

Above: Thoratec's HeartMate VE LVAD is implanted into the abdomen to assist left ventricular function, pumping blood around the body.

# HeartMate<sup>®</sup> opens new market for THORATEC



Finding innovative alternatives to heart transplant is keeping Thoratec ahead of the competition, notes its president and CEO **Keith Grossman**.



Late-stage congestive heart failure is incurable and deadly, unless the patient gets a heart transplant or some mechanical assistance. The latter is provided by a ventricular assist device (VAD), an artificial pump which takes over some or all of the functions of the patient's ailing heart.

**Thoratec** (NASDAQ: THOR) is the world's leading VAD manufacturer with nearly 60 percent of the \$150 million market, says Merrill Lynch. Its main products are the HeartMate VE, which is implanted into the abdomen and assists

# Angiomax simplifies coronary PROCEDURES



A fast-acting and predictable anti-coagulant is opening new markets for The Medicines Company, says its CEO **David Stack**. Nick Cottam reports.



THE **MEDICINES** COMPANY

Treating patients with blocked arteries can be a safer, more predictable procedure using the anti-coagulant Angiomax. What's more Angiomax, which lowers the risk of blood clots during treatment, could have a range of other cardiovascular applications, according to **The Medicines Company** (NASDAQ: MDCO), which is marketing the drug, approved for use in 2000 and launched in 2001, to medical practitioners in the U.S and has licensed it to 5 partners in 63 countries.

"We believe that Angiomax is a \$500 million revenue opportunity in the U.S. alone. Our priority for 2003 is getting the drug on a \$10 million-a-month trajectory," says company CEO David Stack, who noted that in the fourth quarter of 2002, ending 31 December, the number of hospitals purchasing Angiomax increased by more than 20 percent since the results of a ground-breaking clinical trial (REPLACE-2) announced in November.

That means life on the road for Stack and his colleagues as they seek to engage the nation's top interventional cardiologists and demonstrate the added value of Angiomax over heparin, a bi-product

from boiling pigs' intestines, which was previously the only anti-coagulant of its kind on the market. "Heparin," says Stack, "is a pretty nasty drug. It's been around since the 1930s, but because it's a natural product and it's heterogeneous, you don't really know how much anti-coagulant you are giving. Only 30-35 percent of the product is pharmacologically active - the rest is pig junk."

In contrast, Angiomax, which works by directly inhibiting thrombin, a key substance involved in the formation of bloodclots, is synthetic, fast-acting and entirely predictable, he says. "It does the same thing every time you inject it. The data from the REPLACE-2 trial shows the average time a patient needs to be on Angiomax is 44 minutes, while for heparin, with the antiplatelet drugs that need to be used with it, it's 12-18 hours." The result, he suggests, will be more outpatient treatments and significantly reduced bleeding related to angioplasty, which costs \$8,000 to \$10,000 and results in patients staying in hospital for an additional two days.

To prove the point, MDCO has run an extensive program of clinical trials since

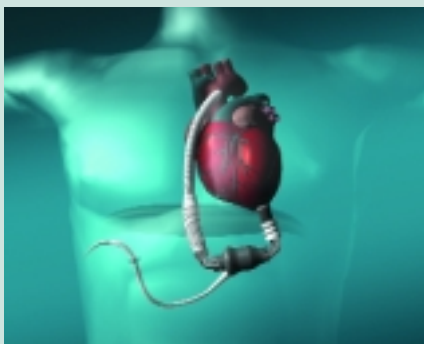
On average every 45 seconds, someone in the U.S. has a stroke, says the American Heart Association, which

or replaces the left ventricle (which pumps blood around body); and the Thoratec VAD, an external device which supports one or both ventricles.

Hitherto, both have been used as a 'bridge to transplant' (keeping patients alive until transplant) – a small market, with around 4,000 U.S. patients a year. Last November, the HeartMate VE was the first VAD to be approved in the U.S. for 'destination therapy'. Covering patients who are ineligible for transplant, this market uses the device semi-permanently – in the U.S., Thoratec estimates there are more than 100,000 patients. In trials, half of patients with a HeartMate survived at least a year, compared with a quarter of those without.

VADs cost around \$60,000 each. With total treatment at around \$140,000, says Thoratec, this compares well to a transplant, which is around \$200,000. A few American health insurers began funding the HeartMate for destination therapy straightaway, but most will wait until funding is approved by Medicare.

Current-generation VADs are suitable only for a small population of patients. But with new developments, Thoratec predicts its VADs could be treating between 5 and 15 percent of candidates by 2007, earning the company between \$350 million and \$1.1 billion. "The opportunities for growth are pretty remarkable," president and CEO Keith



HeartMate II: This next-generation VAD uses a small rotor-based impeller instead of a pump.

Grossman says. "The breakthrough years will probably be 2004-05, once the funding issue is sorted out." Merrill Lynch predicts a compound annual growth rate of 22 percent in the global VAD market over the next several years.

New developments are underway too. The HeartMate II uses a small rotor-based impeller instead of a conventional pump, making it a quarter of the size and promising greater durability. Thoratec hopes for approval in Europe early next year and in the U.S. by early 2005. Using a motor suspended in a magnetic field, the HeartMate III is currently in animal trials. With no bearings, Grossman notes it could last almost indefinitely.

Since merging in 2001 with rival VAD-maker Thermo Cardiosystems, Thoratec's competitors have been one-product

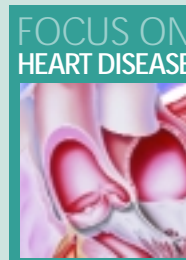
companies – of the four VADs approved in the U.S., three are Thoratec's. "You'll probably need different kinds of pump for different kinds of patients, so the breadth of our range is a key differentiator," says Grossman. "We have more than 70 R&D engineers and a unique expertise in late-stage heart failure that few other companies have."

Around two-thirds of Thoratec's \$130.8 million 2002 revenues came from VADs. Most of the rest came from hand-held coagulation diagnostic devices – not as spectacular a market as VADs, but a highly profitable one in which sales grew 10-12 percent last year. In addition, the company has promising niche products.

For example, the Vectra is a 'vascular access graft' (somewhere to plug in the tube during dialysis), which can be operational within 24 hours of implantation (compared with a month for rival products). Vectra sales doubled in 2002, and Thoratec now claims 10-15 percent of the \$120 million worldwide market.

Although the company recently hired a vice president to look for opportunities outside its core areas, and would consider acquisitions and investing in start-ups, Grossman is clear about the company's direction. "Our number one priority," he insists, "is not to lose our leadership position in VADs." ■

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purchasing the drug from **Biogen** (NASDAQ: BGEN) in 1997 and is predicting sales of between \$70 million and \$90 million for 2003. "The estimate is very wide but this is because our REPLACE-2 angioplasty clinical trial is so recent and we're still working our way through the data," notes Stack. "We've seen a dramatic uptake in the marketplace, with sales doubling between last September and this January."

MDCO plans to submit the REPLACE-2 results to the FDA, so that contemporary

REPLACE-2 data can be included in the Angiomax package insert. MDCO and its European partner, Nycomed, will submit REPLACE-2 data as the basis of approval to market Angiomax in Europe.

In the meantime, the trials and cardiologist networking goes on. "It's amazing the intensity you can bring to a program if you have one drug. At the moment, we don't worry about anything else but selling Angiomax and improving patient care by replacing heparin." The company is beginning another major trial, this time with 14,000 patients, to look at how Angiomax can be used on patients presenting to the emergency department with chest pain.

According to the company, which achieved revenues of \$38.3 million in 2002 (compared to \$14.2 million the year before), more than 12 million patients received therapeutic doses of heparin in 2001, 8.5 million of them for some kind of acute arterial indication. "These are patients who are going to have by-pass surgery, or valve replacement or a pacemaker inserted," explains Stack.

While Angiomax is MDCO's only drug on the market – a second, clevidipine, for

## The Medicines Company Healthcare

controlling hyper-tension during cardiac surgery is entering Phase 3 trials – Stack believes the company is well placed to demonstrate its benefits and boost sales in the short term. "REPLACE-2 involved more than 6,000 patients and was the largest Cath Lab trial of its type ever successfully completed. We have been able to show a statistically significant advantage in controlling bleeding and thrombocytopenia, two safety issues for patients and clinicians," he adds.

The wider brief for the Parsippany, New Jersey-based company, says Stack, is to pick up other late-stage development products in the acute care space. "It revolves around serving high-end customers [for example, interventional cardiologists] who think about how they treat patients, not what category the product is in. We are in the right place at the right time and we are looking at several product opportunities." ■

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