscle of the heart, and then connecting it to the oxygenated blood in the ventricle. His belief was that the shortest path would be from the left ventricle directly to the artery.

So our technology has the advantage of using biomaterials that are well known as implants, but placed into a very different physiologic condition. They're now being put into a muscle rather than into a naturally occurring lumen or vascular system.

What that has meant for us is that traditional stents did not work in this application. Early on, when we tried off-the-shelf technology, we found that it didn't have the radial strength needed to withstand the compressive forces and sheer stresses of the myocardium as the heart is beating. So now we're using a technology that's familiar to coronary stents, but with a much more robust stent design and proprietary coverings and coatings that we believe will help us to keep the device patent.

What is the market outlook for this technology?

Oh, if I only had a crystal ball. Because it is a Class III PMA device, the first thing we have to do is to prove that it's safe and efficacious in humans.

We have a very broad application, in that we have patents for both surgical implantation—called VCab—and for percutaneous bypass in the cardiac catheterization lab—called VPass. The stents used for these applications are similar, but of course the delivery systems are unique for each application. So we really think of the market as two-tiered.

In the surgical market, our advisors have suggested that one suitable population might be patients who are going in for a second or redo bypass surgery. These would be patients who tend to be older and have already had vein or arterial grafts that have reoccluded. For that population, we could provide a very simple approach to revascularization of those arteries. We believe the market in the United States is about 400,000 patients annually who might be candidates for a redo type of procedure.

For the cath lab application, we've just begun studying the feasibility of the percutaneous delivery system, so we've not yet looked at patient indications. There are a number of possibilities, including patients treated for saphenous-vein grafts, patients who have restenosis from traditional coronary stents, and patients who have chronic total occlusions. We're looking at all those possibilities, but it's a little early to predict whether some or all of those applications might be candidates for our device.

Some analysts have suggested that your technology could address 40% of the total coronary artery disease market worldwide, with the potential of a $2 billion annual market size. Does that sound accurate?

Once we've demonstrated that the device provides sufficient revascularization in human patients, I think that assessment could prove to be fairly accurate. And those numbers include both the delivery system and the implanted stent.

It's a very simple device to deploy. In preclinical animal trials, we've shown that the device can be deployed in less than two minutes, so we don't believe there will be an ex-

Photo by STEWART WOODWARD courtesy VISUAL TALENT GROUP

tensive learning curve for surgeons. There may be some technique issues relative to the deployment procedures, but we're optimistic that it should have a fairly broad application in the market.

When are you expecting clinical trials to occur in humans?

It all depends on FDA, of course, but our internal plan is to submit our application for an investigational device exemption (IDE) some time within the next 12 to 18 months. Then, depending on how long the review cycle is, one would imagine that we would be in human pilot trials sometime before the end of 2002.

When could you conceivably have the VStent on the market?

It's too early to say. It will depend on how many patients are required for the IDE, and how long the required follow-up period might be. It could be as early as 18 to 24 months after the trials, or as long as three to five years. We're obviously hoping for somewhere in the middle.

You mentioned Percardia's broad intellectual property portfolio. What will those properties enable the company to do?

Early on, we made a strategic decision to build a very broad and diverse intellectual property portfolio, because there is a lot of prior art relating to stents, catheters, balloons, and delivery systems. Our strategy was to focus on what we were doing that was so unique, and we had an internal goal to own that space. So all of our intellectual properties revolve around the VStent itself—different iterations of the stent, different biomaterials, different delivery approaches, different systems.

We have a portfolio that is broad enough to allow us to practice what we need when it comes to stents in the myocardium. But it's not that diverse when it comes to addressing other technologies; all of our intellectual property relates to the ventricular revascularization stents and their delivery systems.

Value-Added Investors

During the past three years, you've raised more than $32 million in financing for Percardia. How did you target potential investors?

From the perspective of a start-up, there are several important things that one has to do when raising money. When you go out to talk with venture capitalists (VCs), you must have a business plan and you need to have a very persuasive or compelling story.

One of the ways you can make the company's story persuasive is by building on the quality of the company, including the employees you've recruited as well as the board of directors and scientific advisors. Early on, I made sure that we had an experienced management team and the best and the brightest scientific advisors and top-tier investors. It was important that we had such investors who understood we would have a long road ahead to commercialize a Class III PMA device, so we needed people with staying power.

We had a story that was very compelling because the market opportunity is very significant and the technology is really a new business, not just a product-line extension. So if we could demonstrate that the technology worked, it offered VCs a potentially significant return.

But to really access venture capital, you have to match the type of funds you're talking with to your company and the stage of financing you require. It sounds pretty simple, and you would think that people do this, but it isn't always necessarily what people look for.

We looked for VCs that we felt could be value-added investors. In other words, we made sure that we understood the characteristics of the fund, its stage of investment, and whether the partners had previous company experience. We took a very deliberate and strategic approach toward getting them interested in Percardia. Anyone can give you money, but it's really the value-added VCs that will help bring the most to the company as it is growing. This is especially important in the start-up world, because company management faces many challenges as well as opportunities.

So we looked especially for partners who had had some operating experience before becoming VCs. We felt that they would not only bring us the investment capital we needed, but that they could also provide significant contacts and relationships. And because they had experience in our market space, they would understand some of the challenges that management would face and could provide both counsel and stewardship.

We were very lucky because we were successful in raising money from VCs who work in this market segment, understand what we are doing, share our vision, and have a local presence. We were well prepared with good quality people internally, and we targeted the right group—and they, of course, were a good match for us.

Medtronic was an early investor in Percardia. What is the nature of that company's investment?

Medtronic has been involved in every round of financing for Percardia, including the seed round. In fact, I learned about Percardia from friends at Medtronic, and one of the attractions about the opportunity here was the fact that the company already had a corporate investor.

Obviously, as one of the world's premier cardiovascular companies, Medtronic understands that if Percardia's concept works, it will have incredibly far-reaching market implications.

Medtronic manages its investment in Percardia as it would a venture investment. The company does not have a board seat or any special first-offer rights.

What role might Medtronic play in Percardia's future?

I wouldn't want to predict. That's probably a question better asked of Medtronic's CEO, Art Collins.

The next funding round for us is probably a couple of years out, once we've done testing with some human patients. Then we'll be looking for significant cash both to do the pivotal trial and to go commercial. At that point, it will be interesting to see if we might be a fit with Medtronic or another cardiovascular company.

You've had great success in raising venture and public financing for a number of medtech companies, including Percardia, Vista Medical Technologies [Carlsbad, CA], and Target Therapeutics [Natick, MA]. In addition to your solid business background, you also hold an undergraduate degree in psychology. Does that background give you any advantages or special understanding when pitching a company to potential investors?

Actually, I think my MBA in marketing and finance is much more relevant. But understanding psychology never hurts. What's important for investors is that you understand what they're looking for in terms of a return on investment, and that you have a compelling story backed by a credible team.

My psychology background was probably more helpful earlier in my career, when I was at Edwards Laboratories [Irvine, CA] as a heart-valve and cardiology sales rep working with surgeons.

Percardia is a member of the Medical Device Manufacturers Association [MDMA; Washington, DC], which has traditionally pursued an active political agenda on behalf of its members. What is Percardia's involvement in this area?

Last May, at the most recent MDMA annual meeting, Percardia presented an award to Senator Judd Gregg [R–NH] in recognition of his efforts with FDA reform and his ongoing work with the medtech sector. It surprises a lot of people to learn that New Hampshire ranks second in the country in high-tech industrial employment. We're very pleased that our small state has such a well-educated population and close proximity to the resources that a venture-backed start-up requires. And our industry has great support from our senators at the national level.

Do you have specific involvement with MDMA as well?

Personally, no, but a number of our employees are active in the organization. We're also a charter member of MassMedic [Boston], a New England–based group of medical

The Competition

Thanks to its intellectual property portfolio and extensive study in the area of revascularization technology, Percardia (Merrimack, NH) may be on the verge of developing the next technological breakthrough in the field of cardiology. But the company faces some stiff competition. Two rival start-ups also vying for a piece of the market for treatment of coronary artery disease (CAD) are HeartStent Corp. (Minneapolis) and Ventrica Inc. (Fremont, CA). Like Percardia, these companies are developing devices to treat CAD using ventricular revascularization technology and hope to create alternatives to coronary bypass surgery by connecting a coronary artery with the left ventricle of the heart instead of with another spot on the artery.

HeartStent is currently developing a device that creates a ventriculocoronary artery bypass, a permanent transmyocardial channel between the left ventricle and a coronary artery. In animal trials, the company implanted an L-shaped titanium tube with an exterior polyester cuff from the base of the left ventricle to the proximal left anterior descending coronary artery using a beating-heart approach. These trials showed the promise of perfusing ischemic myocardium with systolic flow. HeartStent has been very successful in raising funding and is backed by numerous venture capital firms, including Charter Venture Capital (Palo Alto, CA), Focus Ventures (Palo Alto, CA), Kleiner Perkins Caufield & Byers (San Francisco), Medical Innovation Partners (Minnetonka, MN), Northeast Ventures (Duluth, MN), Piper Jaffray Ventures (Minneapolis), St. Paul Venture Capital (Minneapolis), Technology Partners (Palo Alto, CA), and Winton Partners (Minneapolis).

Ventrica is developing its own approach to revascularizing coronary arteries, which works by shunting blood directly from the left ventricle of the heart and tapping into the body's natural source of oxygenated blood. Founded in 1998, the company is funded by Delphi Ventures (Menlo Park, CA), InterWest Partners (Menlo Park, CA), and MedVenture Associates (Orinda, CA).

device manufacturers. We encourage our team to remain knowledgeable about current regulations and other trends that may affect our business.

So that's why you have chosen to belong to these particular groups?

That's correct.

Challenging the Future

What are your plans for Percardia's future?

Percardia is currently working on a very novel approach to coronary artery revascularization. The immediate challenge in the next 12 to 18 months is to demonstrate that the encouraging results we've seen in our preclinical animal trials can be duplicated in humans. From there, the key will be to continue developing what we believe may be a more-cost-effective, less-invasive approach to treating coronary artery disease.

Have you given thought to the company's future business approach and model? Might the company go public at some point?

Since Percardia is 80% owned by investors and venture capitalists, the exit strategy for the company could be one of many. It could be an IPO, or it could be something like an acquisition by one of the major cardiovascular companies. It's a bit early to tell, but once we've demonstrated the safety and efficacy of the device in humans, then either of those options would be very viable so far as our investors are concerned.

Do you have any feeling about which way the company might go?

In today's market, an IPO would be rather uncertain. But by the time we need funding again, in 18 to 24 months, it's hard to imagine what conditions might be like on Wall Street. In the meantime, we're trying to continue hitting our milestones successfully, demonstrating the science behind our new approach, making sure that we have the highest-quality medical devices we can build, and then getting them into humans for testing. And along with that, we're staying abreast of financing options for the company so that we can continue to fund our growth.

Photo by STEWART WOODWARD courtesy VISUAL TALENT GROUP

Our technology has the advantage of using biomaterials that are well known as implants, but placed into a very different physiologic condition.

What are the larger challenges to the future success of Percardia?

A significant challenge at this point is to continue expanding our knowledge of the physiology of both systolic and diastolic flow. We're already at design freeze for the first generation of the VStent, but that information will be very important for the development of the second-generation technology. By expanding our knowledge and iterating new generations of these stents, we'll be able to continue expanding the patient population that we might serve.

We therefore must continue hitting the milestones for the first-generation device while keeping an eye on the second-generation technologies that will be needed to continue growing the organization and the market.

What about the challenges of the marketplace?

We're very happy that we're in a market space for ventricular revascularization where we're not the only company competing for the lion's share. We have two competitors that are working on devices using similar technologies, HeartStent Corp. [Minneapolis] and Ventrica [Fremont, CA]. It's going to be helpful to have all of us building the market, because it's much easier when there are a number of companies working on demonstrating the basic science and the feasibility of the product concept. Then, when we have approved devices, it'll just be a matter of competing for market share on the basis of which company's product is more elegant or easier to use.

In that sense, we're very happy to have competitors. It's going to help us as we move forward in this very exciting new opportunity for ventricular revascularization.

What's going to be next for you?

Next for me is Percardia.

For the long foreseeable future?

That's right. I have no plans to move. ■