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2006 Medical Innovation Summit

Clinic unveils 'Top Ten' list of medical innovations for 2007

By HOLLAND JOHNSON
***Medical Device Daily* Associate Managing Editor**

CLEVELAND — As an interesting addition this year to its Innovation Summit, the Cleveland Clinic unveiled the first of what promises to be an annual "Top Ten" list of what it predicts as the most promising medical innovations in the coming year.

The 2007 list — which includes therapies for cancer, asthma, heart failure, age-related macular degeneration and vascular disease, including several medical devices — was complied by a panel of clinicians from the clinic who whittled the list from about 100 products to the final 10.

"The top 10 list is the result of a survey of dozens of Cleveland Clinic thought leaders offered to promote widespread discussion on innovation and new technol-

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Dealing with CMS

Reimbursement hurdles seen as benefit as well as barrier

By MARK McCARTY
***Medical Device Daily* Washington Editor**

WASHINGTON — The first day of the reimbursement conference hosted here by the **Medical Device Manufacturers Association** (MDMA; Washington) focused largely on the economic headaches of pulling in early funding and getting the **Centers for Medicare & Medicaid Services** (CMS) to cough up for new technology.

While the industry sees these considerations as major barriers, one speaker observed that a full set of clinical trials — even when a device seems substantially equivalent to an existing device or technology — may be the key to profitability rather than a case study of financial waste in a demand economy.

Maren Anderson, president of **MDA Consulting** (West Newton, Massachusetts), gave attendees an overview of

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Report from Europe

Angiotech's Vascular Wrap trial finds amputation reductions

A *Medical Device Daily* Staff Report

Angiotech Pharmaceuticals (Vancouver, British Columbia), a pharmaceutical and medical device company, reported results from its European first-in-man study for its Vascular Wrap paclitaxel-eluting product, saying the trial "produced evidence" that the Vascular Wrap reduced the overall incidence of leg amputation and prolonged limb retention time for patients in the treatment arm relative to the control group.

It said that for the patients that underwent an amputation during the study period, the mean interval to amputation for patients treated with the Vascular Wrap was 156 days — more than double the mean interval to amputation for the control, which was 76 days.

William Hunter, MD, president/CEO of Angiotech, said, "We believe this is an important step forward in improving the quality of life of patients suffering from end-stage peripheral arterial disease. It appears from this trial that

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Transcend, out of ForSight Labs, gathers in Series A $7 million

By AMANDA PEDERSEN
***Medical Device Daily* Staff Writer**

Transcend Medical (Menlo Park, California), the first company incubated by **ForSight Labs** (Menlo Park, California), has received $7 million in Series A funding from investors, including venture capital firms Morgenthaler Ventures and Split Rock Partners.

ForSight Labs was created late last year with $2.4 million of seed money to incubate new ophthalmic device companies in partnership with **The Foundry** (Menlo Park, California). Morgenthaler Ventures and Split Rock participated in that investment too, along with Versant Ventures (*Medical Device Daily*, Jan. 9, 2006).

The $7 million round will allow Transcend to move forward in the development of an anti-glaucoma device, the leading cause of adult blindness in the U.S., the company said.

"It will allow us to continue on the clinical path and expand the clinical studies internationally and in the U.S.,"

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INSIDE:

AHC Media LLC

Court report

EP MedSystems could pay up to $288,000 in two settlements

A *Medical Device Daily* Staff Report

EP MedSystems (West Berlin, New Jersey) reported executing a settlement with the Bureau of Industry and Security of the **U.S. Department of Commerce** to close issues related to its shipment of products to restricted countries in 2004 and earlier.

The company does not admit or deny guilt, but agrees to pay a fine of $244,000 with no restrictions on commercial or export activities. The company said it has accrued $345,000 for this penalty in its books as of June 30.

The company also said that it has made a settlement offer to the **U.S. Department of the Treasury** in connection with an investigation of these shipments and is awaiting a response. It said the Treasury Department has indicated to it "orally" that the maximum penalty it might seek would be $44,000.

Given that any investigations by the Treasury Department or the **Securities and Exchange Commission** have not been closed, the company said it could not rule out additional civil or administrative penalties. But it said it has made no provision for any future costs associated with these investigations or any costs associated with the "defense or negotiations" to resolve any outstanding issues.

David Bruce, new president/CEO of EP MedSystems, said, "We continue to cooperate with the other governmental entities in hopes that we can close any remaining issues as quickly as possible. "

EP MedSystems develops cardiac electrophysiology (EP) products used to diagnose and treat certain cardiac rhythm disorders.

In other legalities:

• **IntraLase** (Irvine, California), reported filing a lawsuit in the Superior Court for the State of California, County of Orange, against **Carl Zeiss** (Oberkochen, Germany), its subsidiary **Carl Zeiss Meditec** (Dublin, California/Jena, Germany) and certain affiliates.

The lawsuit alleges that Zeiss breached an intellectual property agreement with IntraLase by improperly using proprietary information of IntraLase which Zeiss wrongfully induced IntraLase to disclose. The suit seeks damages for breach of contract and payment to IntraLase of all revenues and profits derived by Zeiss from the sale and use of its laser.

Robert Palmisano, president/CEO of IntraLase, said, "We believe the marketplace rather than the courthouse is the appropriate arena for honest and spirited competition. However, we have a duty to protect our intellectual capital and feel we have no alternative but to take the necessary legal action to protect our interests and ensure that any competition we face is fair competition."

Palmisano added: "The IntraLase FS laser has already been used for approximately one million corneal flap procedures, the first step to LASIK surgery, resulting in superior safety and clinical outcomes. We remain confident that our advanced technology will continue to be the technology of choice for corneal surgeons worldwide."

IntraLase manufactures what it calls "an ultra-fast laser that is revolutionizing refractive and corneal surgery by creating safe and more precise corneal incisions."

• **RehabCare Group** (St. Louis) reported that it has been notified by the Office of Inspector General (OIG) of the **Department of Health and Human Services** that the agency has closed, "without action," its investigation of the company's contract therapy (CT) business in New Jersey.

In April 2005, the OIG issued a subpoena requesting materials related to the company's CT operations in that state. RehabCare said it received notice earlier this week that the OIG has closed its investigation and will not be taking further action in connection with the subpoena.

RehabCare provides rehabilitation program management services in partnership with more than 1,400 hospitals and skilled nursing facilities in 42 states, the District of Columbia and Puerto Rico. The company also operates freestanding rehabilitation hospitals and long-term acute care hospitals. ■

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ASTRO 2006 notebook

Calypso rolls out 4D localization system, reports collaborations

By KAREN YOUNG
***Medical Device Daily* Staff Writer**

Calypso Medical (Seattle) launched its Calypso 4D Localization System at the 48th annual meeting of the **American Society for Therapeutic Radiology and Oncology** (ASTRO; Fairfax, Virginia) that ended yesterday in Philadelphia.

Calypso received FDA 510(k) clearance for the system in July for use with imaging systems for the prostate, which is subject to movement during imaging. The Calypso system uses electromagnetic technology in conjunction with implanted Beacon Electromagnetic Transponders designed to provide "objective, accurate and continuous tumor location information during external beam radiation therapy."

Eric Meier, president/CEO of Calypso, told *Medical Device Daily* that the system is the only one of its kind to pinpoint target location during imaging that is non-ionizing, or in other words, not releasing radiation.

The systems' transponders — smaller than a grain of rice — are placed "in proximity to the tumor," Meier said. When the transponders are coupled with the localization system, they send out "objective location instructions" to the radiation therapist "to register the patient's treatment target to isocenter prior to treatment."

The problem is that, due to respiration and other body movements and functions, organs move during radiation therapy. Thus, Calypso's system is designed to help radiation therapists make appropriate adjustments during treatment.

The system was evaluated in patients undergoing prostate radiation treatment between 2003 and 2006 at leading cancer centers. In those studies, investigators documented clinically-relevant prostate motion present in the majority of patients.

The prostate motion was unpredictable and variable, patient to patient, and throughout the course of treatment. But by using the guidance from the Calypso system, clinicians responded to out-of-threshold conditions in real-time, to manage organ motion with individual protocols.

Calypso also reported two "product collaborations," one with the Radiology Oncology Systems unit of **Philips** (Andover, Massachusetts), another with **IMPAC Medical Systems** (Mountain View, California).

"Integrating continuous, real-time monitoring data with Philips' treatment planning software system builds on our collaboration agreement to co-develop product offering that advance planning and treatment delivery techniques," Meier said. "Plans are under way to bring truly adaptive radiation therapy techniques to the clinical community through our collaboration."

With the collaboration, the Radiation Oncology Systems business of Philips expects to provide enhancements to its treatment planning systems with target localization data from the Calypso 4D Localization System.

Meier said Calypso's system and collaboration with others provides the "'missing' link to advance radiation treatment options with continuous target tracking."

"Today's highly conformal radiation therapy treatment options relay on knowing the exact location of the target moment to moment," Meier said.

Meier said that he expects the collaborations to bear results for the next "product introductions."

Meier also told *MDD* that the company is investigating uses of its system in other "soft tissues."

In other news from ASTRO:

• **Varian Medical Systems** (Palo Alto, California) held a symposium, attended by more than 900 radiation oncology professionals, on the use of new image-guided radiotherapy techniques to improve the effectiveness of cancer care.

Billy Loo Jr., MD, PhD, of **Stanford University** (Palo Alto, California), focused on strategies for improving the precision of treatments for lung cancer and other thoracic tumors by tracking and compensating for respiratory motion.

Loo's team uses image sequences that show the extent of tumor motion to plan more precise treatments. The technique enables him to escalate the dose delivered to the tumor while preserving the surrounding healthy tissues.

Karin Haustermans, MD, PhD, of the Department of Radiation Oncology at **UZ Gasthuisberg** (Leuven, Belgium), discussed ways of using functional imaging — namely, PET-CT and MRI — to detect radiation-resistant regions in rectal cancer in order to target them with higher radiation doses using image-guided treatment delivery techniques.

"Most relapses in high-risk rectal cancer patients occur in areas that were already treated with radiation," Haustermans said. "The aim of our study was to develop methods of detecting the radiation resistant regions in tumors and target them more aggressively."

Haustermans described how tumors changed over time during a course of treatment — both in size, shape and metabolic activity. Her team is now comparing different treatment approaches using this information to improve dose distribution and treatment effectiveness.

Alan Pollack, MD, PhD, chairman of the Radiation Oncology Department at **Fox Chase Cancer Center** (Philadelphia), is leading a clinical study on strategies for shortening the duration of a course of radiotherapy treatment for prostate cancer, normally taking up to eight weeks. His approach involves delivering higher doses with greater precision over fewer treatment sessions, as compared with more conventional treatment approaches.

"Giving higher doses per treatment session has potential advantages, but requires very precise targeting of the prostate to avoid the surrounding normal tissues. We are using 3-D imaging daily before each treatment, which allows for reduced exposure of the bladder and rectum to high radiation doses while ensuring that radiation delivery to the prostate and the potential for tumor eradication are optimized," Pollack said. ■

Deals roundup

Thermo Fisher Scientific formed with close of major merger

A *Medical Device Daily* Staff Report

Thermo Electron (Waltham, Massachusetts) and **Fisher Scientific International** (Hampton, New Hampshire) yesterday reported completion of their merger to create Thermo Fisher Scientific, saying the combination now creates a "world leader in serving science."

The companies combined in a tax-free, stock-for-stock transaction following anti-trust clearance received from the European Commission early Thursday. The new company, to be headquartered in Waltham, has about $9 billion in revenues and 30,000 employees.

"This is a historic day for both companies, as two industry leaders join forces to create Thermo Fisher Scientific," said Marijn Dekkers, president/CEO of Thermo Fisher Scientific. "The new company combines Thermo's industry-leading analytical instrumentation with Fisher's world-renowned laboratory reagents and consumables. As a result, we can deliver advanced technological solutions and integrated workflows to help our customers push the boundaries of scientific discovery, with increased efficiency. In addition, we have unprecedented access to our customers across the globe through the largest sales force in the industry, and through our catalog and e-commerce channels."

Fisher shareholders received 2 shares of Thermo common stock for each share of their Fisher common stock. Thermo's shareholders own about 39% of the combined company, and Fisher shareholders own about 61%.

"With this transaction, we have created the world's only provider of fully integrated, end-to-end solutions in the life, laboratory and health sciences industry," said Paul Meister, chairman of Thermo Fisher Scientific and previously vice chairman of Fisher Scientific.

Thermo Fisher Scientific said it will provide more details about the company, including an update to its 2007 guidance, at an Analyst Day in New York Dec. 14.

The company will trade on the New York Stock Exchange under the symbol TMO.

Thermo Fisher Scientific says it now serves more than 350,000 customers within pharmaceutical and biotech companies, hospitals and clinical diagnostic labs, universities, research institutions and government agencies, as well as environmental and industrial process control settings.

In other dealmaking activity:

• A subsidiary of **LifeCare Holdings** (Plano, Texas) has entered into a master lease line of credit and master lease agreement with **Health Care REIT** (Toledo, Ohio) to provide LifeCare with up to $250 million in capital to acquire and develop long term acute care hospitals (LTACH).

Health Care REIT will purchase designated properties and will provide capital to build hospitals to be leased to LifeCare for a 15-year term.

LifeCare's first project using the line of credit is a 60,000-square foot *de novo* facility to be located in Meridian, Idaho, near Boise.

Health Care REIT also recently completed the purchase of a 6.7-acre parcel of land in Meridian on which a 60-bed, long-term acute care hospital will be constructed and leased to LifeCare. The hospital is expected to be completed in early 2008 and will be designed and constructed specifically for a medically complex patient base, the company said.

"Health Care REIT is a significant force in healthcare real estate financing, " said CEO and Chairman W. Earl Reed, III. "This agreement will advance our efforts to develop hospitals in under-served markets to meet the needs of patients who can benefit from our long term acute care hospital services."

LifeCare operates 19 long-term acute care hospitals in nine states. Long-term acute care hospitals specialize in the treatment of medically complex patients who require intensive hospital care for an extended period of time, generally more than 25 days.

• **Amicus Hyperbaric Group** (Lubbock, Texas) reported acquiring **Southcoast Hyperbarics and Wound Care Center** (Houston). Amicus said that the Southcoast Center will provide hyperbaric services to Texas Specialty Hospital under an exclusive long-term contract.

Don Sprague, MD, formerly medical director at the **Johnson Space Center**, will serve as medical director of the Southcoast Center, and Jay Rain, formerly clinical research specialist with Surgical and Infectious Disease and Hyperbaric/Woundcare Medical Team at **UTMB-Galveston** will serve as chief technologist.

"Acquisition of the Southcoast center is a first step in our multi-phase plan to provide the Greater Houston Metropolitan Area with quality hyperbaric and wound care services," said Jim Bullard, Amicus' president.

Amicus said the acquisition is part of its plan to establish hyperbaric centers throughout the southwestern U.S. to provide treatment for diabetic or geriatric wounds.

Hyperbaric therapy is a Medicare-approved therapy to treat wounds in diabetic and other patients. The majority of hyperbaric services target the treatment of diabetic foot wounds or wounds indirectly related to diabetes.

Amicus Hyperbaric Group was founded in 2003 to provide hyperbaric services to hospitals throughout the U.S. and it says it is one of the largest providers of hyperbaric therapy services in Texas, with operations in Amarillo, Abilene, Houston, Lubbock, McAllen (two hospitals), Fort Worth, Floresville (a suburb of San Antonio) and Odessa

• **Chemed** (Cincinnati) reported that its **Vitas Healthcare** subsidiary has finalized the sale of its hospice program in Phoenix, Arizona. Terms of the transaction were not disclosed.

Chemed operates two subsidiaries: Vitas Healthcare and Roto-Rooter. It says that Vitas is the nation's largest provider of end-of-life hospice care. ■

Grants/contracts

Cleveland BioLabs reports negotiations with threat agency

A *Medical Device Daily* Staff Report

Cleveland BioLabs (Cleveland) said it has entered contract negotiations with the Defense Threat Reduction Agency (DTRA) of the **Department of Defense** (DoD). Cleveland BioLabs submitted a proposal for a collaborative project with the **Armed Forces Radiobiology Research Institute** (Bethesda, Maryland) to complete development of radiation protectors in response to the Radiological Countermeasures research area. The company said it has been identified as an "apparent successful offeror" by the DTRA and negotiations are in progress, according to the company.

"Our participation in this program would be a significant milestone for the company," said Michael Fonstein, PhD, president/CEO. "A contract resulting from this program would support further development of our line of radioprotectant drugs, as well as establish a path for procurement with the DoD."

Protectan CBLB502, the company's lead radioprotectant molecule, has demonstrated its efficacy in a recent study when it rescued more than 70% of lethally irradiated primates and substantially delayed death for those that died. CBLB502 is undergoing an accelerated development program under the FDA two-animal rule, which requires the company to show efficacy in two animal species (including primates) and only safety in humans.

Cleveland BioLabs says it is "leveraging" its discoveries about programmed cell death to treat cancer and protect normal tissues from exposure to radiation and other stresses.

In other grant news:

• **The Minneapolis Heart Institute Foundation** at **Abbott Northwestern Hospital** (Minneapolis) has partnered with three Minnesota healthcare providers to create the Minnesota Cardiovascular Cell Therapy Clinical Research Network (MnCTN), which recently received a $1.5 million grant from the **National Institute of Health** to research stem cell treatments for heart disease.

In addition to the Minneapolis Heart Institute Foundation at Abbott Northwestern Hospital, MnCTN comprises the **University of Minnesota** Division of Cardiology, the **Center for Cardiovascular Repair**, and the **Molecular and Cellular Therapeutics** lab; **Hennepin County Medical Center**; and the **Veterans Administration Medical Center**.

MnCTN is one of five organizations across the country selected to receive the grant and participate in the MnCT-Network, created to facilitate clinical trials to examine the success of new cell therapies for the treatment of heart conditions including heart attacks and heart failure.

Specific areas of research the MnCTN has proposed examining include using bone marrow-derived stem cells to initiate cardiac repair following a heart attack and using patients' own stem cells to treat heart failure. ■

Innovations

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ogy," said Chris Coburn, executive director of CCF Innovations, the clinic's technology commercialization arm.

Four major criteria had to be met in order for a technology to qualify. To receive consideration, a product had to have significant potential for short-term clinical impact; a high probability of success; be on the market or close to introduction; and sufficient supporting data.

Marc Penn, MD, PhD, chair of the clinic's **Bakken Heart Brain Institute**, chaired the project and moderated the eight-person panel presenting the list.

And the picks, in reverse priority:

10) Convection-enhanced delivery (CED) of drugs — a system used to administer medication directly to the site where it is needed, without exposing the rest of the body to a drug's effects.

According to Michael Vogelbaum, MD, PhD, a neurosurgeon at the clinic's Brain Tumor Center and director for the **Center for Translational Therapeutics**, who presented the CED technology for the panel, CED allows a drug to cross the blood-brain barrier, the natural defense against toxins trying to get into the brain.

"It's been estimated that more than 98% of potential neurotherapeutics are excluded by the blood-brain barrier," Vogelbaum said. "Unfortunately, critical targets of drug therapy are most often behind a normal blood brain barrier." CED's major advantage, he said, is relying "on the blood-brain barrier to keep the drug in the brain rather than outside the brain."

The treatment has been primarily used as a treatment for malignant brain tumors. Other neurological applications are also being explored, including for epilepsy, enzyme replacement therapy, stroke movement disorders and spinal cord injury.

9) Left Ventricular Assist System (LVAS) — the first implanted ventricular assist device (VAD) that senses when to increase or decrease blood flow rate. It is designed to take over most of the function of the left ventricle, the heart's primary pumping chamber, and helps generate the force necessary to propel oxygen-rich blood throughout the body.

Nicholas Smedira, MD, surgical director of the clinic's Kaufman Center for heart failure, noted that the most important function of the newest generation of these systems is the introduction of non-pulsatile devices with ceramic bearings. Some of these newer systems — which are made by companies including **WorldHeart** (Oakland, California), **Thoratec** (Pleasanton, California) and **Ventracor** (Sydney, Australia) — may last up to 12 years and have greatly reduced infection rates and so far have not shown the failures of their older, larger, pulsatile counterparts.

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Innovations

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8) Targeted cancer therapies — second-generation, small-molecule tyrosine kinase inhibitors used to block or modulate disease and provide treatments for advanced cancers, such as renal cell carcinoma. Clear cell carcinoma is the most common type of kidney cancer, which represents 2% of all adult cancers.

7) Endografting — a minimally invasive repair technique traditionally used in cardiology and now being used to treat vascular disease, such as thoracic abdominal aneurysms.

Panel presenter Roy Greenberg, MD, a vascular surgeon, said that aortic aneurysms are found in 5% of the population over the age of 65 in the U.S., comprising the 13th leading cause of death.

He noted the lack of prospective randomized data, until recently, showing endovascular repair to be superior to traditional open surgical repair in low-risk patients. Now data is available that shows that to be the case, out to about four years.

Greenberg said he expects the device to lower mortality rates for complex aneurysms, but noted that adoption "requires that we break some barriers of conventional treatment of these patients, requiring cross-specialization in terms of imagining, surgery and interventional techniques." He said the technology also will require "additional developments" for implanting into small vessels and various delivery system challenges.

The specific product referred to most likely was **Medtronic**'s (Minneapolis) Talent system. The company reported the filing of the first module of the premarket approval application for the Talent in November 2005 (*Medical Device Daily*, Nov. 21, 2005). Other companies with technology in this field include **W. L. Gore** (Flagstaff, Arizona) and **Cook** (Bloomington, Indiana).

6) Ranibizumab — a drug therapy, brand-named Lucentis, inhibiting uncontrolled blood vessel formation in the eye, developed by **Genentech** (South San Francisco) and approved by the FDA this summer.

Lucentis was approved specifically for the treatment of neurovascular wet age-related macular degeneration, the leading cause of blindness in people older than 55.

5) Bronchial Thermoplasty (BT) — a therapy being developed solely by **Asthmatx** (Mountain View, California), used to ward off asthma attacks. BT involves the controlled application of heat in the lungs to improve pulmonary function and reduce asthma symptoms. The company has developed a catheter-based procedure that employs BT, via its Alair system, to deliver thermal energy to the airway walls to reduce the presence of airway smooth muscle, the tissue thought responsible for airway constriction and breathing difficulties.

"The existence of bronchial thermoplasty offers us a non-drug, a therapy with a 'permanent' therapy for asthma'," said panel presenter Tom Gildea, MD, medical director for the clinic's Center for Major Airway Disease. Underscoring the word "permanent," Gildea referred to three-year data in animal studies showing "no reaccumulation of airway smooth muscles so far."

Gildea noted that the smooth muscle layer is an evolutional vestige, much like the appendix, and in humans rather useless, but often becoming inflamed and restricting the airways.

4) OCT (optical coherence tomography) — a non-invasive imaging technology used in the treatment and diagnosis of eye diseases, such as diabetic retinotherapy and macular holes and glaucoma.

With the OCT technology, clinicians can now "actually image individual cells in the retina," said Andrew Schachat, MD, vice chairman for clinical affairs at the clinic's **Cole Eye Institute**. Though it is primarily being used in the retina, Schachat said it will ultimately be used in all areas of the eye.

3) Neurostimulation for Psychiatric disorders — such as deep brain stimulation (DBS), is emerging as a treatment option for millions of patients suffering treatment-resistant depression and treatment-resistant obsessive compulsive disorder (OCD).

Ali Rezai, MD, director of the Cleveland Clinic's Center for Neurological Restoration and director of its Brain Neuromodulation Center, said these two mental disorders account for 15% of the disease burden in the U.S. "That's more than all cancers combined."

Companies involved in the neurostimulation space for these conditions include Medtronic, **St. Jude Medical** (St. Paul, Minnesota), **Boston Scientific** (Natick, Massachusetts), **Northstar Neurosience** (Seattle) and **Cyberonics** (Houston).

2) Designer Theraputics Using Selective Receptor Antagonists – used to block receptor activation leading to improved patient outcomes. Examples include therapeutics that block the peripheral side effects, such as constipation and nausea of opioid medications for pain; increased stress response to mediate eating and smoking; increased good cholesterol using niacin.

And — drum-roll here — **No. 1) Cancer Vaccines** — used to prevent the disease and treat patients more specifically according to cancer type.

One example of a cancer vaccine is the HPV vaccine developed to prevent cervical cancer cause by the human papillomaviruses.

Asked by *Medical Device Daily* what items he anticipates to see on next year's top 10 list, Penn mentioned systems for transmitting brainwaves to computers — being undertaken by **Cyberkinetics** (Foxborough, Massachusetts), and RNA interference. Others barely missing the cut this year but possibly making the 2007 roster, he said, include electronic medical records and telemedicine. ■

CMS

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how venture capitalists (VCs) approach small medical device manufacturers, as well as how start-ups should approach VCs, stating that "reimbursement is often the culprit for a bad decision in investment" rather than the technological or clinical feasibility of a device.

Anderson said that among VCs, there is "a tremendous fixation on CMS," but hastened to point out that "there are other payers" and that the smart manufacturer or VC firm should look beyond the behemoth in Baltimore.

She said that the question of the critical payers is only the first. And she asked, "What clinical studies and labeling are critical for coverage?"

Anderson added that firms with products eligible for a 510(k) filing should not automatically assume that this will get them to market faster or bring them favorable coverage decisions by public or private payers sooner than filing the much more arduous PMA.

In some instances, a firm should write an interim reimbursement strategy, she advised, because payers find it easier to reimburse for a device under a code for miscellaneous procedures in the early going. Some companies have taken as long as two years to get through the CMS minefield into a national coverage decision (NCD) and may not be funded to go that entire stretch without income from operations.

However difficult the process may be, Anderson said, "reimbursement is usually successful, [but] it may take longer than you would like." The problem is that some of the adoption curves are initially flatter than investors see as desirable, even though the prospects for the device are quite good in the long term.

"When you're trying to communicate that to an investor, they may not want to hear that," she said. But the difficulty of getting CMS or multiple private payers on board can make it nearly impossible to boost a new product to full market acceptance in a short span of time.

A strategic reimbursement plan addresses the payer mix, a matter of considerable interest for investors. This kind of plan starts with determining which diagnostic codes apply to the condition the device will treat, and determining which members of the field of potential payers already have codes for that condition (at present, ICD-9 is the standard index for diagnostic codes in the U.S., but ICD-10, a significantly expanded list of diagnostic groups, will likely be in play by the end of 2009).

Anderson said that the web site for the **Centers for Disease Control and Prevention** (Atlanta) includes data tables that allow the viewer to "find out not only how many people were treated [for each condition], but who paid for it." She said that the results for payers might be surprising for many users and might rewire the reimbursement expectations for VCs and device makers.

One attendee noted the well-known reality that the burden of clinical proof is greater on smaller rather than large firm and that payers are "more aggressive" in demanding substantial clinical data from small companies.

"The level of clinical evidence that is now required is the same regardless of size," Anderson replied, but "the classic dilemma" is how large a sample to pull together from how many sites and whether European studies are useful in persuading payers. Anderson stated that studies conducted in Europe are accepted by most payers, but the studies should appear in a U.S. peer-reviewed publication.

A device maker can avoid problems by asking payers a few questions in advance about what kind of evidence those payers expect to see. Given the number of payers one might want to appeal to, "you kind of filter that" information and devise a clinical trial that will yield the desired effect without incurring needless cost, Anderson said.

On the other hand, doing studies "on the cheap" can backfire.

Anderson said, "Unfortunately, I have many small company clients who have had to do more than one study, and [conducting a small initial study] becomes a false economy."

"I'll be the first to tell you it's a mistake to do a study of 40 patients in two sites that don't have controls" because payers will not respond, she said. She added that investors are reluctant to fund repeated studies that seem to indicate a lack of appropriate planning.

The question of whether to put a device through the full brunt of PMA application rather than the faster-track 510(k) process hinged to some extent on preliminary feedback obtained from payers regarding meaningful data.

However, Anderson seemed bullish on the benefits of the clinical data that comes with the studies required for PMAs. She said, "If you think you might have to [file a PMA], it can get you over the hump of payment." The reason: "It's an enormous step forward with payers."

Further on the subject of PMA clinical trials, Anderson recommended that entrepreneurs talk seriously with VCs about getting "enough money to do justice by this product," allowing the innovator to "convince very sophisticated medical directors" of the worth of the device.

Start-up companies might also do well to tell a VC representative that the reimbursement plan will start small so as to provide some positive cash flow while company representatives keep working on the rest of the payer population.

As for the overall vitality of venture capital in the U.S. device market, Anderson said that "at the moment, there's a lot of money in healthcare."

But she cautioned attendees against putting "all your eggs in the Medicare basket." Noting the difficulties of dealing with 5,000 payers in the U.S., she said that CMS is "reasonable to work with" but "slow as molasses."

Anderson recommended that start-up firms look to smaller payers because "some of the little guys are easier to move and you can divide and conquer." ■

Wrap

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being treated with our Vascular Wrap provides patients with an option to better manage their disease, and a much greater chance of retaining their leg for a longer period of time following synthetic bypass grafting."

He said that the Vascular Wrap is intended to prolong the effectiveness of vascular surgery, "so to demonstrate a greater than 100% improvement in the duration of limb retention seems to bode well for other potential uses, like for hemodialysis graft patients."

The Vascular Wrap component is a biodegradable mesh implant incorporating Angiotech's paclitaxel technology in a novel biomaterial with the goal of mitigating scar formation caused by abnormal blood flow thereby potentially enhancing graft patency rates in AV-access patients as well as in peripheral bypass procedures.

The objectives of the two-year study were to assess safety and clinical performance of the in combination with an ePTFE vascular graft following surgery to treat patients suffering from advanced peripheral arterial disease in their lower limbs. The Vascular Wrap in combination with an ePTFE graft was compared to a control group of patients that received standard of care — an ePTFE graft alone.

Key findings:

- Adverse events (AE) leading to death occurred in a lower percentage of treated subjects (11%, 8/71), than in controls (18%, 7/38).
- The incidences of adverse events and serious adverse events were comparable in treated (graft with Vascular Wrap) and control (graft alone) groups.
- No adverse events were considered by the investigators to be related to the use of the Vascular Wrap.
- Overall, the action taken to resolve AEs was similar for the two groups, and the outcomes were comparable.
- When comparing the treatment arm relative to the control, the Vascular Wrap maintained the mean diameter of the distal anastomosis during the 24-month trial compared to a decrease in mean diameter in the control arm. This reached statistical significance (p=0.0333).
- The trial produced evidence that the Vascular Wrap reduced the overall incidence of amputation and prolonged limb retention time. The control group had an almost 19% higher probability of losing their limb compared to the treatment arm.
- The treated group had an overall lower incidence of amputations (15.5%, 11/71 subjects) compared to the control group (18.4%, 7/38).
- While the sample size was small, diabetic subjects appeared to experience benefits from the Vascular Wrap.

The single-blind study enrolled a total of 109 patients at nine clinical centers in Europe as well as the Dutch Antilles and randomized patients with peripheral vascular disease in a 2:1 fashion. The treatment arm enrolled patients with a synthetic bypass graft plus the Vascular Wrap paclitaxel-eluting mesh, and the control arm enrolled patients with a synthetic bypass graft alone.

Peripheral vascular disease progresses in the lower extremities to critical limb ischemia (CLI), characterized by leg pain at rest, skin ulceration, gangrene, and ultimately amputation. Among patients diagnosed with CLI, 25% may require amputation within a year.

Limb salvage depends on restoring and maintaining blood flow in the CLI patient. Surgical interventions include endovascular therapy (angioplasty and stenting). However, in patients with severe occlusion and stenosis, small vessel occlusion, calcified lesions, as well as those with diabetes, surgical bypass provides a final option to manage the occlusion(s) prior to amputation.

The success of grafting to restore blood flow depends on inflow and outflow of the graft. The trial results announced today shows trends that suggest that the use of the Vascular Wrap in these procedures may increase the success rates of vascular graft surgery.

Angiotech's Vascular Wrap paclitaxel-eluting mesh/ePTFE graft combination product technology is designed and in development for use in hemodialysis access and peripheral arterial bypass surgery. It consists of both the ePTFE graft and the Vascular Wrap paclitaxel-eluting mesh.

PCA3 gene-based test wins CE mark

A new test to detect prostate cancer based on **DiagnoCure**'s (Quebec City, Quebec) PCA3 gene has received CE-marking, the company said.

"I believe this is a significant moment for our company and for all those concerned with prostate cancer," said John Schafer, president/CEO of DiagnoCure. "We are confident that clinicians and patients will share our excitement at the potential of this important new prostate cancer diagnostic tool."

In 2003, the company granted an exclusive worldwide license for the use of the PCA3 technology in prostate cancer diagnosis to **Gen-Probe** (San Diego).

Gen-Probe said that its PCA3 test, which measures the expression of the prostate cancer-specific gene, PCA3, will be formally launched later this month at the meeting of the **British Association of Urologic Surgeons** (BAUS) in Birmingham, England.

Gen-Probe reports conducting studies at seven European institutions to validate the test. It said four molecular pathology laboratories across Europe are in the process of setting up the assay for the reporting of clinical results.

At a European symposium in October, Dr. Jack Schalken's keynote presentation discussed data suggesting the importance of PCA3 in predicting the outcome of a prostate biopsy. Being able to predict whether a second biopsy is needed could potentially spare many patients the uncomfortable experience of a second procedure.

Dr. Frans Debruyne, emeritus professor of urology at UMCN called PCA3 the most important discovery in his over 20-years as head of the department. ■

Transcend

Continued from Page 1

Mitch Campbell, the newly appointed president/CEO of Transcend, told *MDD*.

"I'm very excited, it's always nice to not have [fundraising] be one of your key focuses when you come into a new position," Campbell acknowledged.

Transcend is developing a device that would treat glaucoma through a "safe, simple and effective way" using a needle-stick approach to reduce intraocular pressure — high pressure within the eye — known to cause the disease, Campbell said.

Though glaucoma is commonly treated today with medicine, Campbell said the advantage of using a device to treat the disease is that the patient would not be able to miss doses.

"Most people start to drop off and don't take the medicine when they should so the effectiveness starts to diminish," Campbell said. "The nice thing about it is, it can be performed right there in the doctor's office, so it's a comfortable setting and only takes about five minutes."

The new technology is so early in the regulatory process that the company has not even opened up clinical trials in the U.S. for it yet, Campbell said. Because of that, he was unable to say when the device might hit the U.S. market, but he estimates that would be "years down the road."

Robert "Robin" Bellas, a general partner with Morgenthaler Ventures, told *MDD* that the investment in Transcend is consistent with the firm's previous medical device investments related to "graceful aging" because eye problems are often associated with aging. Morgenthaler Ventures also funded The Foundry about 10 years ago, he said.

Bellas said Transcend has seen promising results from First In Man clinical trials in Latin America.

Dave Stassen, managing director of Split Rock, said the firm is also interested in the ophthalmology field.

"We believe that ophthalmology is particular ripe for the kind of minimally-invasive device design that The Foundry has pioneered for other medical specialties," Stassen said.

Campbell said the treatment Transcend is developing could be repeated in a patient if necessary.

"It also does not limit you from being able to do one of the other procedures out there," Campbell said. "We're excited about continuing the progress that has been made and building on the early results."

Previously, Campbell was president/CEO and chairman of Refractec through the research and development, clinical trial, FDA approval and market launch of a vision correction device designed to eliminate the need for babyboomers to wear reading glasses.

According to Transcend, more than 2 million people in the U.S. are afflicted with glaucoma, and the numbers are expected to grow to 3 million by 2020.

In other finance news:

• **Osiris Therapeutics** (Baltimore), a stem cell therapeutic company focused on the inflammatory, orthopedic and cardiovascular areas, reported raising $20 million of newly issued convertible debt led by **Friedli Corporate Finance** (Switzerland).

On Oct. 30 Osiris issued $20 million in convertible promissory notes to several Swiss investors. The notes were placed in Switzerland by Friedli Corporate Finance; Peter Friedli, the chairman of the board of directors and largest stockholder of Osiris, is the president and owner. The notes bear interest at a rate of 10% per year, with semi-annual payments of accrued interest due April 30 and Oct. 30 of each year, until maturity on April 30, 2009.

The $20 million in notes issued on Oct. 30 are convertible at the option of the respective holders at any time after Feb. 9, 2007 into shares of common stock at an initial conversion price of $18 per share. The notes automatically convert into shares of common stock at the same conversion price, if at any time after Feb. 9, 2007 and before repayment, the closing price of the common stock for 10 consecutive trading days on the Nasdaq Global Market equals $25 a share or more. Each note is redeemable in whole at any time at the option of the company upon 30 days prior written notice to the holder.

Friedli, individually, bought $4.5 million of the notes, and **New Venturetec**, a Swiss publicly traded company about 3% owned by Friedli who serves as its president, bought $4 million of the notes.

• **Guardian Technologies** (Herndon, Virginia) reported completing the first of two closings of a private placement of its securities under a securities purchase agreement with a group of investors. Investors have agreed to buy $5.1 million of securities, $2.6 million of which were purchased at the first closing and $2.6 of which will be purchased upon effectiveness of a registration statement to be filed by the company with regard to shares underlying the securities. Midtown Partners & Co. acted as the placement agent for the private placement.

At the first closing, Guardian issued an aggregate of $2.6 million in principal amount of Series A 10% senior convertible debentures due Nov. 7, 2008, and warrants to purchase 4.5 million shares of its common stock at an exercise price of $1.2 per share. The debentures are convertible into shares of Guardian common stock at any time at a conversion price of $1.2 per share. The debentures bear interest at 10% per annum due on the first day of each quarter or upon conversion or redemption of the debentures as to the principal amount so converted or redeemed.

Guardian develops imaging technologies for early detection of threats of diseases. ■

PRODUCT BRIEFS

• **AMDL** (Tustin, California) reported that it has completed its pre-IDE for the use of its DR-70 test kit in monitoring colon cancer patients. AMDL, with operations in Shenzhen, Jaingxi and Jilin, China, through its wholly owned subsidiary **Jade Pharmaceutical** (Hong Kong), is an international biopharma company. AMDL together with Jade engages in the development, manufacture and marketing of proprietary pharmaceutical and testing products.

• **BioSphere Medical** (Rockland, Massachusetts), which says it pioneered the use of bioengineered microspheres to treat uterine fibroids, hypervascularized tumors and vascular malformations, reported that the FDA has cleared the 510(k) notification for BioSphere's QuadraSphere Microspheres. U.S. shipments through BioSphere's direct sales force are expected to begin immediately. BioSphere's QuadraSphere Microspheres, which are indicated to treat hypervascularized tumors and peripheral arteriovenous malformations, are delivered by interventional radiologists who perform embolization procedures. QuadraSphere is technically identical to BioSphere's HepaSpheres Microspheres, an embolic currently marketed in Europe. QuadraSphere's spherical shape allows for a "predictable, flow-directed occlusion," the company said. The product expands up to four times its dry-state diameter and thus absorbs aqueous media up to 64 times its dry-state volume. In addition to the absorption process, the negatively charged polymer is also capable of selective bonding with positively charged substances through ionic interaction. Also, QuadraSphere affords atraumatic conformability to the vessel architecture, leading to a more complete vessel occlusion, the company said.

• **Heartscape Technologies** (Columbia, Maryland) reported enrollment of the first patient in the OCCULT-MI trial. The Optimal Cardiovascular Diagnostic Evaluation Enabling Faster Treatment of Myocardial Infarction (OCCULT-MI) trial will measure the impact of a more complete view of the electrical signals of the heart with the PRIME ECG System, compared with the standard ECG, including time to treatment (cardiac catheterization sheath placement) for patients diagnosed using PRIME versus the time to treatment using the standard 12-lead electrocardiogram. The first patient was enrolled in the trial by clinicians at Baystate Medical Center (Springfield, Massachusetts). Designed primarily for emergency department use, PRIME is a new diagnostic system that uses 11 easily-applied, self-adhesive plastic strips containing 80 data collection points, or leads, to cover the front and back of the body. The 11 strips allow analysis of the heart's electrical activity with 360 degrees of spatial resolution, which has the potential to detect critical diagnostic information not visible with a traditional electrocardiogram, the company said.

• **Eastman Kodak** (Rochester, New York) said it has submitted the final module of a pre-market approval submission (PMA) to the FDA for approval of its computed radiography system for mammography. The final module contains data and test results from the clinical trials Kodak has concluded at several sites in the U.S. and Canada. The FDA has already accepted and closed review of the previously submitted modules covering manufacturing information and non-clinical data. The FDA filing is on track with Kodak's plan for obtaining regulatory approval in the U.S., so that when approved, the company may begin selling its Kodak Directview CR Mammography Feature in the U.S. next year. Kodak's CR (computed radiography) mammography feature will offer the ability to produce high-resolution scans for mammography applications (50 microns per pixel—or 20 pixels per millimeter) when using Kodak Directview CR Mammography Cassettes and EHR-M screens.

PEOPLE IN PLACES

• Kevin Keim, PhD, has been appointed chief development officer at **INC Research** (Raleigh, North Carolina), a contract research organization. Keim will also take the helm of INC's new outreach program to the Japanese pharma and biotech business community. Most recently, Keim served as president/CEO and board member of Vela Pharmaceuticals, as well as founder and managing principal of K.L. Keim Consulting Group.

• Austin Noll has been named new president/CEO of **NeoGuide Systems** (Los Gatos, California), a developer of the NeoGuide Endoscopy System. Previously, Noll held leadership positions at Medtronic over a 13-year period. Amir Belson, MD, company founder and inventor of the company's technology, will remain full-time with NeoGuide as a board member and chief technology officer.

• Paul Castillo, MD, has been named chief medical officer of **Veridgm** (Los Angeles), a telemedicine and network communication company. Castillo will oversee the implementation of Veridigm's telemedicine technology and will serve as the company's primary conduit to the professional medical community. He previously was a clinical technology consultant to the U.S. Congress and medical director for a Rand-based venture to build software used to manage chronic diseases.

• Theresa Bachhuber, RN, has been named hospice director for the **VITAS Innovative Hospice Care** (Middlebury, Connecticut), which serves patients and families living in the Eastern Connecticut area and is one of three VITAS programs in Connecticut. Prior to joining VITAS, Bachhuber was a home care administrator at Bristol Hospital.