



Akron planning for seed fund to lure biomedical companies

By **JIM STOMMEN**
Medical Device Daily Contributing Writer

Turnabout is fair play, reasons the city of Akron, Ohio. Miami successfully lured Akron's native son, LeBron James, to leave the Cleveland Cavaliers and come play for the Florida city's NBA team, the Heat. Now Akron is eyeing a similar ploy, albeit one that will generate far less publicity. During his State of the City address last week, Akron Mayor Don Plusquellic said the city is planning to create a seed fund aimed at attracting out-of-region biomedical companies to the northeast Ohio city, as well as to help local start-ups grow.

Plusquellic said the Akron Development Corporation Seed Fund will have a focus of drawing early stage biomedical companies, both the local firms and those from elsewhere, to set up operations in the city.

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Medtronic gains FDA approval for Consulta and Syncra CRT-Ps

By **OMAR FORD**
Medical Device Daily Staff Writer

Medtronic (Minneapolis) reported that the FDA has approved its Consulta and Syncra cardiac resynchronization therapy-pacemaker (CRT-P) systems.

Consulta is the first CRT-P that includes Medtronic's exclusive OptiVol fluid status monitoring, which identifies patients at risk for worsening heart failure before symptoms develop.

OptiVol, measures intrathoracic impedance in heart failure patients using very low electrical pulses that travel across the thoracic cavity (the chest area encompassing the heart and lungs). The system measures the level of resistance to the electrical pulses, which indicates the patient's fluid levels. Used in combination with the Medtronic Cardiac Compass Report, the ability of OptiVol to

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FDA/AAMI annual conference

Foreman sees no support for abbreviated 510(k) program

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

RESTON, Virginia – Christy Foreman, acting director of the Office of Device Evaluation, made an appearance on the first day of the annual meeting held by FDA and the **Association for the Advancement of Medical Instrumentation** (AAMI; Arlington, Virginia), and offered little in the way of breaking news for industry, but her interaction with the audience suggested that at least one channel in the 510(k) pathway may be headed for the history books.

Foreman's principal motive for appearing was to go over the 510(k) program overhaul, but she inquired at one point as to the audience's views of the abbreviated 510(k)

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Agile Therapeutics CEO says he's 'all in' on innovation

By **JIM STOMMEN**
Medical Device Daily Contributing Writer

If you want to get Al Altomari going, ask him about the so-called "innovation gap."

The president CEO of privately held, venture-funded **Agile Therapeutics** (Princeton, New Jersey) doesn't want to hear even a suggestion that medical innovation is imperiled by tight financing and tighter regulation or that it may dry up and move away to friendlier locales.

As part of a lengthy conversation that appears in full form as the *BB&T* Interview in the April issue of *Medical Device Daily's* sister publication, *Biomedical Business & Technology*, Altomari offered his views on a variety of topics ranging from his company's development-stage contraceptive patches to the outlook for the drug-delivery

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Don't miss today's MDD Extra: Neurology



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*Report from Europe***Boston Sci reports first UK implant of Omega stent system****A Medical Device Daily Staff Report**

Boston Scientific (Hemel, UK) reported the first implant in the UK of the Omega platinum chromium bare-metal coronary stent system which recently received CE mark approval. The first implant was performed by Neal Uren, MD, Consultant Cardiologist, **Royal Infirmary of Edinburgh**.

The system incorporates a platinum chromium (PtCr) alloy designed specifically for coronary stenting and is intended to provide interventional cardiologists a bare-metal stent with improved acute performance in treating patients with coronary artery disease. "Omega is a highly deliverable stent, with fantastic conformability to the natural shape of the vessel. The platinum chromium alloy also provides excellent strength and radiopacity. In my opinion, these qualities highlight omega as a definite step-up in the bare metal stent market," said Uren.

The Omega stent system is part of the company's PtCr stent series, which includes the Taxus Element paclitaxel-eluting stent and Promus Element everolimus-eluting stent systems. All three stents feature the novel PtCr alloy and an innovative stent design, which combine to offer greater radial strength and flexibility while reducing stent recoil, the company said.

The Omega stent is offered in 48 different sizes ranging in diameter from 2.25 mm to 4.50 mm and lengths of 8 mm to 32 mm.

"The platinum chromium Promus Element stent has been well received by UK interventional cardiologists since its launch in November 2009, and we are pleased to offer a bare-metal coronary stent built on the same PtCr platform,"

said Tim Coutts, General Manager, UK Group, Boston Scientific.

Asuragen gets CE mark for IVD AmplideX

Asuragen (Austin, Texas) reported that they have achieved CE-marking and commercial launch in Europe of the AmplideX FMRI PCR Kit for the detection of CGG repeats in the fragile X mental retardation (FMRI) gene. The AmplideX FMRI PCR Kit is widely available through Asuragen's recently established network of distributors in Europe. The AmplideX FMRI PCR Kit is used as an aid in the diagnosis of fragile X syndrome and associated disorders, such as fragile X-associated primary ovarian insufficiency and fragile X-associated tremor/ataxia syndrome. The Kit provides a high throughput PCR and CE analysis workflow that can accurately resolve sample zygosity and reproducibly detect the full range of full mutation alleles in a single reaction. These assay capabilities reduce the need for Southern blot testing to 2% or less of all samples.

According to Dr. Sara Seneca from the **University of Brussels, Belgium**, "This new technology has distinct advantages over existing methodologies and was easy to adopt for routine use in our clinical lab."

"As we expand our molecular diagnostic portfolio for oncology and genetics with the launch of our proprietary CE-marked AmplideX FMRI PCR Kit, we have put in place an experienced and effective network of European distributors already dominant in the molecular diagnostic testing arena," said company President, Rollie Carlson PhD. "Our distribution partners will also serve a critical role in accelerating clinical validation and CE-marking of our portfolio of molecular diagnostic products."

Archimedes in partnership with Novo Nordisk

Archimedes (San Francisco) a healthcare modeling

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*Financings roundup***Accretive offers 6.5M shares of common stock****A Medical Device Daily Staff Report**

Accretive Health (Chicago) a provider of services that help healthcare providers generate sustainable improvements in their operating margins and healthcare quality while also improving patient, physician and staff satisfaction, reported the pricing of the public offering of 6.5 million shares of its common stock at a price to the public of \$23.50 per share. All of the shares are being offered by selling stockholders.

In addition, the underwriters have a 30-day option to purchase up to an additional 975,000 shares from the selling stockholders. The company will not receive any proceeds from the sale of shares in this offering.

In other financings:

- **HealthSpring** (Nashville, Tennessee) reported that it has priced its underwritten public offering of 7.5 million shares of its common stock. The shares were resold by the underwriters at a price of \$35.95 per share. The company has also granted the underwriters a 30-day option to purchase up to an additional 125,000 shares of common stock. The closing of the sale of the common stock, which is subject to customary closing conditions, is expected to occur on or about March 29.

The net proceeds from the offering, after estimated offering expenses and underwriting discounts, are anticipated to be about \$262 million, not including any proceeds from the potential exercise of the underwriters' option to purchase additional shares. HealthSpring expects to use at least 50% of the net proceeds for the repayment of indebtedness and the balance of the net proceeds for general corporate purposes, which may include acquisitions of similar or complementary businesses.

- **AssureRx Health** (Mason, Ohio) reported the closing of an \$11 million Series B financing. The personalized medicine company, which provides clinically-relevant information to help physicians select the right drug and the right dose for individual neuropsychiatric patients, will use the funds to expand direct sales and marketing for its first product, GeneSightRx, and for second generation product

MDD's Fun Facts

Editor's note: In an effort to enlighten your day, we now offer a weekly ponderance or two . . .

Old age . . . seniors rule!

What age relegates a person to senior citizen status?

You can join AARP, the world's largest senior advocate lobby group, at 50, although traditional retirement age is more than a decade away. The post-baby boomer Generation X thinks 50, or any age that has ever disparaged "new technology," is the Living Dead threshold. The U.S. government and corporate doctrines essentially release you from indentured servitude at 65.

Actual senior citizens (the Greatest Generation) regard 75 as the Dawn of Dependency, although they are happy the benefits begin at 65. Baby boomers (the first wave reached 65 on 1/1/11) misguidedly disavow age as just a number. My own keepin'-it-real diagnosis is that your body condition will dictate your portal to old age, usually with annoying-to-acute symptoms that begin around the mid-40s.

The census counted 3 million U.S. residents 65 and older in 1900; 35 million in 2000; and 40 million in 2010. All of us citizens reading (and writing) this will be included in a seniors class of 72 million in 2030 or as part of the Medicare brigade of 89 million in 2050. Oh, so many blinking turn signals!

– Michael J. Harris, Fact of the Week Editor

development activities.

The financing was led by Claremont Creek Ventures and Sequoia Capital and included participation of existing investors Cincinnati Children's Hospital Medical Center, Mayo Clinic and CincyTech, as well as new investor Allos Ventures. John Steuart and Dr. Brad Webb of Claremont Creek Ventures have joined the AssureRx board of directors, increasing board membership to seven. ■

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Agreement/contracts**Teleflex to distribute Polysite implantable infusion ports****A Medical Device Daily Staff Report**

Teleflex (Limerick, Pennsylvania) reported a global distribution agreement with **Perouse Medical** (Savigny-Le-Temple, France) under which Teleflex will distribute the Perouse line of Polysite intravenous implantable infusion ports.

With this agreement, Teleflex complements its Arrow vascular access product lines with a range of implantable infusion ports used for facilitating the administration of chemotherapeutics, related medications and fluids. The Polysite family, an established brand currently available in several European countries, includes a full range of port sizes, designs and catheter types. Perouse has more than 30 years of experience designing medical devices used in oncology, cardiovascular and interventional imaging.

Through its Arrow brand, Teleflex is a provider of catheter-based vascular access solutions. The Arrow family of products includes the ARROWg+ard Blue PLUS central venous catheters with Chlorhexidine-based technology and the recently introduced Arrow Evolution PICC with Chlorag+ard antimicrobial technology. Central venous access catheters, peripherally inserted central catheters, multi access catheters and acute hemodialysis catheters are now available in ErgoPack Maximal Barrier Precautions Trays, a system designed to support compliance with best practice and guidelines for catheter insertion.

In other agreements/contracts news:

- **Crospon** (Galway, Ireland) and **Smart Medical Systems** (Ra'anana, Israel) have signed a collaborative agreement whereby Smart Medical will produce a custom version of their NaviAid external channel endoscope accessory for Crospon, to permit deployment and positioning of Crospon's EndoFLIP imaging catheter.

John O'Dea, CEO, Crospon said, "This partnership with Smart Medical represents an excellent example of open innovation. We were first introduced to the NaviAid eighteen months ago and saw excellent potential for a modified version of the device to meet our needs in terms of deploying our EndoFLIP catheter to hard-to-access areas within the gastrointestinal tract. This endoscope accessory will play a key role as we move EndoFLIP into the bariatric revision market, in particular for gastric bypass pouch stoma repair. In the medium term it will also provide the means for us to deploy EndoFLIP within the colon for the assessment of distensibility disorders such as IBD and Crohn's disease."

Crospon makes minimally invasive medical devices for monitoring, diagnosis and therapy in the gastroenterology area.

SMART Medical makes medical devices in the field of gastro-intestinal (GI) endoscopy. Its NaviAid family of

products provides a standard endoscope with the means to overcome major challenges in GI endoscopy, through a series of single-use balloon devices and delivery systems.

- **Althea Technologies** (San Diego) has extended its service offering to include labeling, packaging, storage and distribution of drug and biological products through its co-marketing partner, **Sherpa Clinical Packaging** (San Diego). Sherpa is located adjacent to Althea's clinical and commercial-scale biologics and drug product manufacturing facilities. The proximity of the facilities to one another simplifies supply chain logistics for clients of each organization. Additionally, the co-marketing agreement will provide Althea's clients developing complex biologics products the option of producing, labeling and packaging of drug and biological products during a single campaign.

"Contract packaging services offered through our co-marketing partner, Sherpa, will allow our clients to meet aggressive manufacturing timelines. We are very excited to present these capabilities to our existing and potential clients," said Valerie McDonnell, VP, sales and marketing, Althea.

Althea is a contract development and manufacturing organization that provides services for plasmid DNA, recombinant proteins, and sterile products. Sherpa Clinical Packaging is a privately held firm specializing in providing Clinical Trial Material management services, including packaging, labeling, distribution and returns reconciliation, for pharmaceutical, biotechnology, medical device, *in vitro* diagnostics and dietary supplement companies. ■

Med-Tech Notes**MRI-compatible pacemaker implanted in Illinois**

Lee Ryan, 74, a Worth, Illinois man was among the first in Chicago to receive a MRI-compatible pacemaker. His pacemaker was implanted at **MetroSouth Medical Center** (Blue Island, Illinois), a hospital known for its cardiac care.

Ryan, who suffers from coronary artery disease, was having bradycardia, a heart arrhythmia condition that causes a slow heart rate. His heart rate was 35 beats a minute, which compares to 60 to 100 beats per minute for a person without a heart condition.

Until now, patients with pacemakers weren't allowed to have MRIs because the magnetic field produces heat, causing the pacemakers to malfunction or induce arrhythmia. The new **Medtronic** (Minneapolis) Revo MRI system is made out of nonmagnetic metal and has extra insulation on the leads – the wires that attach to the heart – which better absorbs the heat.

There are approximately 15 million Americans with pacemakers. About 200,000 of them have to forego MRIs and often undergo more invasive and risky diagnostic procedures because they have pacemakers.

Akron

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The city is aiming at raising about \$15 million for the fund from corporate donations and other sources, with the first investment expected to be made by this summer or perhaps sooner. The individual investments are likely to range from \$100,000 to \$250,000.

Deputy Mayor for Economic Development Bob Bowman said that the fund is designed to help companies through the especially difficult period during the costly development stages of potential products and before they are generating revenues. He said the investments from the city's fund might help provide stability for companies and help them attract venture capital or other funding.

Plusquellic told the *Akron Beacon Journal* that the money will be used to provide funding for biomedical companies when they are ready to expand on their own to buy equipment, land, buildings or other expenses.

He said the city's economic development efforts "are getting a great deal of traction out in Akron's Biomedical Corridor," which he first announced five years ago. Plusquellic noted that the state had recognized Akron last year as a Biomaterials Commercialization Hub, with a particular focus on orthopedics and wound-healing technologies.

In emphasizing the existing and future role biomedical companies have in his city, the mayor threw out what could almost be a long-form slogan: "The world is coming to Akron for its needs in new procedures, new instruments and new materials for medicine."

Plusquellic cited job growth at one of the start-up companies located in the city's Global Business Accelerator, saying that FMI Technologies has hired 15 new employees thus far in 2011. He added that the company had received an investment of \$18 million from an investor group in Shanghai, China, that he and other local officials had met with in that country last fall.

He noted that another biomedical company recruited from Israel, **Ni Medical** (Kfar Mallal), "is in the process of hiring salespeople and contracting with distributors. It plans to establish its worldwide center for technical support in Akron."

In his address, Plusquellic also cited what appears to be pending success after hosting a delegation from the Finish Funding Agency for Technology and Innovation. He said representatives of that group "are returning to Akron this spring with several companies that are considering operations here."

He said he is proposing to make Akron "Start-Up City USA," using the lessons learned from the Israeli playbook for developing new companies, including an impressive record in the medical space. "There are more Israeli companies on Nasdaq than all of Europe combined, more than India, China, Japan and Korea combined. They have pulled off one of the fastest-growing technology economies the world has seen, by nurturing start-up companies."

Plusquellic said "the idea that I've been advancing since labeling the Biomedical Corridor is that it has the promise to grow start-up companies into nationally known brands and provide jobs for our local residents in the process."

He reminded his listeners that Goodrich, Goodyear and Firestone, all huge names in the making of tires and all connected with Akron, "were once start-up companies too. With investors, innovation and leadership, they gained global greatness."

The first contributor to the seed fund is Cleveland-based Medical Mutual, which has pledged \$1 million to the fund. Power company FirstEnergy also has committed to an investment, without the amount having yet been specified.

"This seed fund will be directed at attracting early stage home-grown and other biomedical companies to set up operations in our Global Business Accelerator, then help them grow into their own space, Plusquellic said. "Forty out of 50 companies in our Accelerator are 'home-grown,' but we cannot ignite the huge potential for job growth by not reaching out across the U.S. and global marketplace to get our share of investments and jobs."

He also cited the work of the **Austen BioInnovation Institute** (Akron), which is readying new headquarters facilities in downtown Akron, praising that organization's president and CEO, Dr. Frank Douglas, "for the great work he has been doing in the short time he has been in Akron." The institute was established in 2008 to bolster the region's innovation in healthcare and has set a goal of bringing 2,400 jobs and 60 biomedical companies to the community within 10 years. ■

Med-Tech Notes

HTG changes name to HTG Molecular Diagnostics

HTG (Tucson, Arizona), a provider of molecular technology solutions, today announced it has officially changed its name to HTG Molecular Diagnostics. The company, formerly known as High Throughput Genomics or HTG, made the change to convey the company's strategic vision and direction in providing molecular testing capabilities for clinical researchers, pharmaceutical clinical development and clinical testing laboratories.

HTG's clinical sample-based testing solutions consist of multiplexed and multi-parameter assays for precise, cost-effective, and rapid management of mRNA, miRNA, gene fusions, translocations, and single nucleotide variants. The company is working with many tumor types and initial, proprietary programs are focused in melanoma, lymphoma and lung cancer.

"We're excited about the future of HTG Molecular Diagnostics and will continue to focus on supporting our customers in advancing their research, developing new drugs and finding better treatment options for patients," said TJ Johnson, CEO, HTG Molecular Diagnostics.

Medtronic

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monitor fluid status over time can provide physicians with important insights in conjunction with ongoing monitoring of other patient symptoms, which may lead to timely clinical intervention.

Additionally, both Consulta and Syncra are the first CRT-Ps that include Leadless ECG Waveform, which together with the Medtronic CareLink Network device data monitoring system, offer the possibility of remote follow-up in heart failure patients implanted with these devices. The company said that shipments of Consulta and Syncra will begin immediately.

"We are pleased to offer two unique, next-generation CRT-P options, which provide top-of-the-line features that may benefit hundreds of thousands of heart failure patients and the physicians who treat them," said Pat Mackin, president of the Cardiac Rhythm Disease Management business and senior VP at Medtronic. "These new innovations in the CRT space confirm our commitment to the development of novel, best-in-class cardiovascular technologies that are backed by industry-leading clinical research."

Both next-generation systems are the most comprehensive cardiac resynchronization therapy-pacemaker systems offered by Medtronic, providing fully automatic capabilities and adaptive therapies that help to ensure CRT, even during atrial fibrillation, and enable physicians to monitor their heart failure patients in the office or remotely. Additionally, both systems include unique programming flexibility to avoid phrenic nerve stimulation, which helps prevent the need for more invasive surgical approaches.

While both Consulta and Syncra systems include the same technology, they have differentiating features. Consulta includes Medtronic's OptiVol Fluid Status Monitoring, as well as Complete Capture Management, which helps improve patient safety and preserve the longevity of the device by continuously and automatically adjusting the pacing of the device to changing patient physiologic needs. Complete Capture Management also provides flexibility for clinicians so they may eliminate certain manual checks and devote more time to patients, procedures and complex cases.

"Atrial arrhythmias are the number one cause of reduced cardiac resynchronization therapy; therefore, there is a real need for next-generation devices that can deliver lifesaving CRT in this patient population," said Robert Canby, MD, **Texas Cardiac Arrhythmia and Seton Medical Center** (Austin, Texas). "These new innovative technologies allow physicians to proactively manage their heart failure patients, and offer cutting-edge features that contribute to patient safety and physician ease-of-use."

Consulta has been approved in Europe, Syncra has not.

To date the firm's cardiovascular division has been firing on all cylinders. Most recently it reported the worldwide launch of the Contour 3-D Annuloplasty, a device that could

help in the treatment of these patients (*Medical Device Daily*, March 15, 2011).

But the company's orthopedics division hit a huge bump in the road when the FDA sent it a letter saying that it wouldn't be able to approve its Amplify rhBMP-2 matrix without getting additional information from the firm (*MDD*, March 14, 2011).

Amplify is a recombinant human bone morphogenetic protein-2 solution, a synthetically produced version of a naturally occurring protein in the body, which is used to stimulate bone formation. ■

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Europe

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company, reported a collaboration with **Novo Nordisk** (Bagsvaerd, Denmark), a leader in diabetes care, to evaluate the effects of standardized vascular health checks on expected health outcomes. Archimedes will simulate these effects in a variety of European populations using the Archimedes Model.

Archimedes will generate a simulated population of patients that matches the demographic characteristics and other risk factors in the UK, Germany, France, Poland, Italy and Denmark. The health check, a multi-faceted preventative intervention, will be simulated in a variety of ways, but will be modeled after the program outlined in the Best Practice Guidance designed by the United Kingdom National Health Service.

Peter Alperin, MD, Archimedes' VP of medicine said, "Our collaboration with Novo Nordisk complements the work we have been doing within the healthcare industry to demonstrate the benefits of healthcare modeling when determining the best approaches to clinical care. The partnership adds further confirmation that the industry is interested in evaluating the potential benefits of various interventions using healthcare modeling, which can provide an accurate representation of how patient outcomes are affected by different interventions."

The simulation, which will forecast the effects of such checks over a period of 30 years, has already commenced. Researchers hope that quantitative information on the benefits of the health check will encourage increased participation. The study is expected to conclude during the first half of 2012, at which time the companies will determine the best means of disseminating the results. ■

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FDA/AAMI

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mechanism. While the survey was anything but scientific, it appeared that this portion of the device clearance process is not the stuff of industry's water-cooler chatter. Foreman noted that the total annual abbreviated 510(k) filings numbered 153 last year compared to the thousands of total 510(k) filings each year, and she asked the audience, "would anyone see it as a great loss if we didn't have an abbreviated program?" Nobody indicated it would present a problem for their firm.

Foreman may have the classic worst-of-both-worlds jobs. She currently serves as the acting director of the Office of Device Evaluation (ODE) at FDA's Center for Devices and Radiological Health, and has said she is not interested in the permanent job, but CDRH is apparently having a tough time filling the slot. Hence, Foreman has all the responsibility but not all the leverage. Her predecessor, Donna-Bea Tillman, PhD, left the job about a year ago, but Foreman is not the only member of the CDRH management team whose title includes the term "acting." A glance at the CDRH organizational chart indicates that more than 20 positions are held on an interim basis, while a number of positions are vacant. Foreman's prior post, deputy director for science and regulatory policy at ODE, is currently held by Johnette Foy, PhD, whose title also includes the modifier "acting."

Addressing the agency's review of the 510(k) program, Foreman said "it was a fairly comprehensive evaluation," noting that the working group had recommended that CDRH provide additional guidance on a number of standards, and consider revising the requirements for declarations of conformity. "The abbreviateds specifically use declarations of conformity," she noted, although special and standard 510(k) filings often use them as well.

Foreman also said of the proposal to build an online repository of 510(k) devices, which would include pictures, that FDA is "going to have a public meeting April 7," which will take place at the FDA campus in Silver Spring, Maryland. She also noted that CDRH is working on draft guidances for clinical trials, *de novo* applications, standard 510(k) applications, pre-submission interactions with FDA, and product codes. However, she also said CDRH intends to implement an assurance case study for infusion pumps as a pilot for assurance case studies in general, but as was already announced by others at CDRH, center managers also want to "establish notice-to-industry letters as a standard of practice . . . as an addition to guidances."

"We're also going to draft a transfer of the 510(k) ownership program," Foreman said, a move prompted by "too many mysteries about whom it was sold to." She said other ideas will wait for the upcoming report on the 510(k) program by the Institute of Medicine, including the proposal to fuse the terms "intended use" and "indications for use," the idea behind which she said was "to parallel the statutory language a little better." The dependence on the

IOM reporting date extends also to the proposal to require 510(k) filings to include more data on possible off-label use, but this is also the case for the notion of adding a class IIb category to the device clearance mechanism. Foreman claimed that FDA's intent with the IIb proposal is "to provide transparency" as to which applications will require clinical data – a claim industry views with some skepticism – but she also noted that FDA "received significant comment on that and we're going to defer" action until the IOM report, which is due in June.

Regarding the controversial topic of 510(k) review times, Foreman said "there's a trend" in that "the average number of FDA review cycles . . . is going up." Her chart indicated that the metric for average reviews was at 189 in 2010 vs. 143 in 2003. "We're trying to find out why."

"We have to send more and more deficiency letters" to industry for their applications, Foreman said, stating that despite the increase in "the total time to market, FDA is meeting its performance goals," including that 98% of applications are decided on within 150 days, "The manufacturer response time is increasing," she said.

Foreman was not as confrontational as CDRH director Jeff Shuren, MD, was in a recent hearing in a House Energy and Commerce subcommittee, after which he told reporters that the increased times were "all on industry." In response to a question posed by *Medical Device Daily* about a correlation between reviewer experience and requests for additional information, Foreman said "we did analyze the program six ways to Sunday" and that CDRH managers "didn't necessarily see an increase in the number of cycles, but [did see] an increase in the number of questions." One way to alleviate this issue as a flashpoint between FDA and industry might be to add industry's time to respond to FDA queries to the calculation of review times, but it is difficult to see why CDRH managers would feel compelled to go along with the idea.

Foreman said "the majority of requests [for additional information] were for failure to address guidance documents and or recognized standards," while the second most common request was prompted by what reviewers saw as inadequate device descriptions. However, Foreman indicated that the paperwork might be a stumbling block, asking attendees if they find form 3654 cumbersome. "What changes would you recommend we make?" she asked. ■

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ing on today's med-tech.

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Agile

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space in general to whether medical innovation is indeed imperiled in the U.S.

"I don't agree with those who think innovation can't happen," he said. "I'm an optimist; I see so much innovation out there. It's a matter of getting the right amount of people in the room who are very focused on getting the job done, and figuring out ways to finance themselves. It isn't easy, but it can happen."

Altomari agrees that financing is a big issue, "but you're seeing management teams being tremendously resourceful in finding ways to fund themselves." Because of the financing issues, "not everyone is going to make it, but those that do are going to be strong companies going forward. I'm all in, I'm excited about what's happening in these sectors."

In addition to discussing where his company's development of contraceptive patches (more on that later), he talked about transdermal drug delivery in general and how the drug-delivery space is developing.

"You're starting to see more and more attention being paid to transdermal delivery," Altomari said. "I'm aware, for instance, of work being done with nanotechnology on a transdermal delivery basis. Another company is working with an ionophoresis platform to deliver antifungals to the nails via ionophoresis charge."

He added, "There's a lot of really good stuff being done out there. The idea is how can we deliver drugs other than through the mouth or through the systemic system, can we deliver it more locally, either in a patch form or via nanotechnology or even mechanically with an ionophoresis platform."

Noting that "it makes sense to bring the drug right to the site of action without having to go through systemic action," he expressed the view that the drug-delivery space will see "more and more device-like combinations."

The key to earning FDA approval of such products, Altomari said, is that "if you're working with known molecules, then it's just a matter of working on delivering the drug in a new way."

That is what Agile is doing with its initial products, especially with its lead AG200-15 patch. "The simplest way to describe what we're doing is that we're taking two hormones that are some of the best and most well-known hormones. AG200-15 is a weekly contraceptive patch containing the active ingredients levonorgestrel and ethinyl estradiol," he said. "These two hormones are very well-known; they've been around for years. The FDA and physicians and women will know them."

The AG200-15 patch is applied once weekly for three weeks, followed by a fourth, patch-free week. "It's a soft patch, not rigid like a Band-Aid – it's like a soft fabric," Altomari said. "It has to hold up [over seven days of wear]; it has to be rugged enough to stay on the skin, but not so

rugged that when you take it off the skin is irritated."

And, "At the end of the day, it has to perform. This is . . . a matrix patch, meaning that it is almost like a film of drug that is in there. So it's not really a reservoir like some patches where the drug can actually be dumped out of there. Ours is a matrix; it actually comes out very slowly over time."

Enrollment in the phase III trial for the patch was completed last fall, reaching the planned 1,500-patient mark two months early. Altomari said that "definitely moves up" the timetable for filing a new drug application with the FDA, now targeted to occur in 1Q12.

In addition to an earlier filing, he said hitting enrollment early means the work necessary to move toward eventual commercialization also needs to be ramped up. "That means we have to marshal a lot of resources toward preparing for that filing and then for commercialization," he said.

As for dealing with the FDA, he has a high degree of confidence. "We're not bringing the FDA any new chemicals; we're taking them two hormones they know well. We're putting them together into a patch, so we're only changing the delivery. We have a lot of safety data and a lot of patient exposure – this is a pretty big trial."

Altomari added: "We have a lot of talent involved with this and we believe we have a very good proposition to bring forward to the FDA."

Beyond the two patches currently under development, a number of other products could feasibly become part of Agile's pipeline. "Our initial labeling is for contraception, but physicians also use birth-control pills for treating acne, for treating certain kinds of mood disorders for women, so we can look at other indications as our next step," he said. Another use might be in extended regimens for birth-control purposes.

He added that "another big idea that we have spent very little time on yet is that you certainly can use a patch to deliver other things, not just hormones. All of our efforts to date have been focused on getting these two products into the clinic, but we have plenty of ideas for the future."

Altomari noted that his background "has been more as a commercial guy, which essentially is my training. I came up through 23 years at **Johnson & Johnson** [New Brunswick, New Jersey] on the finance and commercial side of the business. Here at Agile, we're really more of a development-stage company, so for the first time in my career I'm really running all the development within an organization and a little bit of the commercial. It's a challenge, but that's why I signed up." ■

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Product Briefs

- **Carl Zeiss** (Peabody, Massachusetts) has introduced the IOLMaster 500, which it says is the fastest optical biometer available, and offers the best cataract penetration in the industry as well as proven keratometry. In addition, the IOLMaster 500 delivers highly precise measurements that are especially critical for meeting patient expectations for outcomes with premium intraocular lenses.

- **Elana** (Columbia, Maryland) has received FDA approval for a humanitarian device exemption (HDE), enabling a lifesaving cerebral bypass. "The Elana Surgical Kit may help those with a rare condition for whom there previously was no treatment option," said Jeffrey Shuren, MD, director of the FDA's Center for Devices and Radiological Health. The company expects that annually a thousand patients worldwide are eligible to be treated with the device. The Elana Surgical Kit is used in neurosurgery in numerous European countries as well as in Canada. In the U.S. the device has been used under a clinical study in St. Luke's Roosevelt Hospital in New York, University of Illinois at Chicago, University of Texas Southwestern Medical School and the University of Arkansas for Medical Sciences.

- **GerMed** (Garden City, New York) reported the introduction of the Sequential Suture Holder, also referred to as the Vijay-Robinson Sequential Holder. This surgical instrument is designed to easily attach to a surgical drape. As the sutures pass through the annulus of the heart valve, they're applied to clamps and placed into the Vijay-Robinson Sequential Suture Holder. This innovative idea for the sequential suture holder has revolutionized the way surgeons perform surgery. The sutures are detached one-by-one, in sequential order and applied to the sewing ring of the artificial heart valve. Then the needles are cut and all the sequential sutures in the holder are lifted up to maneuver the heart valve into the proper position. Then without any strings hanging below, the sutures are tied and cut. The Sequential Suture Holder is an aluminum, steel and plastic model of the Vijay-Robinson Sequential Suture Holder.

- **Sphere Medical** (Cambridge, UK) reported that the IVD-GE02 blood analyzer received FDA clearance. The firm claims the device is the first multiple-use, microchip-based blood analyzer to attain 510(k) approval. Based on Sphere's silicon microchip technology that allows the simultaneous analysis of a range of analytes, the IVD-GE02 platform is designed to measure glucose, pH, carbon dioxide, oxygen, and potassium ions in blood samples, with a performance that matches that of a standard clinical laboratory analysis. Sphere says it working to add new analytes to the panel, including hematocrit, lactate, sodium, and ionized calcium.

- **TranSI** (Wilmington, North Carolina) reported FDA clearance of the AxiaLIF 1L+ product line, an instrumentation and implant system for L5-S1 lumbar fusion. The AxiaLIF 1L+

system represents the next generation of the original AxiaLIF 1L system first launched in 2005 that has a clinical history of over 10,000 implants. "Our new AxiaLIF 1L+ system further demonstrates TranSI's commitment to continuously advance our proprietary AxiaLIF core technology. The 1L+ system builds upon our successful 2L+ system launched last year," said Ken Reali, TranSI's president/CEO. "The modular approach of the 1L+, coupled with the tapered tip design, allows for more precise distraction capabilities and improvement in pull out strength. Further, through our minimally invasive pre-sacral access, the 1L+ implant provides a biomechanically stable implant at the base of the spine."

Med-Tech Notes

SBI's STAR covered in more states

Small Bone Innovations (SBI; New York) said that 38 of the 39 independent member companies of the BlueCross and BlueShield Association will cover SBI's STAR Total Ankle Replacement system to benefit an estimated 98.5 million insured in 49 states.

SBI is an orthopedics company focused exclusively on serving patients and their physicians with technologies and treatments for joint replacement (arthroplasty) and post-traumatic reconstruction of the small bones & joints of the thumb, fingers, hand, wrist, elbow, toes, foot and ankle.

According to SBI, more than 90% of the approximately 175 million members of commercial insurance plans in the U.S. now have access to the STAR ankle replacement surgery, when deemed clinically appropriate by experienced surgeons.

MedQuist to voluntarily delist from Nasdaq

MedQuist (Franklin, Tennessee) has given formal written notice to the Global Market of The Nasdaq Stock Market of its intention to voluntarily delist its common stock from Nasdaq. The company will file a Form 25 with the SEC on April 4. The company anticipates that Nasdaq will suspend trading in the common stock within ten days of submission of its written notice and expects the delisting from Nasdaq to become effective April 14, ten days after filing its Form 25.

Through a series of transactions MedQuist Holdings has increased its holdings (direct and indirect) of the outstanding common stock of the company from 69.5% to approximately 97%. The company's board authorized the delisting of the company's common stock from Nasdaq after examining the positions that constitute the approximately 3% of the outstanding common stock of the company not held by holdings and determining that it is in the best interests of the company's shareholders to remove the company's common stock from listing on Nasdaq.

MedQuist makes medical transcription services and technology-enabled clinical documentation workflow.

MDD'S NEUROLOGY EXTRA

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

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Keeping you up to date on recent developments in neurology

Breakthrough in understanding of brain function . . . A team of researchers from the **University of Montreal** and **McGill University** (both Montreal) have discovered a type of “cellular bilingualism” – a phenomenon that allows a single neuron to use two different methods of communication to exchange information. “Our work could facilitate the identification of mechanisms that disrupt the function of dopaminergic, serotonergic and cholinergic neurons in diseases such as schizophrenia, Parkinson’s and depression,” wrote Louis-Eric Trudeau of the University of Montreal’s Department of Pharmacology and Salah El Mestikawy, a researcher at the Douglas Mental Health University Institute and professor at McGill’s Department of Psychiatry. An overview of this discovery was published in the *Nature Reviews Neuroscience* journal. Their results show that many neurons in the brain are able to control cerebral activity by simultaneously using two chemical messengers or neurotransmitters. This mode of communication is known as “cotransmission.” According to Trudeau, “the neurons in the nervous system – both in the brain and in the peripheral nervous system – are typically classified by the main transmitter they use.” For example, dopaminergic neurons use dopamine as a transmitter to communicate important information for many different phenomena such as motivation and learning. The malfunction of these neurons is involved in serious brain diseases such as schizophrenia and Parkinson’s. “Our recent research, carried out in part with Dr. Laurent Descarries at the University of Montreal, shows that dopaminergic neurons use glutamate as a second transmitter. That means they are able to transmit two types of messages in the brain, on two time scales: a fast one for glutamate and a slower one for dopamine.” Other research conducted by Salah El Mestikawy’s team at the Douglas Mental Health University Institute observed the same kind of bilingualism in brain neurons that use serotonin, a group of cells that communicate important information for controlling mood, aggression, impulsivity and food intake, and also those that use acetylcholine, an important messenger for motor skills and memory that is unbalanced by Parkinson’s disease, antipsychotic drugs and in drug addiction.

‘Sleeping Sickness’ pandemic offers insight into Parkinson’s . . . A bizarre disease that caused sufferers to fall into a deep ‘sleep’ while still being aware of their surroundings can offer us insight into the nature of Parkinson’s disease. Paul Foley from **Neuroscience Research Australia** says the pandemic of encephalitis lethargica, which swept the world in the 1920s, caused Parkinson’s-like symptoms in many sufferers, most of whom were less than 30 years old. “While we don’t know for sure what caused encephalitis lethargica, there is strong evidence that it was a virus that ultimately caused neurological symptoms to appear many years after the initial infection,” said Foley. “We can use this as a model to investigate the notion that there may be an infectious involvement in other brain diseases, such as Parkinson’s disease, and even Alzheimer’s disease and multiple sclerosis,” he said. Encephalitis lethargica had two distinct phases. During the first, acute phase, victims seemed to fall asleep, but often maintained an awareness of their environment. “They would close their eyes, and just didn’t have the will power to move themselves,” said Foley. As many as one third of sufferers died during this initial phase. In the second, chronic phase, which often commenced after a healthy interval of many years, most victims developed incurable neurological symptoms resembling Parkinson’s disease. People in this stage were depicted in Oliver Sacks’ book, ‘Awakenings.’ Foley says his research indicates that around 30% of those who developed chronic symptoms did not experience any acute phase symptoms. This suggests that it is possible an infection can have long term consequences for brain function, even where the initial infection is mild or even negligible,” he said. Foley said that encephalitis lethargica can help us investigate other infections that cause neurological symptoms after a long lag time, and can possibly help us understand the cause of some brain diseases. “The idea of an infectious involvement in diseases like schizophrenia and Parkinson’s disease is controversial today, just as it was in the 1920s,” he said. “But by the end of the 1920s, researchers had built up evidence with regards to encephalitis lethargica to show an infection can have serious psychiatric and neurological outcomes.”

Cooling treatment could reduce brain damage . . . More people who suffer cardiac arrests could soon be offered a cooling treatment to reduce the risks of them dying or becoming severely brain damaged. This comes as new NICE guidance advises doctors that the treatment is safe and works well enough for routine use in certain patients. "Therapeutic hypothermia" is a procedure used in some critical care units for people who have just been resuscitated following cardiac arrest due to a heart attack or other trauma. The treatment involves lowering a person's body temperature to 32-34°C while unconscious, using a blanket or mattress filled with air or fluid, or a special cap. The aim is to cool the person's brain and slow down the rate of cell damage. Up until now, there have been significant uncertainties among doctors about the procedure's risks and its potential to reduce brain damage and save lives, compared to standard intensive care treatments. This has meant while certain hospitals in the NHS may be offering this to some of their critically ill patients, others may not be considering it at all. The new guidance from the **National Institute for Health and Clinical Excellence** (NICE; London) advises that healthcare professionals could consider therapeutic hypothermia as a treatment option for people who are at risk of brain injury after cardiac arrest, under their hospital's usual arrangements for clinical audit/research, governance and consent. Bruce Campbell, chair of the interventional procedures advisory committee which produced the guidance for NICE said: "The evidence shows that controlled cooling of selected patients who have suffered cardiac arrest can increase their chances of survival. The therapy can also reduce the risk of severe brain damage, which can occur when blood flow to the brain is disturbed. While the outcomes of therapeutic hypothermia seem to look promising, we still need to find out more about precisely which patients are most likely to benefit from its use. This is why we are encouraging further research in this area." The NICE guidance does not advise whether or not the procedure should be funded – these decisions are made locally.

Research offers clue to halt Huntington's . . . Surprising findings from a study into the brains of transgenic mice carrying the Huntington's disease mutation could pave the way for treatments which delay the onset and progression of this devastating genetic disease. Researchers at the **Queensland Brain Institute** (QBI; Australia) have found that the brains of mice with Huntington's disease nevertheless retain populations of the precursor and stem cells which can give rise to new neurons. The potential for stimulating the production of new neurons in Huntington's disease patients thus remained high, according to Tara Walker, the postdoctoral fellow who carried out the work in the laboratory of Perry Bartlett. "Combined with previous findings which show that environmental enrichment and antidepressant treatment delayed both the onset and progression of Huntington's disease in mice, these findings are encouraging," Walker said. Huntington's disease (HD) is a neurodegenerative disorder that results in progressive motor, cognitive and psychiatric deficits which eventually lead to death. Currently, there is no known cure. However, the research, published this week in PLoS ONE, holds out hope that retained cell populations in the brains of Huntington's disease patients could one day be manipulated to replace degenerating neurons. "Now we know that the capacity to generate neurons is retained in animals in even advanced stages of Huntington's disease, further research will need to explore what stops this process from occurring," Walker said. "This may not only allow the restoration of neurogenesis, but may also allow this process to be harnessed to repair other areas of neuronal cell loss."

– **Compiled by Rob Kimball, MDD Staff Writer**
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