

Device Company Creation

The New Device Incubators

Universities focusing on translational research and regional economic development groups are turning to new kinds of medical device incubators for value creation.

By Mary Stuart

Stanford. MIT. Harvard. The Hutch. The names of the universities capable of spinning off high-quality life science companies are well known to investors, entrepreneurs, and business development folks alike. But one other class of professional has been watching these centers very closely as well—officials from other universities.

For years, university and economic development officials residing outside of those entrepreneurial hubs have tried to draw investors and businesses to their own research and engineering labs, hoping some of the good fortune being enjoyed by those major centers would rub off on their own universities and regions.

No more. Today, universities and other research institutions are making their own luck. They've come to realize that they need to change their own approaches to the development and commercialization of their inventions.

Although they've always run incubators—the kinds of fee-for-service structures that offer laboratory space and perhaps some shared administrative services—today many universities have a mandate to actively create new companies around university technologies. These university officials realize they no longer can count on corporations or venture capitalists to find them. Instead, they're opting to do the heavy lifting themselves to create start-ups that will fuel their economic engines. David Schetter of the Office of Technology Alliances at the **University of California, Irvine** (and a co-founder of **Orange Coast Medical Ventures**, profiled below) says that in 2003, start-ups accounted for 47% of the university's active license agreements; 30% of licenses from UCI's active invention portfolio; 20% of UCI's industry research funding; and 40% of UCI's royalty and fee income. He's working on gathering the current numbers now, but he bets they will only go up, demonstrating the strength of starting new companies.

What's also new is that universities are making a concerted effort to attract in companies from beyond their hallowed gates to enhance internal research programs.

While we tend to think of medical device incubators as the kinds of organizations in which founders fund a management

company that creates companies, take equity in spin-off companies, and actively seek external funding for portfolio companies—the model of dozens of for-profit medical device incubators like **The Foundry**, **The Innovation Factory**, or **Coronis Medical Ventures**—here it is a little different. Certain universities are collaborating with interest groups with common goals to develop new, external business incubators, which they don't necessarily own, but the connection to which gives them some intangible benefits. Models vary, because they're tailored to particular regional environments and to individual goals. Unlike the incubators formed out in industry, the incubators in which universities participate aren't driven by the profit motive as much as by a variety of competitive and funding pressures related to the institution's *raison d'être*. The university exists to educate, and to conduct basic research for the benefit of humanity. Indeed, while tech transfer departments may take equity in exchange for granting a license to technology, the university-owned business incubators we spoke with never do. Many of the self-described university business incubators are essentially service organizations that provide resources to member start-up companies and entrepreneurs as they need them, to help early-stage companies move up the value creation chain, but for reasons that aren't necessarily financial.

Cliff Robinson, PhD, the director of the business incubation program at **Boston University** (BU) explains that business incubation helps his university accomplish several of its goals, including attracting research funding. "As a large research university—with one of the better biomedical engineering departments in the country—we attract substantial federal funding to support our faculty. Today, the funding agencies want to see commercial value from that research. The name of the game is translational research," Robinson says. He explains that federal funding agencies are especially interested these days in research that can be translated into products with clinical efficacy and patient benefits. In 2002 the **National Institutes of Health**, for example, began an initiative known as the "NIH Roadmap for Medical Research" that articulates a vision for a more productive system of medical research with a greater impact on health care. Institutions with a focus on translational medicine optimize their chances of winning grants, Robinson says.

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The Business Incubation Program is part of BU's Office of Technology Development (OTD), which provides a host of capabilities to start-up companies. In addition to business incubation, OTD focuses on patenting and licensing intellectual property, assisting in the formation of start-up companies by providing internal and external venture capital funding, mentoring for start-up founders and executives, and opportunities to partner with industry.

Robinson says that BU's incubation program differentiates it as an educator. The university's business school teaches entrepreneurship and recently formed the Institute for Technology Entrepreneurship and Commercialization. "Students today are demanding education in entrepreneurship. We are training the next generation of business leaders, especially with respect to technology business. Today, businesses have to be constantly innovating and inventing new products and new businesses. As a university we have a responsibility to prepare our students properly for a career in the workforce."

Robinson explains that BU has a business incubator located right in the heart of the university campus, which houses about a dozen well-financed and well-managed start-up companies. Students have the opportunity to work as interns in these companies, and some find employment there after graduation. Start-ups may have been formed around a license to BU technology, or may have been invited into the incubator because of skill-sets or a focus that benefits university programs, but they are independent companies with their own management and external funding. **Solx Inc.**, for example, was an external company with its own funding that matched up with photonics expertise at BU. Solx grew up in the incubator, and it was acquired by ophthalmic device firm **Occu-Logix Inc.** in August 2006. (See "An Early Peek at Glaucoma Devices," *START-UP*, February 2006.)

"We immerse students in the real world of companies. They will become better employees for technology companies as a result of having been at BU," he says. **Stanford University** similarly hopes to give its students an edge in medical product industries, through its Stanford Biodesign program, which gives students hands-on experience in biomedical technology creation as they work with successful entrepreneurs and clinicians. (See "The Device Industry's Training Ground," *this issue*.)

Many of the benefits of the new business incubators are intangible. The **Cleveland Clinic**, a founding member of **BioEnterprise Corp.**, believes that creating a vibrant local commercial environment will help it attract leading clinicians and researchers; it's what it needs to remain competitive with other parts of the country like Palo Alto or Boston. BioEnterprise also serves the economic development goals of the state of Ohio, as it forms companies and attracts others to the state, creating jobs and increasing the tax base.

Incubators can expand the capabilities of research institutions. The **Advanced Technology Development Center** (ATDC) has helped the **Georgia Institute of Technology**, with its expertise in electrical engineering, acquire biomedical capabilities. It combines resources with the **Emory University School of Medicine** to create biomedical start-ups. The two universities have formed a joint department of biomedical engineering, a unique collaboration between a private and a public university. Lee Herron, associate

director of ATDC Biosciences says, "We tend to see a lot of convergence opportunities—clinical problems that need or require an engineering solution." **CardioMEMS Inc.**, the developer of an implanted sensor for the monitoring of congestive heart failure and abdominal aortic aneurysms, is a graduate of ATDC. (See "Remote Patient Monitoring: The Markets Near and Far," *START-UP*, April 2006.) The primary mission of ATDC, like many incubators, is economic development for its region.

Picking Up Where Tech Transfer Leaves Off

While serving the goals of higher education or society, university business incubation groups might have one ancillary, but great benefit in improving the process of technology transfer, especially for medical devices. Business incubators add capabilities that pick up where tech transfer leaves off, and they might even improve access to university technologies for smaller entrepreneurs.

Technology transfer can be a confusing, cumbersome process spanning multiple departments that reside in "silos." UC Irvine's David Schetter says, "Most universities are segmented. The sponsored projects office may not talk to the foundation development office, which doesn't work with the tech transfer office, which is unaware of what goes on at asset management." This is a setup for confusion, and that's not the only thing that's wrong with the technology transfer process, particularly for medical devices. Adam Dakin, for one, has had his share of frustrations with the tech transfer process.

Dakin is CEO of **Bioconnect Systems Inc.**, the developer of an improved anastomotic connector for hemodialysis. The company was incubated by **MentorTech Ventures**, an \$11 million venture fund that invests in medical device start-ups (as well as information and marketing technology) that have some association, loosely defined, with the **University of Pennsylvania**. Dakin ticks off a list of five things that make tech transfer departments difficult to work with, starting with slow turnaround time. "There is no sense of urgency. Small companies are anxious to get the process moving. We're burning capital while we're waiting, but there is a stark contrast between academic and industry time lines." Dakin also laments that many tech transfer departments spend the majority of their time doing pharmaceutical deals, and they don't understand that device deals need to have a completely different structure. "They try to strike high-royalty-based arrangements, and that doesn't work with devices." Next on the list: the process of protecting intellectual property is often inadequate, according to Dakin. "Tech transfer departments don't want to spend a lot of time and money on any one patent. They might just file a provisional patent, or even a utility patent, but they don't instruct their counsel to do a really comprehensive job on the IP." Holes in IP may exist because the inventing research scientist, who filed the claim, might not understand the potential market applications for particular devices.

A high rate of turnover can be another big problem for entrepreneurs. Dakin says he wasted a year and a lot of money on legal fees negotiating an agreement with a tech transfer department,

but when the agreement was on the verge of completion, the tech transfer officer left the organization, and his successor, who didn't understand the medical device industry, refused to sign the agreement.

Finally, because tech transfer organizations give preference to large companies with which they have ongoing relationships, IP can be tied up unproductively for long periods of time. Dakin says, "There were times when we were interested in licensing a piece of technology, but they said, 'We're in talks with a big company and we want to see where that goes first.' It's going nowhere," says Dakin, "because the technology is too early for a large device company." Dakin acknowledges that if a university has a relationship with a large company like **Johnson & Johnson**, the big company will probably politely consider the patent disclosure, especially if it comes from a famous clinician. But it won't result in a deal, he says, and meanwhile access to the IP is blocked. Because many of the new business incubators are billing themselves as "go to" places that match entrepreneurs with resources—IP counsel, help on reimbursement strategies, faculty with specific expertise—they might smooth out the process of tech transfer, especially for small companies.

No matter what the primary motive, the new incubators share the goal of filling the gaps in skill-sets related to the development of early-stage technologies at a particular institution or in a region by making connections to outside resources, to shepherd a start-up toward the point where it can attract venture capital or corporate attention. We've profiled two incubators below that have very similar goals but very different structures. In Cleveland, BioEnterprise is trying to create a competitive environment far from the biomedical clusters of two coasts, which means it is working without a preponderance of local venture capital firms or a large corporate biomedical base from which to draw management. Cleveland has some of the latter—remnants of an orthopedic industry that left the state when Johnson & Johnson's **Depuy Inc.** bought AcroMed and moved it to Massachusetts. It also has prestigious research institutions—the Cleveland Clinic and **Case Western Reserve University**—and strong support from the state, which is managing a \$1.6 billion fund, the Ohio Third Frontier program, to create centers of excellence for translational research. BioEnterprise operates as a not-for-profit charitable organization that takes no equity and requires no fee-for-service from start-ups.

In contrast, the brand new incubator Orange Coast Medical Ventures (OCMV) will have a for-profit structure, taking equity much like an incubator in the private sector. OCMV is attempting to solve a different, but less obvious, problem. Located in (but not owned by) the University of California, Irvine, Orange Coast Medical Ventures is based in a part of the country that has a university with a long-history of biomedical tech transfer; a medical school; a world-leading photonics research center, the Beckman Laser Institute; large venture capital firms that invest in the life sciences, for example, Versant Ventures, Fjord Ventures, Crosspoint Venture Partners, and Enterprise Ventures; a large base of large medical companies including **Edwards Lifesciences Corp.**, **Allergan Inc.**, **Advanced Medical Optics Inc.**, **Nestle SA's Alcon Inc.**, **Baxter International Inc.**, **ev3 Inc.**, and a whole slew of medical start-up companies. Its challenge is simply to get all of the resources to work in unison for early-stage device incubation, for the ultimate

goal of regional economic development. UC Irvine's Schetter says, "We have all the venture capital, all the facilities, we have UC Irvine's expertise, and we have new technology and start-ups, but we somehow need to pull this together and deliver a coherent program." It's like a super-saturated solution, Schetter says, and the new incubator will be the crystal that makes it coalesce.

Orange County Rises Above the Gathering Storm

Orange Coast Medical Ventures (OCMV) arose from, indirectly, a nationwide teleconference sponsored by the National Academy of Sciences in September 2006. The Convocation on "Rising Above the Gathering Storm" was a workshop designed to respond to some of the issues raised in the report of the same name, about America's future competitiveness (or loss thereof) in a future, global economy. UC Irvine's David Schetter was among the thought leaders chosen, in each of 50 states, to head up a committee on university-industry and technology economic development issues. His task force was to discuss what needed to be done in Orange County to address some of the concerns that were raised.

After an hour and a half of discussion, Schetter's group, which included the senior VPs of the Boeing Company, Northrop Grumman, Edwards Lifesciences, Versant Ventures, and others, came to the conclusion that Orange County needed an incubator for new business. "This is one of the capitals of the medical device world," says Schetter "and the fact that we did not have any kind of incubation capability here to speak of was a big missing piece."

Schetter was conscripted to head up the Orange County Business Incubation Network (OCBIN), a non-profit consortium of university, civic, and industry partners, which would coordinate resources in Orange County to launch start-up companies and tide them over with whatever they needed to succeed from the invention phase to commercial viability. OCBIN identified four key industry segments for which dedicated incubators would be created: medical devices, aerospace, information technology, and biotechnology.

The overarching goal of the incubators is economic development, and on an operational level, individual incubators will create and fund, through core sets of resources, an infrastructure that will have all the business planning, legal, and regulatory capabilities, and everything else that a start-up would need to get to the first institutional funding round, Schetter explains.

The first incubator, Orange Coast Medical Ventures (OCMV), is coming together at lightning speed. The Aubrey Group, an Irvine firm that specializes in the design and manufacturing of electronic and electromechanical devices for medical applications, is providing incubator space, plus access to design, prototyping services, and equipment. Greg Ruehle, currently CEO of **Allvivo Vascular Inc.**, has taken the helm. Ruehle spent the early part of his career at device icons Medtronic, St. Jude Medical, and Boston Scientific but has spent the past eight years working on launching start-ups, including Allvivo, the developer of a biomimetic coating for vascular devices such as stents. Shepard Bentley, a principal at Bentley Biomedical Consulting, has joined the team as an expert

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on regulatory affairs. Schetter and Ruehle are accepting investments for the incubator now—from VCs, angels, and corporate investors—with a goal of raising \$10 to \$15 million. They've gotten some initial funding, and they have started to put together a select board of clinicians to help with commercial, reimbursement, and other strategic issues. The incubator also has a great resource in its access to UC Irvine, with its clinical trials and research capabilities, and UC Irvine has three companies ready to go into the incubator.

With many of the functional pieces in place, OCMV still needs to finalize its business model, which will likely be for-profit. Ruehle points out that there are 1,200 to 1,300 incubators in the US right now, and less than 5% are for profit. He is bringing in an expert from outside of Orange County to help his incubator determine the feasibility of a particular model for the unique environment in Orange County. "We not only have a university, but a large contingent of venture capitalists with roughly 200 medical companies that can help nurture this, and some of them are very large." Ruehle suggests that the incubator will be patterned after for-profit accelerator **Coronis Medical Ventures**. Coronis was launched in early 2006 by four device industry veterans, Mark Klopp, Wil Samson, Carl Simpson, and Roger Stern. Coronis takes advantage of a relationship with **StellarTech Research Corp.**, an outsourcer of contract manufacturing services for sophisticated medical devices, to create virtual companies that use the StellarTech services on a contract basis. (See "Coronis: Creating Virtual Companies," START-UP, January 2007).

As Schetter describes it, "Instead of trying to start companies one at a time and having to deal with infrastructure and whatever's needed for each one, we will create one infrastructure with the kind of high-level leadership that Greg can provide when it's needed, with connections, assistance with regulatory affairs, or anything else. The goal would be to spin three or four companies a year out of that program." OCMV investors will probably fund and own the incubator, and then portfolio companies will take advantage of external investments. Coronis invests about 40% of its funds in core infrastructure and the remaining amounts in actual creation and development of three to four companies annually. That's a good model, Schetter says, because "then you can afford to hire experienced people like Greg."

Like Coronis, the OCMV incubator will probably work with pre-funding or seed-stage companies that, not yet having all the details figured out, probably need mentoring. "There are a couple of critical things that we're going to help with," says Ruehle. One is to make sure that a company's IP is solid. The university has its own set of skills for that activity, but the incubator's oversight board also includes Fish & Associates, a firm that deals with patent law. "We have lined up various engineering groups, both large and small to help with prototyping, and from a funding perspective, we have three or four medium-sized venture capital groups. The incubated companies will probably get an initial bolus of money to get going, and then a milestone or certain time frame will release additional funds," Ruehle says. The incubator will be able to acquire

and retain some equity in all the companies that it forms, and it will sustain itself without having to go to public sources or donations, Ruehle hopes.

Sourcing technologies for start-ups doesn't look like it will be a problem. Schetter says, "It's difficult to believe, but at UC Irvine, we are getting one new invention per business day. About 75% of our technology is in life sciences, and a large percentage of that relates to medical devices. I'm looking to the incubator as a very important vehicle for out-licensing a lot of our technologies. It also turns out that start-ups are becoming more interesting to the faculty."

In Schetter's experience, there is a new emphasis on getting companies started. "The big pharma and big medical device companies have moved downstream. They aren't doing that much discovery research in collaboration with universities any more. They are waiting for the biotechs and medical device start-ups to figure it out, get the rights, get it organized, and then they'll either do a strategic partnership, a sub-license, or buy the company," he says.

Ruehle suggests that OCMV's first

Exhibit 1

Orange Coast Medical Ventures

Industry Focus: Medical devices

Academic Affiliation: University of California, Irvine

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Mission: 1) Economic development in Orange County; 2) Facilitate tech transfer in a sector where company creation is desirable; 3) Remove early stage risk in preparation for external funding round

Competitive Advantages: Generous funding for the incubator attracts seasoned management from industry; large corporate base in the region provides management and financial resources

Funding Sources: Incubator will have external funding and will grant seed money and early milestone-based funds to spinouts

Incubator's Return on Investment: Incubator will hold equity in start-ups

Representative Investment: CODA Genomics (out of the UC Irvine, pre-dates the incubator) developed a scalable, rational process for protein manufacturing. www.codagenomics.com

Source: University of California, Irvine

graduating class might include some companies in the photonics area, a minimally invasive optical coherence imaging technology, for example, and a vertebral pain management system. This came to the incubator from a neurosurgeon and a trauma surgeon who had gotten their own initial funding. "This is a perfect fit," says Ruehle, "because they've done some self-funding but they need regulatory and quality capabilities, and they need prototyping."

It pre-dates the incubator, but Schetter suggests that **CODA Genomics Inc.** is a good example of the kind of company the incubator hopes to nurture. The start-up, which has developed a process for routinely assembling synthetic genes that manufacture large amounts of protein, was spun out in 2005 from the UC Irvine, where it existed as a virtual company operating under sponsored research agreements. Schetter says the company has raised \$10 million in capital and by the end of the year will have 30 employees, most of whom are high-end professionals. "That is just one company, and it is bringing \$10 million and 30 employees to the county. That is where we are going."

A Favorable Microclimate for Bioscience Innovation

Cleveland Rocks! Most people know that Cleveland, Ohio, is the home of the Rock and Roll Hall of Fame, but few are aware that since 2002, it has been quietly transforming into a haven for early-stage biomedical start-ups. Two things happened that year; in February 2002, the Ohio Department of Development launched the Third Frontier Project, a 10-year initiative that will dispense \$1.6 billion in funding to programs that build up the commercial infrastructure to support Ohio's native research capabilities. \$800 million of that fund has been invested to date in distinctive translational capabilities around the state of Ohio with a heavy emphasis on biosciences, and within biosciences, the grants have been weighted to medical devices. The Third Frontier program has created several centers of excellence in some of the hottest emerging markets for medical devices, for example, neurostimulation, macular degeneration, and atrial fibrillation.

The same year saw the formation of **BioEnterprise Corp.**, an accelerator and partnership launched by the **Cleveland Clinic, Case Western Reserve University, University Hospitals,** and **Summa Health System** in Cleveland. These different constituencies got together, president and CEO Baiju Shah explains, because they wanted to collectively commit to

growing the bioscience economy and convert the IP resident in the research institutions into products that would have broader societal and financial benefits.

Beyond that common goal, each group had its own reasons. The university felt it would benefit from tech transfer opportunities. For the researchers and clinicians, getting IP out of the lab and into patients was a motive; the health systems felt that an entrepreneurial environment for physicians would be a competitive advantage in recruiting, as would the acclaim that would come with developing renowned medical technologies. Creating and attracting new business would also serve the goals of the regional economic development groups

In 2001 Shah was with consulting firm McKinsey & Co., which the clinical and research institutions engaged—on a pro bono basis—to identify ways to foster biomedical entrepreneurialism. Shah says, "As I looked around the country (and not necessarily just with respect to device-focused tech transfer) I saw only one model of start-up success in an environment that was like Cleveland that was responsible for a great deal of company formation around an institution. That was **Yale University's** Office of Cooperative Research in New Haven." Yale was BioEnterprise's inspiration, rather than MIT, Stanford University, Berkeley, or the University of California San Diego, because those institutions live in close proximity to rich venture capital communities. That's not the case

Exhibit 2

BioEnterprise Corp.

Industry Focus: Medical devices, biotechnology, and health care services

Academic Affiliations: Case Western Reserve University, Cleveland Clinic, Summa Health System, University Hospitals

Contact: Baiju Shah, President and CEO, telephone: (216) 658-3972; e-mail: bshah@bioenterprise.com

Mission: 1) Accelerating health care start-ups from entrepreneurs and institutions; 2) Promoting Cleveland's health care sector; 3) Regional development

Competitive Advantages: Cleveland Clinic, one of the largest and most prestigious health systems in the world; availability of early-stage funding: Ohio Third Frontier program, \$1.6 billion for translational research and development; local non-profit seed funds like JumpStart, Case Tech Ventures, Cleveland Clinic Innovations, numerous health care venture funds

Funding Sources: The partner institutions (Case Western et al., above); philanthropy from regional foundations, BioOhio, and state development funding

Incubator's Return on Investment: Funded by philanthropy, takes neither equity nor fee for services; incubator is a donor-funded service organization benefiting local constituencies in more or less intangible ways, for example, the state of Ohio achieves goal of economic development (creation of jobs, tax base, etc.); spin-outs enhance the reputation of research institutions (attracting grant money and top tier innovators)

Representative Company: Synapse Biomedical (www.synapsebiomedical.com)

Source: BioEnterprise Corp.

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for New Haven, to which, despite the relative lack of local venture capital, Yale spin-offs have attracted more than \$2 billion since 1996. “Research Triangle evolved over 40 years, and innovation in Minneapolis is an outgrowth of an entrepreneurial corporate community dating back to 3M,” says Shah. But the Yale model felt right for Cleveland. “Yale is a great institution, but in an environment that doesn’t have a great deal of existing industry, and it doesn’t have significant venture capital in its back yard either. Their model has made New Haven a health care hotspot in under a decade.” (Today, Connecticut does have its share of medical investors, for example, CHL Medical Partners, Foundation Medical Partners, Thomas, McNernery & Partners, and Canaan Partners.)

Yale’s approach is brilliantly simple, Shah says, yet very few incubators follow it. “Their model is to figure out what investors want to invest in and help them find it. That’s it. That’s what we do at BioEnterprise,” he says.

Shah says the team spends more than a third of its time, by sector (BioEnterprise works in devices, health care services, IT, and biotech) meeting with VCs. “We are always on planes, mostly to the East Coast and Silicon Valley, listening to what VCs want to invest in.” BioEnterprise then uses that intelligence to find suitable emerging opportunities from the Cleveland area institutions or in the regional entrepreneur community, and it provides the support

and connections to advance them to the point where those same investors are then interested in taking a serious look at them. “It sounds obvious, but it is the exact opposite of what most tech transfer offices and most regional accelerators do,” Shah says. Following this simple model from New Haven, “Cleveland has gone from ‘nowhere’ to one of the emerging hotspots in health care venturing,” he adds. Cleveland is now getting a level of health care venture investments equivalent to that of Minneapolis or Research Triangle; in the first half of 2007, the region’s companies have already attracted more than \$170 million. (See Exhibit 3.)

BioEnterprise is a not-for-profit. It is funded by its founding institutions, philanthropy from local foundations, and the state bio-science trade association. The accelerator also gets support from the state of Ohio. “We are in a partnership with these institutions; we do not take an equity stake or a separate payment for our services. We don’t charge anyone for what we do in any way, shape, or form” whether it comes out of the local institutions, regional entrepreneurs, or an overseas start-up that’s been recruited to the region, Shah asserts.

The incubator operates along three different models. It will support technologies that come out of the research institutions, the typical tech transfer type of situation where companies are built around in-licensed IP; from regional entrepreneurs; and it ac-

Exhibit 3

Selected BioEnterprise Medical Device Start-Ups

Company	Description/ Key Funders
Cardiovascular	
CardioInsight	Electrocardiac imaging technology developed at Case, non-invasively images electrical activity on the surface of the heart./Draper Triangle, JumpStart, Case
Icon Interventional	Novel stent developed by interventional cardiologist Jay Yadav, MD, formerly with the Cleveland Clinic./Angels
Interventional Imaging	Vascular imaging and the detection and treatment of vulnerable plaque, formed by Case Western Reserve University and technologies from the University Hospitals./Ohio Tech Angels, Case
Orthopedics	
OrthoHelix	Comprehensive set of instruments and implants for use in small bone reconstruction: foot, ankle, and hand surgeries./Mutual Capital Partners
SpineMatrix	Non-invasive device that identifies the origin of low back pain, determining whether the injury is to the spinal disc, the facet joint, or the surrounding musculature./Nationwide
OrthoMEMS	Wireless implantable pressure sensor to assess and treat orthopedic and spine conditions
NeuroStimulation	
Synapse Biomedical	Diaphragm pacing device restores normal breathing, eliminates dependence on ventilator in patients with spinal cord injury, trauma, or ALS./Palo Alto Investors, Case, JumpStart, Vivo Ventures
Intellect Medical	Portfolio of deep brain stimulation and gene therapy from Ali Rezai, MD, a functional neurosurgeon at the Cleveland Clinic./Wilson Greatbatch (via Biomec)
NDI Medical	Commercialization services to start-up neurostimulation companies and medical device companies pursuing the neurostimulation market
Undisclosed sleep apnea device company	Device that delivers selective nerve stimulation to maintain airway patency, from Case Western Reserve

SOURCE: BioEnterprise

tively recruits companies from overseas, particularly Israel, Russia, and soon Hungary, that want to move or co-locate to Cleveland.

BioEnterprise is focusing on these particular countries somewhat opportunistically because there happen to be large Israeli, Russian, and Hungarian communities in the Cleveland area. Surprisingly, Cleveland is home to the largest Hungarian community outside of Budapest, Shah says. There is business wisdom to this strategy, too; all of these countries are known for the high quality of their scientific and bioscience research. Hungary, for example, has a disproportionate share of Nobel Prize winners and was a designated bioscience industry center in the Soviet planned economy. The medical markets in these countries are relatively small, however, and their start-ups need to access the US market.

There are now six Israeli companies, two Russian start-ups, and one Japanese firm in BioEnterprise's portfolio. Israeli company **Simbionix Ltd.** has been particularly successful. It has developed the equivalent of flight simulators for endoscopic surgery, which look and feel just like a patient case. Surgeons use the technology to train on new techniques and tools. The Cleveland Clinic, a leading center for minimally invasive surgery, is the principal reason why Simbionix came to Ohio. Working alongside prominent clinicians would help the company expand surgical applications of its technology. The Clinic lent its support by investing in Simbionix and recruiting other investors as well, including local fund Early Stage Partners, which has continued to back the company. The company resides in the BioEnterprise incubator space, and since its arrival, it has expanded its line of products from laparoscopic simulators to GI, urological, and interventional cardiology simulators.

Simbionix has gone on to raise several rounds of funding, tapped into a number of loans and grants from the Third Frontier program, set up contract manufacturing in Cleveland with a medical device manufacturing company, and is in the midst of a significant venture round, Shah says. After the success of Simbionix and several other Israeli co-located companies, in 2005 BioEnterprise supported the launch of a \$10 million venture fund, the Bridge Investment Fund, specifically to support medical device companies from Israel that are willing to co-locate in Cleveland. Most Israeli companies migrate to the United States for clinical and market development.

Portfolio company **Synapse Biomedical Inc.** provides a case study of some of the benefits BioEnterprise can offer to spin-outs of Cleveland institutions. Founded in 2002 with a license to technology from Case Western and University Hospitals, Synapse developed *NeuRx*, a neurostimulation system for diaphragmatic pacing, targeting patients with a very high level spinal cord injury. The company was incubated with the assistance of Case Western's technology office, JumpStart, and BioEnterprise.

Synapse's device paces the diaphragm to help restore normal breathing and wean patients off ventilators. The company was funded primarily through grants until 2005, the year that neurostimulation technologies became hot in the wake of **St. Jude Medical Inc.**'s merger with **Advanced Neuromodulation Systems Inc.**, which followed **Boston Scientific Corp.**'s acquisition, the previous year, of **Advanced Bionics Corp.** At that point, local seed funds JumpStart, Case Western Reserve's Case Technology Ventures,

University Hospitals, Cleveland, Scitech of Columbus, local angel investors, and Palo Alto Venture put \$1.3 million into the start-up. JumpStart also provided the company with a professional CFO.

One of the initial patients to benefit from the Synapse system was the late Christopher Reeve, who also helped draw attention to the company. Meanwhile, the company assessed additional potential indications and the competitive landscape for therapies to expand their addressable market. BioEnterprise assisted the company with market research, health economic models, product development advice, and fund-raising support.

Synapse is now also targeting ALS patients and trauma victims who have become ventilator dependent. In 2006 and 2007 Synapse raised an additional \$5.5 million from Vivo Ventures and Palo Alto Investors to fund clinical trials and market development for its expanded indications.

When asked how BioEnterprise is able to blend the structure of a charitable organization with the goal of helping to develop early-stage start-ups into commercially successful, profitable companies, especially with all the experience and expertise that's needed, Shah says, "We've been blessed that the community has put enough resources behind us to hire a very professional team. Our annual budget is \$4.5 million per year, and that allows us to hire experienced and well-connected professionals." Mike Lang, BioEnterprise's VP of medical devices, is a veteran of five different medical start-ups in the cardiovascular and biomaterials sectors, and before that, he was involved with minimally invasive surgery in the early days of Ethicon Endo-Surgery. "We have been able to hire this type of individual because we have been given the resources to be able to afford it." Shah also says that BioEnterprise is backed up by the core technology transfer offices of the research institutions. "We're not dealing with one- or two-person operations or reformed lawyers. Our technology offices are staffed with individuals with significant business development and technical backgrounds, who can expertly review the invention disclosures and advise on the development of companies." Collectively, BioEnterprise and the partner technology offices have more than 40 professionals committed to developing new health care ventures, Shah says.

In April 2007 BioEnterprise announced that it would expand its capabilities by collaborating with the Pittsburgh Life Sciences Greenhouse in a cross-border co-development arrangement. "Cleveland and Pittsburgh are less than two hours apart, and in this little corridor we have \$1 billion of health care research, over 700 health care companies, and \$250 million of annual health care investment going on. This belt has a greater collection of health care assets and deals than most regions in the country."

Shah has statistics that reflect the early success of BioEnterprise. "When we started, the venture community did not recognize Cleveland as a health care start-up region. Since July 2002, we have supported more than 50 companies that have attracted \$515 million in new funding. Local technology offices have collected more than \$65 million in revenues, and more than 160 technology transfer deals have been completed with industry partners. This year, we've already had 16 venture financings totaling \$170 million in equity capital, and all but one have been led by funds from New York, Boston, and Silicon Valley."

Comments? Send an e-mail message to the author at mstuart@windhover.com