

# MEDICAL DEVICE DAILY™

THE DAILY MEDICAL TECHNOLOGY NEWSPAPER

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## *MDMA annual meeting*

### Schultz: *de novo* 510(k) path not used to 'maximum effect'

By MARK McCARTY

**Medical Device Daily Washington Editor**

WASHINGTON – Dan Schultz, MD, director of the Center for Devices and Radiological Health at FDA, gave a brief address at this year's annual meeting of the **Medical Device Manufacturers Association** (MDMA; Washington), and had a lot to say about a lot of things.

One of the things he said is that with all the criticism of the 510(k) program at CDRH, more devices could end up as *de novo* 510(k)s if only because it is one of the center's regulatory options that are not used "to their maximum effect."

Schultz opened his remarks Tuesday by observing, "I get told a lot that the goalposts are moving" at FDA. "Of course the goalposts are moving," he said, and "there are a lot of reasons" for this, including the fact that technology is changing. "That's your fault," he told the audience, but

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## *International report*

### China MED draws 26,000-plus to 21st exhibition in Beijing

**A Medical Device Daily Staff Report**

The recent staging of China MED 2009, the 21st International Medical Instruments and Equipment Exhibition held in Beijing, featured 505 exhibitors from 22 countries showcasing their products over 322,900 square feet of exhibit space to 26,408 attendees.

Sponsor **Messe Duesseldorf**, which puts on the world's largest medical trade exposition, MEDICA, said CHINA MED 2009 featured not only IT technology, medical software, surgical instruments, medical diagnostics and imaging equipment, but also special exhibits for medical consumables, orthopedics, dental and rehabilitation equipment.

Messe Duesseldorf said the number of visitors confirmed the rapid growth and development of the Chinese medical care industry. About 30% of the visitors were from medical organization and R&D institutes, while 60% were wholesalers and distributors.

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### ev3 discusses Chestnut deal, its future during BMO 'chat'

By OMAR FORD

**Medical Device Daily Staff Writer**

Some companies take on the jack-of-all-trades approach, fighting to become a market leader in nearly every segment that its hands are in. Those listening to the **BMO Capital Markets** (New York) fireside chat with **ev3** (Plymouth, Minnesota) yesterday found that quite the opposite is true for that company.

During a session moderated by BMO med-tech analyst Joanne Wuensch, ev3 President/CEO Robert Palmisano told listeners that the company is interested in maintaining its position in the neurovascular market and that it plans to further grow that market.

Nothing could be further from the truth, especially since the company signed an agreement to acquire **Chestnut Medical** (Menlo Park, California), a company that holds many synergies for ev3.

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### JDRF study: CGM benefits people with Type 1 diabetes

By AMANDA PEDERSEN

**Medical Device Daily Staff Writer**

For people with Type 1 diabetes – even those who manage their blood sugar levels well, life is a balancing act, Aaron Kowalski, PhD, told *Medical Device Daily*. They know that the higher their HbA1c level is, the higher their risk is of developing long-term complications such as blindness and kidney disease; but if their blood sugar level gets too low they run the risk of becoming hypoglycemic and driving their car into a tree or passing out at work.

*See Diabetes, Page 9*

#### **A little something Extra**

You asked for it . . . you got it. Tacked onto the end of your regular issue today are two pages of *MDD's Ortho Extra*, which we have tagged "Additional Developments in One of Med-Tech's Key Sectors." This is the latest added weekly feature of the publication as part of increasing *MDD's* value to you.

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**AHC Media LLC**

*Digestive Disease Week notebook*

## Trial results point to positive Barrett's esophagus treatment

### A Medical Device Daily Staff Report

Clinical trial results presented at this week's Digestive Disease Week (DDW) meeting in Chicago reveal that endoscopic radio frequency ablation performed in a community practice setting is safe and effective for eradicating a precancerous esophageal condition known as Barrett's esophagus.

The study, titled "Radiofrequency Ablation of Barrett Esophagus: Outcomes of 429 Patients from a Multi-center Community Practice Registry," was presented by Ronald Pruitt, MD, of **Nashville Clinical Research** (Nashville, Tennessee), at a scientific session sponsored by the **American Society for Gastrointestinal Endoscopy** (Oak Brook, Illinois).

Pruitt reported on 429 patients with Barrett's esophagus, with and without advanced dysplasia (cellular signs of advanced progression towards cancer), who were treated with radiofrequency ablation using the HALO ablation system from **Barrx Medical** (Sunnyvale, California) over the last four years.

He added that the adverse event rate was favorable, with a low stricture risk (about 1%) and no serious adverse events. After an average of two ablation procedures and 20-month follow-up, 77% of patients were cured of their Barrett's disease. For those patients that had baseline evidence of dysplasia, 100% had complete eradication of all signs of dysplasia.

"We believe that the results of our trial are unique and relevant to the scientific knowledge-base, as this is the largest patient experience reported to date and the first multi-center trial conducted at community practice centers for using radio frequency ablation to eradicate Barrett's esophagus," said Pruitt. "Most importantly, we found that the safety and efficacy outcomes garnered in this clinical

### Today's MDD food for med-tech thought

"If there's a word you're going to be hearing more of in the next four years, it's going to be 'transparency.'"

– Daniel Schultz, MD, director of FDA's Center for Devices and Radiological Health, discussing the direction that agency regulation is heading, "Schultz: *de novo* 510(k) path not used to 'maximum effect'," pp. 1, 6.

setting comport with those from reported trials conducted as predominantly academic tertiary referral centers."

Study centers were comprised of large community practices with expertise in therapeutic endoscopy and the management of Barrett's esophagus. Radio frequency ablation was applied with a balloon-based circumferential device and an endoscope mounted focal device.

Patients underwent biopsy sampling of tissue from the esophagus at regular intervals to determine if all Barrett's disease had been eradicated. To be considered a "complete responder," all biopsy samples had to be normal.

"This study is highly relevant and represents an important contribution to the science related to Barrett's esophagus therapy," said David Utley, MD, chief medical officer at Barrx Medical. "The study's strengths lie in its large number of studied patients, relatively long follow-up and objective histology endpoints."

Barrx Medical develops treatment solutions for Barrett's esophagus, a precancerous condition of the lining of the esophagus caused by gastroesophageal reflux disease, or GERD. Its main product, the HALO360 System, provides a uniform and controlled ablation effect, which removes the diseased tissue and allows regrowth of normal cells.

The HALO90 System is mounted on the end of an endoscope and used to treat smaller, non-circumferential areas of disease.

In other news from Digestive Disease Week:

• **Ethicon Endo-Surgery** (Cincinnati) said that multiple studies presented this week demonstrate that the com-

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*Deals roundup***Medtronic buys CGM assets from Danish firm PreciSense****A Medical Device Daily Staff Report**

**Medtronic** (Minneapolis) reported this week that it has bought substantially all glucose monitoring assets from **PreciSense** (Horsholm, Denmark), a development company focused on continuous glucose monitoring (CGM) technology. Financial terms of the acquisition were not disclosed.

"This strategic acquisition is an effort to expand Medtronic's already robust continuous glucose monitoring pipeline, and to develop a new CGM platform to aid development of our 'closed-loop' system," said Chris O'Connell, president of Medtronic's Diabetes business unit and a senior vice president at Medtronic. "This potentially disruptive technology could significantly broaden the use of CGM, and help improve diabetes care for more patients."

The announcement was made during a webcast presentation delivered by O'Connell on the state of Medtronic's Diabetes business unit and its strategic plan. O'Connell also discussed the significant increase in R&D spending in the Diabetes business, and he gave an update on the business unit's next generation insulin pumps, Personal CGM and Professional CGM, diabetes management software, and closed-loop product platforms.

According to the company, CGM is one of the most significant advances in diabetes management technology because it shows people their changing glucose levels in real-time. Medtronic said it has the only diabetes management system that integrates the power of CGM with insulin pump therapy, the MiniMed Paradigm REAL-Time Continuous Glucose Monitoring System. This device is designed to allow diabetes patients to better deliver insulin and monitor their glucose levels. With trend graphs, directional arrows and alarms, the device can also alert patients to dangerous high and low glucose values and allow them to take preemptive action to better manage their diabetes, Medtronic said.

A closed-loop system, sometimes referred to as an "artificial pancreas," mimics the insulin delivery of a normal pancreas using technology that automatically responds to and treats glucose fluctuations in patients with diabetes, Medtronic noted. Using advanced mathematical algorithms, Medtronic's closed-loop system is being designed to continuously monitor glucose levels and automatically adjust insulin delivery in patients.

In other dealmaking activity:

- **CenterSpan Communications** (Sacramento, California) reported an agreement to purchase a license, and other intellectual properties, relating to a new drug delivery system from **Hamilton PNG** (North Miami, Florida), in exchange for preferred shares amounting to 96% of the issued and outstanding equity of the company.

CenterSpan said it has been seeking new business opportunities since it concluded its prior business in 2003. The Hamilton PNG technology includes a new drug delivery system for dermatology uses and at least one new drug being submitted to the FDA and other countries in the future. The drug delivery system and new drugs are significant improvements over current systems and are the result of more than 15 years of development in the U.S. and Thailand, according to the company.

Following this purchase, expected to close on June 11, CenterSpan will issue 5 million preferred shares convertible to 96% of the outstanding common shares in return for this new drug delivery system and new drugs. The new officers and board of directors will include the existing directors of Hamilton PNG. CenterSpan is assuming no debt or liabilities in connection with this acquisition of assets. The value of the assets being purchased for stock is about \$82 million as determined by prior arms length private sales.

CenterSpan said it intends to rename as Biophile Corporation and relocate to offices in California, Florida, with satellite offices in New Jersey, and Bangkok, Thailand.

- The **Premier** (San Diego) healthcare alliance has acquired **Phase 2 Consulting** (P2C; Salt Lake City), a provider of consulting services to hospitals and health systems.

The acquisition of P2C, a division of **RehabCare Group** (St. Louis), will complement Premier Consulting Solutions (PCS), as well as provide resources to help meet the growing demand for PCS' services, the company said. In 2008, PCS added more than 60 new customers, along with 225 new customer engagements.

- **Community Health Systems** (Franklin, Tennessee) reported that a subsidiary of the company has acquired from **Akron General Medical Center** (Akron, Ohio) all of its joint venture minority interest in **Massillon Community Health System** (Massillon, Ohio), which indirectly owns **Affinity Medical Center** (Massillon), a 268-bed acute-care hospital. The deal closed Monday. ■

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## DDW

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pany's investigational Toolbox enables natural orifice transluminal endoscopic surgery (NOTES) procedures without laparoscopic support in porcine models.

One of the studies concluded that a new adaptable, minimally invasive surgical platform for NOTES and single-site laparoscopy (SSL) was successfully used to complete a variety of key surgical activities critical to pure natural orifice surgery and SSL.

The seven studies presented at DDW, which involved porcine models and a variety of NOTES procedures, follows 15 studies involving Ethicon Endo-Surgery devices presented at the **Society of American Gastrointestinal and Endoscopic Surgeons** annual meeting in April.

Ethicon said that in the coming months, the Toolbox for natural orifice surgery will be evaluated in a human clinical trial under an investigational device exemption from the FDA.

"To date, most NOTES procedures performed in humans have been with laparoscopic support. In our study, we found several of the devices in the Ethicon Endo-Surgery Toolbox could successfully be used to address some of the critical visibility and access obstacles present with a pure NOTES approach, warranting further investigation," said Klaus Thaler, MD, of the department of surgery, **University of Missouri Health System**.

Investigators of the study titled, "The Development and Testing of an Adaptable Minimally-Invasive Surgical Platform – The Hydra," found that this surgical platform addressed several challenges with NOTES, including visibility, platform stability and adaptability to be used in multiple interventions and procedures.

The surgical platform was used both transgastrically and transvaginally completing multiple key surgical activities that included dissection, ligation, and specimen retrieval. The study, presented as a poster at DDW, involved porcine models and was conducted by investigators from **Sahlgrenska University Hospital** (Gothenburg, Sweden) and **Imperial College** (London).

"With the introduction of this adaptable minimally-invasive surgical platform, we believe we will be able to further address many of the issues experienced when NOTES or SSL procedures are performed with conventional surgical equipment designed for standard endoscopic or laparoscopic use," said Kenneth Sumner, PhD, vice president, clinical and regulatory affairs at Ethicon Endo-Surgery.

"We plan to continue our research to investigate the existing contents of the Ethicon Endo-Surgery Toolbox for natural orifice surgery, as well as develop additional products for inclusion in it that may help fulfill the promise of this approach to minimally invasive surgery," he said.

Another poster presentation titled "Hybrid Transgastric NOTES Cholecystectomy in a Porcine Model Using a Magnetically Anchored Cautery and Novel Instrumentation,"

conducted by the **University of Texas Southwestern Medical Center** demonstrated preliminary feasibility for a particularly difficult NOTES procedure, transgastric cholecystectomy.

Several devices specifically designed for natural orifice surgery were utilized in the study, including a live video manipulation (LVM) system and magnetically anchoring and guidance system (MAGS). Study investigators specifically cited the retraction abilities of the grasper and improved visibility of the provided by LVM, the latter which greatly reduced the workload on the surgical team.

The content of the Ethicon Endo-Surgery Toolbox includes Tissue Apposition System, Steerable Flex Trocar with Rotary Access Needle, Flexible Bipolar Hemostasis Forceps, Flexible Maryland Dissector, Articulating Hook Knife, Articulating Snare, Articulating Needle Knife, Articulating Graspers and Articulating Biopsy Forceps.

Those devices listed will be used within the IDE trial. The Adaptable Minimally-Invasive Surgical Platform and MAGS are limited to non-clinical applications at this time.

Ethicon Endo-Surgery is a **Johnson & Johnson** (New Brunswick, New Jersey) company.

- **GI Dynamics** (Lexington, Massachusetts), a developer of non-surgical, endoscopic approaches for the treatment of Type 2 diabetes and obesity, said that its EndoBarrier Gastrointestinal Liner was highlighted by leading experts in metabolic disorders and endoscopy at DDW.

"This is proving to be a very successful year for GI Dynamics and our development efforts in support of the EndoBarrier," said CEO Stuart Randle. "Based on the data we have seen to date, we believe EndoBarrier, as part of a multidisciplinary approach, has the potential to dramatically change the treatment paradigm for Type 2 diabetes and weight problems due to its unique profile as a non-surgical and non-pharmaceutical treatment option.

"Notably," he said, "EndoBarrier may provide the benefits of gastric bypass surgery without the complications and risks associated with a highly invasive procedure, and unlike traditional pharmaceutical approaches, our implantable device removes the burden of dose regimen compliance from the patient."

The EndoBarrier Gastrointestinal Liner is placed in the GI tract endoscopically (via the mouth) to create a barrier between food and the wall of the intestine. The company said physicians believe that preventing food from coming into contact with the intestinal wall may alter the activation of hormonal signals that originate in the intestine, thus mimicking the effects of a Roux-en-Y gastric bypass procedure without surgery.

It said a "growing body of pre-clinical and clinical evidence supports the potential for EndoBarrier Gastrointestinal Liner to dramatically change the treatment landscape for people living with Type 2 diabetes, obese people at risk for Type 2 diabetes, and people with severe weight problems." ■

*Financings roundup***Active Implants gets \$10M in preferred stock offering****A Medical Device Daily Staff Report**

**Active Implants** (Memphis, Tennessee), a developer of advanced polymer technology for the hip and knee segments of the orthopedic market, said it has raised \$10 million in its Series C preferred stock offering and has appointed Charles Martin to its board of directors.

"This new financing enhances our ability to move forward toward achieving our development, clinical, regulatory, and early commercialization milestones," said President/CEO Michael Mainelli.

Martin is the recent past CEO/chairman and a current director of Zephyr Associates, a financial services software development firm. He was the past CEO/chairman of Third Party Solutions and DirectComp Rx, both national health-care service companies.

In other financing activity:

- **Quest Diagnostics** (Madison, New Jersey) reported that the following principal amounts of its 5.125% senior notes due 2010 and 7.50% senior notes due 2011 have been validly tendered and not validly withdrawn in connection with its previously disclosed cash tender offer to purchase up to \$200 million total aggregate principal amount of the notes.

Because the aggregate principal amount of the 5.125% senior notes due 2010 validly tendered and not validly withdrawn as of the early tender date does not exceed the tender cap, the amount of each series of notes that may be purchased in the tender offer will be determined in accordance with the tender cap and the acceptance priority levels based on the principal amount of the notes tendered midnight, Eastern Time on June 16, unless extended. The notes may be subject to proration, in each case as described in the offer to purchase and related letter of transmittal.

Quest has retained Banc of America Securities to act as lead dealer manager and Calyon Securities and Mitsubishi UFJ Securities to serve as co-dealer managers. Global Bondholder Services has been retained to serve as the depositary and the information agent for the tender offer.

- **Endoscopic Technologies** (San Ramon, California), a provider of cardiac surgery devices, said it has completed \$8 million in equity financing through the sale of its preferred stock. This is in addition to the \$11.3 million the company raised in September 2008. NBI Ventures led the financing. Also participating in the financing were previous investors Saints Capital Everest, Telegraph Hill Partners and Waveland Venture Partners.

- **Orasi Medical** (Edina, Minnesota) said it has completed a \$3.5 million Series B financing round. The company said it would use this capital to expand the develop-

ment and use of its diagnostic test into the pharmaceutical and clinical markets.

According to Orasi, pharmaceutical companies will use this test to determine the efficacy of compounds intended to treat various neurological diseases. The company said it is currently in discussions with several pharmaceutical companies to finalize the structure of these clinical trials and the inclusion of the Orasi test.

Orasi is an early-stage device company engaged in the development and commercialization of technology to diagnose and monitor neurological disorders using electrical brain activity.

- **Catheter Connections** (Park City, Utah) reported that it has raised \$1.3 million in seed capital, led by Kickstart Seed Fund. The funding enables the company to further develop and commercialize its lead product, a device designed to prevent hospital-acquired infections resulting from catheters.

- **Tenet Healthcare** (Dallas) reported the pricing of its previously disclosed private offering of senior secured notes maturing in 2019. A total of \$925 million aggregate principal amount of notes, which will bear interest at a rate of 8.875% per annum, will be issued. The notes will rank *pari passu* with Tenet's 9% senior secured notes due 2015 and 10% senior secured notes due 2018, which were issued in March, and similarly will be guaranteed by and secured by a pledge of the capital stock and other ownership interests of certain of Tenet's subsidiaries.

The proceeds from the offering will be used to purchase Tenet's 9.875% senior notes due 2014 in a tender offer. The 8.875% senior secured notes have not been registered under the Securities Act of 1933 or any state securities laws. Accordingly, the notes are being offered only to qualified institutional buyers outside the U.S. ■

*Patent watch***QuantRX wins approval for intellectual property suite****A Medical Device Daily Staff Report**

**QuantRX Biomedical** (Doylestown, Pennsylvania), a broad-based diagnostic company focused on the development and commercialization of diagnostic products, reported that the U.S. Patent and Trademark Office has issued a new patent extending its lateral flow testing intellectual property suite.

This new patent offers significant new protection as QuantRX enters the market with its hypersensitive point-of-care lateral flow based system. Coupling this technology with the patented Q-reader technology enables QuantRX to provide CLIA (Clinical Laboratory Improvement Amendments) waived point-of-care tests that other technologies cannot offer. ■

## MDMA

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added that as a physician, "I appreciate that."

All the same, "public expectations continue to evolve" with regard to safety, Schultz remarked, so even though "because of the technology you make, the operating room is a safer place," expectations are higher still. "The sense is that we're somewhat victims of our own success," he said, adding that rates of adverse events "that would have been acceptable and even laudable even 10 years ago" are now scarcely acceptable. "I think we need to explain risk and benefit in a way that I think we haven't done in the past," he stated.

The discussion of *de novo* 510(k)s came at the end of Schultz's remarks, and his initial response to a question about whether more devices would end up as *de novos* was "I'm not sure I would frame it as lowering the threshold" to bring more devices into the *de novo* part of the 510(k) program. "Everyone in this room understands that a 510(k) is not the mindless rubber stamp" that it is often perceived to be, a message he said FDA will try to convey, although he cautioned that such an effort is not necessarily going to work.

As for the technological drift induced by the continuous build-on of predicate devices, Schultz said "we need to do a better job of defining that path and making it much clearer how those decisions were made along the way. There are a lot of people who don't trust the system and we need to build that trust back up," he said.

Schultz said the agency is keenly aware that device firms are more and more commonly multi-national entities, remarking, "Clearly, the regulatory system was not designed for a global marketplace." This subject touches on the intent of the Food and Drug Administration Globalization Act of 2009, which would put FDA in the position of conducting more overseas inspections for makers of drugs, devices and food products (*Medical Device Daily*, Jan. 30, 2009). "It doesn't matter where the finished device is made if the components are made all over the place," Schultz said.

"If there's a word you're going to be hearing more of in the next four years, it's going to be 'transparency,'" he said, a message he said seems to be coming from "on high" rather than just from within FDA.

Earlier in the day, FDA had announced the opening of the FDA Transparency Blog and the formation of the FDA Transparency Task Force, which will meet June 24 to begin work on processes designed to make the agency's operations more open. In a June 2 statement on the blog, Secretary of Health and Human Services Kathleen Sebelius said, "our administration is committed to eliminating the barriers between the American people and their government, and the Task Force is another big step in the right direction." Deputy FDA commissioner Joshua Sharfstein will chair the task force.

"Reliance on interactive review, I think, is reborn," Schultz, acknowledging that the agency and industry "got off track" on the idea. Greater participation in interactive review would allow FDA to "reserve the [deficiency] letter for the larger

issues" that cannot be dealt with over the phone. "When we have interactive review, we do a better job" and devices that should go to market get there more expeditiously.

The unique device identifier "is something that is clearly coming," Schultz advised the audience, adding that the electronic medical device report (e-MDR) is also looming on the horizon. "I would strongly encourage you to give this some consideration."

Following Schultz's talk, a panel took the dais to review recent developments on Capitol Hill. Leading off the session was John Manthei, a partner at **Latham and Watkins** (Washington), who said the Senate will soon vote on "the biggest series of reforms at FDA" in decades. "I can't think of a more contentious, controversial" change than putting tobacco into FDA's portfolio, he said.

The reference is to the Family Smoking Prevention and Tobacco Control Act of 2009, which the House passed earlier this year by 298-112, while the Senate Health, Education, Labor and Pensions Committee forwarded the upper chamber's version to the full Senate in April (*MDD*, April 28, 2009).

"It's a new day in Washington," Manthei said, echoing comments he made about the traditional five-year legislative hits absorbed by FDA at the FDA/FDLI annual conference earlier this year (*MDD*, April 27, 2009). "Those days are over, and industry has to brace itself" for annual updates to legislation affecting the agency and, by extension, industry.

Manthei noted that Congress is likely to undertake an "evaluation of the 510(k) program," adding that the program "may be materially reformed." He suggested that industry defend the process. He also said more enforcement activity can be expected, and noted that the approaches of inspections of device manufacturers' facilities will have to be reconciled and which is "another area in which it's important that industry is heard."

Later in the discussion, Manthei and Nick Shipley, director of government relations at the healthcare consultancy the **McManus Group** (Washington) and formerly a Democratic staffer, said the 510(k) program is of intense interest in the House Energy and Commerce Committee and would fall under the committee's health subcommittee, which is chaired by Rep. Frank Pallone (D-New Jersey). However, Pallone's involvement in the Menaflex 510(k) by **ReGen Biologics** (Franklin Lakes, New Jersey) could make any such moves ticklish for Pallone, and he recently told *Medical Device Daily* that he could not be sure when hearings on the 510(k) program might move onto the top of the subcommittee's list (*MDD*, May 14, 2009).

*MDD* asked Manthei and Shipley whether such an investigation might be handled by the Oversight and Investigations Subcommittee, chaired by Rep. Bart Stupak (D-Michigan). Shipley said "there is definitely an opportunity for Stupak to step up and take over" the 510(k) question, while Manthei said, "if I had to handicap it, I would put it in Stupak's committee." ■

## BMO

*Continued from Page 1*

"This acquisition really fits into our wheelhouse," Palmisano said. "We would have loved to have paid less, but we're glad to take part in the deal."

Under the terms of the agreement, ev3 will acquire 100% of the equity of Chestnut for total up-front consideration of \$75 million paid upon closing, 30% to 40% of which is payable in cash, with the remaining portion payable in ev3 common stock.

An additional milestone-based contingent payment of up to \$75 million is payable in a combination of cash and ev3 common stock upon the receipt of U.S. FDA premarket approval of the Pipeline device. ev3 will finance the up-front payment due upon closing through cash on hand. Any contingent milestone payment is not expected to be paid until 2011. The transaction is subject to customary closing conditions and is expected to close within approximately 45 days.

"This acquisition directly supports our stated strategy of bringing breakthrough neurovascular therapies to our markets and adds an innovative new product platform to benefit the large number of patients suffering from brain aneurysms that currently are not well treated with either surgical or endovascular techniques," Palmisano said. "In addition, this acquisition is expected to be an immediate revenue contributor, leverage the strong global distribution capabilities of ev3's neurovascular sales organization and provide another growth engine for delivering enhanced value to our shareholders."

But don't expect for the company to delve much into cardiovascular products after this deal.

When asked if that was going to be the next logical step, Palmisano said it was best that ev3 best stick with what it knows.

"That would be a task that would defer us from what we know we can do well and we're sticking to what we know," he said when asked about getting into the cardiovascular market.

Its neurovascular franchise holds the No. 2 spot in the \$700 million worldwide hemorrhagic stroke market, with industry-leading products such as the Axium Detachable Coil System and Onyx Liquid Embolic System. Momentum should continue in 2009, with the launch of the Axium PGLA and Axium Nylon coils, and new access products.

In the \$3 billion peripheral vascular market, ev3 sells a portfolio of atherectomy products (plaque removal), stents, balloons, thrombectomy (thrombus removal), and embolic protection devices. In January, the company initiated the worldwide launch of its EverCross and NanoCross PTA balloons. The company also is conducting a series of clinical trials, the DEFINITIVE trials, designed to evaluate its SilverHawk and RockHawk atherectomy devices.

Perhaps one of its greatest accomplishments was its merger with **FoxHollow Technologies** (Redwood City, California) (*Medical Device Daily*, July 24, 2007). The \$780

million cash and stock transaction plan created a new company with a market capitalization of about \$1.7 billion. It grew ev3 to a size that would be one of the largest in the endovascular space at nearly twice the size of the applicable business units of other industry behemoths such as **Johnson & Johnson** (New Brunswick, New Jersey), **Boston Scientific** (Natick, Massachusetts), **Abbott Laboratories** (Abbott Park, Illinois), and **Medtronic** (Minneapolis).

But don't count on a repeat of a move like that in the future.

"We don't see us doing what we did with FoxHollow a couple of years ago," Palmisano said. "We're looking right at the products that we know about things we would be looking at would be in our wheel house. We really want to avoid integration." ■

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### *Restructuring roundup*

## Northfield Labs begins move to Chapter 11 bankruptcy filing

### **A Medical Device Daily Staff report**

**Northfield Laboratories** (Evanston, Illinois) reported that it has filed a voluntary petition for relief under Chapter 11 of the U.S. Bankruptcy Code in the Bankruptcy Court for the District of Delaware. The filing was made to facilitate the company's previously-announced plan to wind down its business operations and carry out an orderly disposition of its assets.

The decision to file was made after an exhaustive review of alternative options and is seen as the most favorable means for the company to continue its wind down process and liquidate its remaining assets for the benefit of its creditors and other parties in interest.

The company expects to file with the bankruptcy court a liquidating plan and related disclosure statement. Northfield expects that it will seek approval of the plan as expeditiously as practicable pursuant to relevant notice requirements, the Bankruptcy Code and applicable law and procedures.

Northfield also said that it had received a letter from the staff of Nasdaq, indicating that the company's common stock will be delisted from the Nasdaq Global Market as of the opening of trading on June 11 in accordance with Nasdaq Listing Rules 5100 and 5110(b) and IM-5100-1.

Receipt of the Nasdaq letter follows the company's announcement on June 1 that it had filed a voluntary petition for relief under Chapter 11 of the U.S. Bankruptcy Code in the Bankruptcy Court for the District of Delaware. The filing was made to facilitate the company's previously-announced plan to wind down its business operations and carry out an orderly disposition of its assets.

In view of the company's plan to wind down its business, the company does not expect to appeal the determination of the Nasdaq staff with respect to the delisting of its common stock. ■

## International

*Continued from Page 1*

According to the People's Republic of China customs statistics, the export of medical devices, equipment and products from January to November 2008 was worth \$3.2 billion, an increase of 31.4% compared to the same period of 2007.

Messe Dusseldorf said it is estimated that the peak for the Chinese medical industry development will be between 2008 and 2010.

It said CHINAMED 2009 exhibitors were pleased with the visitor quality and quantity. "It is encouraging that we have found both clients and supplier in this trade fair. The platform provided by CHINA MED enhances the interaction among the participants effectively. The large visitor participation makes me confident about China's future," said Thomas Guttridge of **Blu-med**. Zhang Ning of **Ningbo Xingaoyi Co. Ltd.** agreed, saying, "The percentage of trade visitors seems higher than ever. This is our first time we participated as an exhibitor and the results are good."

Jim Litter, vice president of service at **Vital Image**, said, "Sometimes we were too busy to have lunch because there were always visitors interested in our products."

The exhibits at CHINA MED 2009 were complemented by more than 50 symposiums on topics such as medical imaging equipment, logistics and large equipment quality assessment as well as seminars about orthopedic trauma, tumor imaging diagnosis and clinical laboratory science.

The next staging of CHINA MED is scheduled for March 2010 in Beijing.

### Trial results reported for regen system

Clinical trial results using the regen system by **Pollogen** (Tel Aviv, Israel), the newest aesthetic solution powered by third-generation TriPollar RF technology on cellulite treatment and body contouring, have been published in the online *Journal of the European Academy of Dermatology and Venereology*.

The study, conducted by Dr. Manuskiatti, et al., at the **Mahidol University Hospital** (Bangkok, Thailand), was titled "Circumference reduction and cellulite treatment with a TriPollar radiofrequency device: a pilot study."

The company said the study "demonstrated long-term measurable and durable body circumference and fat thickness reduction using objective measurement system (ultrasound)."

The study involved 37 patients treated once a week with the regen system for a total of eight treatments. Results showed that there was significant circumference reduction of 3.5 cm on average at the abdomen with a maximum of 14.4 cm, and 1.71 cm reduction at the thigh with a maximum of 9.1 cm. These results were maintained four weeks following the last treatment. In addition, ultrasound measurements of the distance between the epidermis and the superficial fascia showed an average reduction of 10.5% in the thickness of adipose tissue with a maximum reduc-

tion of 39% at the thigh region.

"TriPollar is a truly innovative technology that delivers what patients worldwide have been waiting for- a pain free, safe and effective solution for body contouring," said Manuskiatti, lead investigator for the trial and associate professor in the department of dermatology at the **Siniraj Hospital**.

The company said the study "clearly demonstrated that TriPollar RF technology provides beneficial effects on the reduction of abdomen and thigh circumferences and an overall improvement in the appearance of cellulite."

Pollagen CEO Yfat Scialom said, "The study [showed] that the innovative TriPollar RF technology . . . delivers consistent and effective results without pain and adverse side effects as proven once again by the leading scientists and labs in the world. Since the launch of Pollogen's professional anti-aging and body contouring products two years ago, we have successfully captured the attention of physicians and estheticians in over 50 countries worldwide."

Pollogen manufactures professional medical aesthetic devices, powered by the TriPollar third-generation radio frequency technology. The technology powers a full line of clinically proven, non-invasive and non-surgical treatment platforms for wrinkles, cellulite, circumference reduction and skin tightening.

The company's flagship aesthetic devices, apollo and regen, offer anti-aging treatments that deliver what the company described as "immediate and long-lasting results."

### \$500,000 in grants for Compugen

**Compugen** (Tel Aviv, Israel) reported that it has been notified by the Office of the Chief Scientist of Israel that it will receive grants totaling about \$500,000 to support the company's drug and diagnostic product candidate discovery activities and continued capabilities enhancement.

The product candidate programs that will be supported by this funding are focused on discovering additional drug targets for antibody therapeutics and pre-clinical nucleic acid biomarkers for drug-induced toxicity. These activities, in large part, will be based on modifying and enhancing certain of the company's 10 existing discovery platforms

In addition, a portion of the funding will support the company's ongoing activities with respect to extending and enhancing its predictive discovery capabilities infrastructure.

Dr. Anat Cohen-Dayag, co-CEO of Compugen, said, "We are delighted by the continuing support of the Israel OCS with respect to multiple aspects of Compugen's broadly based predictive drug and diagnostic discovery efforts. The programs to be supported with these latest grants should result in both additional product candidates for development and licensing and further applications of our unique discovery capabilities." ■

## Diabetes

*Continued from Page 1*

Fear of low blood sugar emergencies often prevents many people from achieving tight control, and remains a constant concern for those who manage their diabetes well, said Kowalski, program director for Metabolic Control at the **Juvenile Diabetes Research Foundation** (JDRF; New York) and a Type 1 diabetic.

This population of people with diabetes who have been successful in managing their disease can still benefit from using a continuous glucose monitor (CGM) devices, according to a major multi-center trial by the JDRF. Kowalski said that in designing the trial, the researchers decided it needed to be broken into two subgroups of people – those who had not reached targeted HbA1c levels, and those who had. The latter group, he said, often are not well-studied because they are already able to manage their blood sugar levels.

CGM devices, manufactured by several companies and approved by the FDA as an adjunctive therapeutic for diabetes, provide both a real-time snapshot of the glucose levels of a person with diabetes, as well as trend information on whether glucose is moving upwards or downwards, and how fast. Devices also provide warnings when the glucose is becoming too high or too low.

According to the JDRF study, using CGM devices enables people who have achieved excellent control (with HbA1c levels below 7%) to continue to tightly manage their diabetes while cutting down on the frequency of low blood sugars, called hypoglycemia.

"In this group we looked at reduction in hypoglycemic exposure, a problem that can be very dangerous and is a limitation," Kowalski said. "The reason I am so pleased with this paper is that it demonstrates quite convincingly that CGM devices really do help people who are under 'good control' do even better."

Kowalski told *MDD* that the results of this study really resonates with this group of patients because they feel like somebody finally understands that being "at target" is often very difficult and CGM devices can really help.

Surprisingly, he said, in the original cohort (those patients who had not achieved control) the researchers saw a drop-off in benefit in kids and teens, likely because the younger patients weren't using the device as much. In the other group, however, the results showed a benefit across the board.

"I see this as a huge step forward for people with diabetes . . . we hit a population of people who aren't often studied," Kowalski said.

The JDRF noted that the landmark Diabetes Control and Complications Trial (DCCT) showed that with intensive insulin therapy, excellent blood glucose control was obtained, but at the expense of a considerable increase in hypoglycemia. The JDRF study has shown that, with CGM, hypoglycemia can be reduced while maintaining excellent

blood sugar control.

Kowalski said that in planning this study, the change in HbA1c was not selected as the primary outcome measure because the researchers did not anticipate being able to lower HbA1c levels in the CGM group, given their already exquisite level of control. He noted that the study group expected that there might even be small and clinically insignificant increases in HbA1c values in the CGM group if the devices were able to help them reduce the frequency of glucose levels below 70 mg/dL. Instead, the CGM group was able to maintain HbA1c levels with less biochemical hypoglycemia, whereas HbA1c levels rose over time in the control group. He noted that all the HbA1c outcomes favored the CGM over the control group.

People with diabetes try to maintain their blood sugar levels between 70 mg/dL and 180 mg/dL. When blood sugar becomes very low, people can become confused, lethargic, and even slip into a coma or die, according to the JDRF. Very high blood sugars can also be dangerous, the organization said. And long term, lack of control increases the risk of developing devastating complications, including eye, kidney, nerve, and heart disease. HbA1c is a measure of long-term blood sugar control; standards of good control are generally below 7% for adults, and below 7.5% to 8% for children, depending on age. According to the DCCT findings, every one-point reduction in HbA1c reduces the risk of long-term complications by about 40%.

Kowalski said that for people who want to manage their diabetes better, he believes the CGM is going to become the new standard of care. For him personally, he says he could not fathom not using the device.

The CGM study was a randomized and controlled trial involving 129 adults and children ranging in age from 8 to 69 at 10 sites, including the **Atlanta Diabetes Associates**, the **Joslin Diabetes Center** (Boston), **Kaiser Permanente Southern California** (San Diego), **Nemours Children's Clinic** (Jacksonville, Florida), the Lucile Packard Children's Hospital at **Stanford University** (Palo Alto, California), the Barbara Davis Center for Childhood Diabetes at the **University of Colorado Health Sciences Center** (Denver), the **University of Iowa** (Iowa City), the **University of Washington** (Seattle) and **Yale University** (New Haven, Connecticut).

It was coordinated by the **Jaeb Center for Health Research** (Tampa, Florida). All participants had good diabetes control when they enrolled in the trial, and were randomly assigned to either a group that used CGM devices or one using standard finger-stick glucose testing for 26 weeks.

According to the study, for those using CGM devices, the time the blood sugar level was below 70 mg/dL decreased by 37 minutes a day. This compared with a decrease in the control group of only 5 minutes a day. In

*See Diabetes, Page 10*

*Court report***Appeals court backs verdict in Medtronic-DePuy case****A Medical Device Daily Staff Report**

**Medtronic** (Minneapolis) reported results from a U.S. Circuit Court of Appeals review of a December 2007 patent infringement verdict regarding the Vertex line of multiaxial screws, which are no longer on the market. The appeals court upheld the verdict of patent infringement, but reversed a substantial portion of the damages award to **DePuy Spine** (Raynham, Massachusetts).

The appeals court also reversed a sanctions determination against Medtronic, finding that it was legally incorrect and could not be sustained. The court affirmed an award of \$149.1 million in lost profits, but eliminated another \$77.2 million in damages to DePuy Spine, along with another nearly \$10.5 million in sanctions and attorneys' fees.

In other legalities:

A class-action lawsuit filed on behalf of Georgia surgery centers against **Blue Cross Blue Shield of Georgia** (BCBSGa; Atlanta) claims the state's largest health benefits provider has discouraged visits to out-of-network providers by reimbursing procedures at a tiny fraction of

"usual and customary" charges.

The class of plaintiffs is represented by Butler, Wooten and Fryhofer, with offices in Atlanta and Columbus, and J. Tom Morgan of Decatur.

The suit was filed against Blue Cross Blue Shield Health-care Plan of Georgia and Blue Cross and Blue Shield of Georgia. According to the suit, BCBSGa health plan members paid higher premiums in exchange for the flexibility to receive coverage for care from providers who are not part of the plan's preferred network.

The suit alleges that BCBSGa has targeted these out-of-network providers, including outpatient non-hospital providers of surgical services, known as ambulatory surgery centers, for a drastic and unprecedented slash in reimbursement to a mere fraction of usual and customary charges.

These actions violate federal and state laws protecting patients and providers, as well as Blue Cross Blue Shield's own contracts, according to the suit. The lawsuit seeks monetary damages for BCBSGa's failure to pay the contracted reimbursement rate and injunctive relief to require BCBSGa to honor its agreements. It was filed in the U.S. District Court for the Middle District of Georgia, Macon Division. The case is pending before Judge Ashley Royal. ■

**Diabetes**

*Continued from Page 9*

other words, people in the CGM group spent almost two hours more time per day in the target blood sugar range of 71 to 180 mg/dL compared with the control group, and about half an hour less time per day with glucose values in the potentially dangerous hypoglycemia range. The authors demonstrated a number of other significant benefits in this population including:

- More people in the CGM group had an improvement in HbA1c of more than 0.3% (31% vs. 5% in the control group).
- Fewer had a worsening of HbA1c greater than 0.3% (28% vs. 52%).
- More CGM users had a HbA1c level below 7% at 26 weeks (88% vs. 63%).
- More people in the CGM group than the control group had a decrease in HbA1c of more than 0.3% without experiencing a severe hypoglycemic event (28% vs. 5%).

The study is the second major publication resulting from JDRF's CGM trials, established to clinically document the benefits of CGM devices in helping people with type 1 diabetes manage their disease more effectively.

In results published last fall in the *New England Journal of Medicine*, the JDRF Continuous Glucose Monitoring Study Group reported that CGM substantially improved blood sugar levels without increasing the frequency of hypoglycemia in adults over 25 years of age in a randomized trial of 322 adults and children with type 1 diabetes and HbA1c levels above 7%. ■

## M E D - T E C H N E W S A N D N O T E S

**IntuiSkin launches IOMA locations**

**IntuiSkin** (Durham, North Carolina) reported the launch of its first U.S. flagship locations for its IOMA Concepts. The very first IntuiSkin flagship locations include the Iatria Spa and Health Center in Raleigh, North Carolina, Fearington Plastic Surgery in Raleigh, Natura Medspa in Parkland, Florida, and San Diego Beauty Academy in Poway, California.

IntuiSkin technology provides actual measurements of a patient's skin condition and then stores the data for retrieval at a later date, allowing dermatologists and plastic surgeons to make recommendations for treatment and measure the effectiveness of that treatment over time. Sandra Fearington, MD, of Fearington Plastic Surgery, said: "Until now, photography was our primary source of skincare analysis and documentation, which is relatively subjective. The unique new IntuiSkin System provides objective data which is independent of the user. Our patients and clients know that they will directly benefit from the newest technology available for skincare analysis, which is now only available at the flagship locations, and a few select others in the U.S. We also have the unique opportunity to use the IntuiSkin technology to measure the effectiveness of our other services."

## PRODUCT BRIEFS

- **Align Technology** (Santa Clara, California) said it is implementing a product proficiency program in North America to help ensure that Invisalign-trained doctors have the experience and confidence necessary to achieve high quality treatment outcomes for Invisalign patients. The Invisalign System is a procedure that requires regular usage and ongoing education to develop proficiency with the product and technique. Invisalign-trained doctors now have a range of Invisalign products that provide treatment solutions for most day-to-day treatment needs. In 2008, Align introduced three new product offerings with new features, tools and delivery options to meet specific clinical demands while providing a family of end-to-end solutions for doctors. With the launch of these new products, the Invisalign product family includes: Invisalign Express for simple/limited treatment cases, Invisalign Full or Invisalign Assist for comprehensive or complex cases, Invisalign Teen for younger patients, and Vivera Retainers for post-treatment retention.

- **athenahealth** (Watertown, Massachusetts) said the Certification Commission for Healthcare Information Technology (CCHIT) has approved the software component of athenahealth's service-based electronic health record (EHR), athenaClinicals Version 9.15.1, as a conditionally CCHIT Certified 08 Ambulatory EHR pending advanced electronic prescribing verification, additionally certified for Child Health. According to CCHIT, athenahealth's EHR serv-

ice meets the Certification Commission's electronic health record (EHR) criteria for physician office-based use.

- **Canon USA** (Lake Success, New York) reported the expansion of its line of digital radiography (DR) systems with the introduction of the Canon CXDI-40G Compact Digital Radiography System. The new flat panel detector, which is Canon's tenth-generation DR offering, can be retrofitted onto existing radiography equipment. The new system is equipped with a large image sensor and high-quality capabilities similar to the CXDI-40EG but in minimal housing. It is equipped with a 17" x 17" imaging area that enables X-ray images to be confirmed on an optional preview monitor about three seconds after exposure; the system contributes to timely and effective patient care.

- **Magellan Spine Technologies** (Irvine, California) reported the first human implant of its DART (Disc Annular Repair Technology) System for use after lumbar discectomy procedures. Following a standard discectomy procedure for a lumbar disc herniation, the patient was implanted with the Magellan DART device. The device is designed to prevent recurrent disc herniation and maintain disc height. The DART is an implant that provides a seal of the annulus following a standard lumbar discectomy procedure. When implanted, the DART is placed near the central axis of rotation along the posterior edge of the vertebral body. The device is aligned with the vertebral body load column, the strongest of the three primary spinal vertical load columns and is secured in place at the apophyseal ring. The DART has structural integrity similar to interbody fusion devices and provides support to maintain disc height.

## PEOPLE IN PLACES

- Meredith Mathews, MD, was named senior VP of **Blue Shield of California** (San Francisco). Most recently, he was chief medical officer for DaVita VillageHealth. Blue Shield of California is a not-for-profit health plan.

- **Compugen** (Tel Aviv, Israel) reported the appointment of Anat Cohen-Dayag, PhD, and Martin Gerstel as co-CEOs. Cohen-Dayag joined Compugen in 2002, and most recently was VP of R&D. Gerstel joined Compugen in 1997 as chairman of the board, and served in that role until January of this year when he was appointed president and CEO. Compugen is a drug and diagnostic product candidate discovery company.

- Tony Remington has been named VP of U.S. sales for **Endoscopic Technologies** (San Ramon, California), a provider of cardiac surgery devices. Most recently, Remington was VP of sales at Ekos, a venture capital-funded start-up company in the peripheral vascular field. Prior to Ekos,

he was regional manager at Guidant Cardiac Surgery, regional manager at Medtronic Urology and VP of sales at LeMaitre Vascular.

- Joachim de Jong was named operations manager for Europe for **HealthLink Europe** (Tilburg, the Netherlands). The company says that Joachim's past successes include managing order to cash and logistics projects for a prominent multinational medical corporation, which resulted in a number of company success stories. HealthLink Europe is a medical device distribution company.

- **LCA-Vision** (Cincinnati) reported that David Thomas has been promoted to COO from senior VP of operations, and Rhonda Sebastian has rejoined the company as senior VP of Human Resources. Sebastian most recently was VP of organization & management development at SENCORP. LCA-Vision is a provider of laser vision correction services under the LasikPlus brand.

- Alan Arroyo was promoted to VP of global sales and marketing for **Nextrials** (San Ramon, California). Arroyo had previously been a senior director of business development. Nextrials provides clinical research software and services.

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# MDD'S ORTHO EXTRA

ADDITIONAL DEVELOPMENTS IN ONE OF MED-TECH'S KEY SECTORS

THURSDAY, JUNE 4, 2009

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*Keeping you up to date on recent headlines in orthopedic healthcare:*

## **Award for pioneering stem cell research to mend broken bones . .**

■ ■ Funding from the Biotechnology and Biological Sciences Research Council (BBSRC) could lead to the development of new and better treatments for broken bones and other orthopedic problems associated with aging. Nearly £4 million has been awarded to scientists from the universities of **Keele, Imperial College London, Nottingham** and **Southampton** and who will work together combining stem cell science and tissue engineering to look at the development and repair of human skeletal tissue. Fractures, bone loss due to trauma or disease and other orthopedic conditions pose a significant clinical and socioeconomic problem, especially with an aging population, but as yet there is no large scale effective treatment for replacing or repairing damaged bones. Professor Richard Oreffo of the **University of Southampton**, who is leading the study, said: "Despite intense research, significant challenges for the reconstruction of tissues such as bone remain. Bone and cartilage tissue repair is a highly complex development process. A key requirement for these regeneration strategies to succeed remains our ability to understand skeletal cell activity, develop appropriate scaffolds and to understand how the environment the cells find themselves in affects their ability to interact with other cells to form new bone or cartilage." Over the next five years, the scientists will combine their expertise in skeletal stem cells, scaffolds and materials chemistry to identify the key growth factors, matrix proteins and physical conditions that will enhance tissue regeneration and ultimately lead to more effective skeletal repair strategies. "We believe a paradigm shift in approach is required if we are to lead internationally in regenerative medicine. Our findings of how stem cells, scaffolds and the physical environment can be combined to induce new bone and cartilage will be used to augment and accelerate bone repair. This will allow us to develop new regimes for cartilage and bone regeneration ultimately leading to more effective treatments" Oreffo said.

## **Combined ACL reconstruction and hemiarthroplasty effective but still experimental . . . .**

Combined ACL reconstruction and knee hemiarthroplasty can be performed safely with acceptable satisfaction rates. However, orthopedic surgeons should thoroughly discuss the procedure with patients beforehand and consider it experimental until further research is conducted, according to a knee specialist from the **University of Ottawa** in Ontario. "When it goes head to head with osteotomy, generally there is a faster recovery," Geoffrey Dervin, MD, said at the 28th annual meeting of the **Arthroscopy Association of North America** (Rosemont, Illinois) held recently in Las Vegas. "There is longer survivorship in the few randomized studies that have been done, [and it is] potentially an easier revision for total knee . . . and a more physiological alignment of the limb." The consecutive case series review involved 15 patients with a median age of 53.1 years who had a KT side-to-side difference of greater than 5 mm, a positive Lachman test result and symptomatic medial compartment arthritis. The first patient received a staged procedure, with the ACL reconstruction preceding the hemiarthroplasty by 4 months. The other 14 patients underwent an ACL reconstruction concurrent with the hemiarthroplasty. According to the study, patients were assessed at a mean of 31 months. All the WOMAC scores showed significant improvement, and seven of nine KT measurements showed less than 5 mm side-to-side differences. Dervin reported no infections or bearing dislocations, although femoral loosening resulted in one revision to total knee arthroplasty. Dervin said he considers the procedure to be effective, given its numerous benefits. "Potential benefits are that it is bone-preserving, has at least similar satisfaction to total knee [replacement] and allows for a better revision scenario for younger patients," he said.

## **Discovery of faulty genes could reveal risk of bone disease . . . .**

The discovery of faulty genes by **University of Edinburgh** (Edinburgh, Scotland) researchers could help people with Paget's disease, a painful bone condition. Omar Albagha, MD, has found three genes associated with the disease which, if detected early enough in people, could hasten diagnosis and treatment. Paget's disease affects around 3% of the population over 55 in the UK. The carefully regulated system of

renewing bone is disrupted. New bone cells (osteoblasts) increase dramatically, are overactive and enlarged causing weak, misshapen bones leading to pain deformity, osteoarthritis, fractures and even deafness. Genetic factors are important but until now, only one gene is known to be linked to one-third of the people with the disease. The research team in the rheumatology section at the university wanted to find other gene abnormalities that might predispose people to the disease. Speaking at the European Symposium on Calcified Tissue in Vienna, Albagha said, "This discovery is important so that we can better understand the development of Paget's disease and identify those at risk." There were 750 patients with Paget's disease in the study. They did not have the known faulty gene, but 104 of them had a family history of the disease. One thousand healthy people were in the control group. In the analysis of more than 300,000 gene variations covering all known human genes, three genes were found to be associated with Paget's disease. Further research is now under way to determine how these faults cause the disease. "Now we have identified the faulty genes, we will be able to develop ways to screen people ideally in their 30s with a family history of the disease. If necessary, we give them treatment early before the damage is done," Albagha said.

**Injured marines at risk for abnormal bone growth . . . .** Marines and other military personnel who are wounded in combat as the result of a high-energy trauma, such as a bomb blast, are likely to develop an abnormality known as heterotopic ossification. In this condition, bone forms within the soft tissues, such as muscle located near a fracture or other bone injury. New research conducted at the **National Naval Medical Center** (Bethesda, Maryland), is helping to pave the way for a better understanding of the mechanisms of the condition, and better courses of prevention and treatment. A discussion of the study appears in the May issue of *The Journal of Bone and Joint Surgery*. "The purposes of this study were to report our experiences with high-energy wartime extremity wounds, to define the prevalence of heterotopic ossification in these patients, and to determine the factors that might lead to development of the condition," said lead author Lt. Commander Jonathan Agner Forsberg, MD. Forsberg and his team compared data from 243 patients who were treated for orthopedic injuries between March 1, 2003, and Dec. 31, 2006, at the medical center, including patients who underwent amputation; external or internal fixation of one or more fractures; removal of damaged, dead or infected tissue, or 'debridement.' Heterotopic ossification is often associated with injuries to the brain or spinal cord, which can cause the entire body to react as though it is under attack. This type of response is known as a systemic inflammatory response. Forsberg said he believes this unique response to massive injury is the key to understanding why the abnormal bone growth occurs more often in military wounds than in those commonly treated in the civilian population. "Systemic inflammation is detrimental to this patient population," he noted. "We believe that this sort of response contributes significantly to the development of heterotopic ossification, and is the reason why the condition is more prevalent in the war-wounded population." Forsberg also said further study to be conducted at the medical center will focus heavily on treatment methods geared toward prevention of the condition. "Once we develop a better understanding of the events that cause heterotopic ossification, one of our primary recommendations will be treatments to prevent the condition from occurring."

— **Compiled by Holland Johnson, MDD Managing Editor**

Don't Miss these Upcoming Audio Conferences by

# **BioWorld<sup>®</sup> Today and Medical Device Daily<sup>™</sup>**

- ◇ **Parallel Trade in the EU: How to Comply with Unclear Requirements** (T09561)  
Tuesday, June 16, 2009 - 1pm to 2:30pm (EST)

In March 2009 CDER met with 16 makers of long-acting opioid drugs to discuss a sweeping new Risk Evaluation and Mitigation Strategy (REMS) for these extended-release pain killers. The FDA already approved REMS for 14 drugs and was seeking REMS on at least a dozen more even before the March meeting. In this *BioWorld Today* audio conference, REMS expert Arnold Friede, Esq. reveals how we got here, where we are going, and how to prepare for and manage the risk if your product makes the REMS hit parade.

- ◇ **Clinical Trial Agreement Indemnification Clauses: Protect Your Interests, Get Approval** (T09565)  
Thursday, June 18, 2009 - 1:00pm to 2:30pm (EST)

In a new 90-minute *BioWorld Today* audio conference, attorney J. Michael Slocum discusses how to negotiate challenging clauses in one of the most controversial issues in clinical trial negotiations. He describes the core aspects of indemnification analysis, and will showcase real-life language you can include in your CTAs that will cover you, and be acceptable to all involved.

- ◇ **CME and Off-Label Promotion: Find and Fix Noncompliance Before the Feds Do** (T09566)  
Tuesday, June 30, 2009 - 1:00pm to 2:30 pm (EST)

In a new *BioWorld Today and Medical Device Daily* audio conference, attorney Elizabeth Gobeil and former federal prosecutor Holly Pierson will detail the rules of CME and promotion. They'll examine what constitutes legitimate education, and identify the red flags that investigators are looking for. They'll also describe recent enforcement activities with an eye toward governmental priorities for the future.

- ◇ **Is the FDA asking too much of your 510(k)?** (T09567)  
Wednesday, July 8, 2009 - 1:00pm to 2:30 pm (EST)

On May 12, 2009 the FDA announced they would be "re-examining" Menaflex, a device cleared for marketing via 510(k). Will more devices follow? In this *Medical Device Daily* audio conference, device submissions expert Mark DuVal will discuss what FDA is asking for in 510(k) submissions, and how you can effectively respond to FDA's ever increasing demands for more medical and scientific information.

- ◇ **Comparative Effectiveness: Risks and Opportunities in the New Reimbursement Landscape** (T09568)  
Thursday, July 9, 2009 - 1pm to 2:30pm (EST)

In a new 90-minute *Medical Device Daily and BioWorld Today* audio conference, expert attorney Bernadette M. Broccolo will provide insight on reimbursement strategies in this new environment, and on the benefits the newly allocated \$1.1 billion stimulus can provide to smart companies in research, health IT and more.

- ◇ **BiMo Inspections: What You Need to Succeed** (T09569)  
Wednesday, July 15, 2009 - 1:00pm to 2:30pm (EST)

In this 90-minute *BioWorld Today* audio conference, former FDA inspector Carl Anderson discusses how to prepare for a BiMo inspection. He'll examine recent trends, describe what inspectors look for, and share dos and don'ts that he has seen in the field so you can be in compliance.

- ◇ **FDA Unapproved Drug Initiative-Determine, Prove and Ensure Compliance** (T09570)  
Thursday, July 16, 2009 - 2pm to 3:30pm (EST)

On March 30, 2009, the FDA fired its latest salvo against marketed unapproved drugs, giving nine companies 90 days to stop shipping certain narcotics. In a new 90-minute *BioWorld Today* audio conference, attorney Kurt R. Karst describes what a company can do to avoid being swept up in the FDA Unapproved Drug Initiative, and what to do if it is currently marketing an unapproved drug.

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