

# Cover: Taking the Pulse of the Stent Market

*Investment Dealers' Digest*

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*October 16, 2006*

As any healthcare watcher knows, after a contentious, months-long bidding war, Boston Scientific swooped in this January and snared Guidant for \$27.2 billion, winning the deal from industry rival Johnson & Johnson. However, when the company secured that deal, it certainly didn't foresee that just nine months later it would have to warn of lackluster demand globally in the coronary drug-coated stent market, citing US market retrenchment in particular. But on Sept. 21, the company did just that, saying it expects worldwide sales of its drug-eluting stent to come in between \$550 million and \$580 million in its third quarter, which it will report Wednesday, Oct. 18. That represents nearly a 10% drop in drug-coated stent revenue versus a year ago.

Boston Scientific's drug-eluting stent, Taxus, is one of only two such devices on the US market, the other being J&J's Cypher. The company remains adamant that its US market share in drug-coated stents is "stable," but keeping that position will only be more difficult over the coming months and years, as the battle for market share is being waged on three fronts by the leaders, start-ups and emerging independents.

## Next Generation Stents

Although the big boys currently own the drug-eluting stent market in the US, with Boston Scientific holding a slight edge at 55%, it is the start-ups that often define the next generation of medical device technology. The stronger players are often snapped up by the larger players, and of course, given their prominence in financing circles, private equity firms are active in the early-stage stent market, placing bets on their favorites.

"Clearly, there is a need for better drug-eluting stents. That's where we would invest, into companies with superior products," says Stephen Shapiro, a special venture partner with private equity shop Galen Associates and venture capital firm Advanced Technology Ventures (ATV).

One prominent early-stage company is Biosensors International Group, which reported \$8 million in sales in its most recent fiscal quarter. Biosensors, which has no venture affiliations, is developing what it believes will be the next generation of stent technology. Its stent, BioMatrix, uses a proprietary biodegradable polymer that does not remain in the body after the drug is eluted, so ultimately a bare metal stent remains. Biosensors has also developed its own antirestenotic drug, dubbed Biolimus A9 and designed to prevent renarrowing of the arteries, to be used in conjunction with the stent, and it has its own stent delivery platform technology.

By developing the entire stent-delivery package, Biosensors is able to diversify its revenue stream with upfront licensing fees for its drug and its biodegradable polymer. "We have received north of \$80 million combined from all of our partners," Yoh-Chie Lu, CEO of Biosensors, tells *IDD*.

Lu's company has an exclusive partnership with Terumo in Japan through which it agrees not to license its products to anybody else in that region. It has not, however, opted to take that route in the US, where the opportunity is just too large to pursue with one partner. Biosensors is in the midst of a breach-of-contract lawsuit with Guidant, which once had exclusive rights to Biosensors' biodegradable polymer.

The product will debut in the European market, and Biosensors' management is anxiously awaiting CE Mark approval, the equivalent to FDA approval in the US. "We don't have 100% control over [the product] when we get it, but we think it will be soon," says Lu. Once the European regulatory hurdles are cleared, he plans to target Euro-Asian countries where his company can achieve quick approvals from local authorities. "The growth for drug-eluting stents in India is much faster than once imagined," Lu adds.

And all this while Lu keeps his sights set on the alluring US market. In an effort to make its US splash known, Biosensors has teamed up with two venture-backed specialty platform developers in the US: Xtent, a Menlo Park, Calif.-based stent manufacturer that recently filed for an IPO (its shares are expected to begin trading in November), and Irvine, Calif.-based Devax, which is also planning its public-market debut, says an analyst.

"In terms of market size and usage, the US represents the largest market, and we will have to find a way to enter into it," Lu says. "The company expects to begin human trials for its biodegradable polymer stateside in coming months."

Biosensors is listed on the Singapore Exchange but not yet in the US. With no debt on the company's balance sheet, Lu is weighing the best approach to the US equity market and has been approached by intrigued domestic bulge-bracket firms. "We've not entered into anything official," he says. "We are talking to a lot of bankers and trying to decide the best course of action for us."

"Clearly, there is going to be a struggle for market share with new products coming to market," says Robert Andrews, director of healthcare banking at Houlihan Lokey. "That's a testimony to the size of this market. These are expensive, large clinical trials, and you don't spend that kind of money and take that kind of time for small markets."

Although the timing of Biosensors' US debut may be unclear, it's facing competition from others that already have a foothold in the US drug-eluting stent market. Like Biosensors, Conor MedSystems, a publicly traded company with a \$900 million market cap, is developing its own biodegradable polymer for drug-coated stent delivery, analysts say. The company, which has a drug-eluting stent in the European market, is on the radar of the industry giants as a takeover candidate, according to those same analysts.

#### Troubles for Current Products

The promise of the new products can't be discussed without acknowledging that the market has its share of problems. Most recently, Boston Scientific's Taxus has been linked to late stent thrombosis, a blood clot that can cause a potentially fatal heart attack.

Theories differ about the cause. One is that the layer of polymer attached to the metal that remains in the body may cause the clot. The US Food & Drug Administration is in the process of defining the risks tied to coated stents in light of the Taxus scare. This has called into question the efficacy of drug eluting stents over bare metal stents, the first generation of this technology.

Despite the Taxus setback, however, the worldwide opportunity in stents is forecast to widen to some \$6.3 billion annually by 2010 from \$5.6 billion today. This has created an atmosphere conducive to M&A and new offerings in a crowded market with a string of new products in various stages of clinical trials coming down the pike.

"Investment bankers are seeing a mixture of capital raising and M&A," says Holly Sheffield, an investment banker at Credit Suisse. "Large companies have the economic muscle to afford multiple shots on goal. Earlier stage companies have the option of remaining independent, or monetizing in a sale to a larger company."

And despite the controversy surrounding coated stents, market players have no intention of abandoning these devices, and they continue to invest heavily in R&D and clinical trials. "The market is not going back to bare metal stents, and anyone who says otherwise is kidding himself," says Gary Shaffer, a partner in the life sciences and components teams at Morgenthaler Ventures.

However, despite the vigorous efforts of medical device makers, not every new product sees the light of day. Abbott Labs, which paid \$4.1 billion for Guidant's vascular business earlier this year (a deal necessary to win regulatory approval for Boston Scientific's purchase of Guidant), put the brakes on one of its coated stents only weeks ago.

Abbott stopped clinical trials for ZoMaxx, its drug-eluting coronary stent system, in order to focus its development effort on Xience V, the drug-eluting stent it picked up in the Guidant deal. Xience V was launched in most European countries on Oct. 3, and Abbott hopes to introduce Xience V to the US market in the first half of 2008.

"Once they get their drug-eluting stent approved in the US, I think they will be viewed as a significant player," says Keay Nakae, an analyst at CE Unterberg, Towbin.

Also, through the acquisition of the Guidant division, Abbott assumed development of a biodegradable stent, which would permit the drug, polymer and actual device to break down in the body. Abbott is in the midst of a clinical trial called Absorb that will enroll up to 60 patients in Belgium, Denmark, France, New Zealand, Poland and the Netherlands.

#### Early Bird Investors

Biosensors' VC-free development process is an anomaly. Several stent start-ups rely on early-stage capital to fund their R&D process, which includes capital-intensive clinical trials. However, while the opportunity in the stent market is appealing to some, it carries just too much risk for others to stomach.

"We don't invest in the pre-revenue-stage stent market," says David Jahns, a managing director at Galen, a firm devoted to healthcare. "It's a risky market, and there are lots of competitors. The actual time to realization on a regulatory approval process is risky and time consuming."

Les Funtleyder, a healthcare strategist at Miller Tabak, an institutional trading firm, has similarly avoided this segment to date, but may change his tune come the next generation of drug-eluting stents. "Biodegradable stents might be the Holy Grail in the stent market," he says. "But there are some engineering challenges."

Shapiro, on the other hand, is not convinced that the next wave of stent technology will favor biodegradable polymers. "I'm not convinced the next generation is biodegradable stents," he says. "I'd say it presents an interesting opportunity and has theoretical potential to address the needs of a large market."

ATV, the VC shop in which Shapiro is a partner, is among the investors in Xtent, a stent maker (and Biosensors partner) that has raised \$76 million in venture funding. Lead underwriters on the Xtent IPO include Piper Jaffray, Cowen and Co., Lazard Capital Markets and RBC Capital Markets. Morgenthaler has been investing in the stent market for the past four years and is Xtent's majority shareholder.

"Building significantly better mousetraps for the major stent makers - that's our business," says Morgenthaler's Shaffer. "Companies like this are of interest to both corporations and the public market because historically there has been considerable room for innovation." Xtent's claim to fame is its size-adjustable stent, which allows cardiologists to customize the stent to the diseased sections of the artery, or lesions.

Morgenthaler is also backing CardioMind, another California-based stent developer that is considering an IPO. The VC shop was co-lead investor alongside Latterell Venture Partners in the first two rounds, and CardioMind plans to raise its third round of venture capital next year.

CardioMind has developed a promising stent delivery system that eliminates an entire layer of the stent system - the catheter. The stent is minuscule - the size of the guide wire - and therefore no balloon catheter is needed. "The million-dollar opportunity is in the delivery system," says Shaffer. "With positive human clinical data, there will be strong corporate interest." CardioMind is targeting the European market first, where regulatory approval is much faster, and expects to market its stent in the next year. Then management will focus on FDA approval in the US.

"The next wave of IPOs specifically in this category will be focused on third-generation stents and beyond," says Credit Suisse's Sheffield.

#### Looking Ahead

Next week, top cardiologists from around the globe, along with top corporate players and bankers, will be gathering at the year's most important meeting for interventional cardiology when the Cardiovascular Research Foundation hosts its annual Transcatheter Cardiovascular Therapeutics (TCT) convention in Washington DC.

One of the highlights of the symposium will be a roundtable discussion devoted to the topic of late-stent thrombosis. That discussion will include interventional cardiologists and FDA panel members, including

Kenneth Cavanaugh. Investors and analysts expected to attend include Steve Shapiro and Credit Suisse's Sheffield.

Also, the FDA has convened a formal panel to define the proper use of drug-eluting stents in response to the Boston controversy, a pathway that could very well dictate the directions that the next generation of stent technology takes. And whether the softening in the coronary stent market that Boston Scientific is experiencing evolves into a trend will also become clearer in coming months.

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