Medical Device Daily™
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FDA unveils plan to implement 25 changes to 510(k) program

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

The FDA yesterday unveiled a plan containing 25 actions it intends to implement this year to improve the most common path to market for medical devices, the 510(k) process. Key actions include: streamlining the *de novo* review process for certain innovative, lower-risk medical devices; clarifying when clinical data should be submitted in a premarket submission, guidance that will increase the efficiency and transparency of the review process; and establishing a new Center Science Council of senior FDA experts to assure timely and consistent science-based decision making.

Jeffrey Shuren, MD, director of FDA's Center for Devices and Radiological Health (CDRH), told reporters yesterday during a media briefing that these actions will result in a

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Deals roundup

Boston Scientific to acquire Atritech for up to $375 million

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

Boston Scientific (Natick, Massachusetts) continued with its recent string of acquisitions yesterday, when it reported that it signed a definitive merger agreement to acquire **Atritech** (Plymouth, Minnesota), a company that has developed a device designed to close the left atrial appendage (LAA) in patients with atrial fibrillation who are at risk for ischemic stroke.

The agreement calls for an upfront payment of $100 million plus additional potential payments of up to $275 million upon achievement of specified regulatory and revenue-based milestones through 2015 with the closing of the transaction expected to be completed in 1Q11.

Atritech has been working on getting its Watchman left

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Report from Europe

EKOS EkoSonic gets CE mark to treat pulmonary embolism

A *Medical Device Daily* Staff Report

EKOS (Bothell, Washington) reported that its EkoSonic endovascular system is the first endovascular device approved for the treatment of pulmonary embolism (PE) in Europe. The EkoSonic system, which was originally designed and approved to dissolve blood clots in the arms and legs, now has the added indication for treating this unmet medical need.

Robert Hubert, president/CEO said, "The CE mark is an important milestone for EKOS and a clear demonstration of our ongoing commitment to champion a better solution for treatment of PE. Hospitals in Europe may now begin ordering and using the EKOS device for this indication."

PE occurs in about 1 million patients in Europe annually

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Device launches new frontier for treating hypertension

By DIANA TUCKER
***Medical Device Daily* Contributing Writer**

After a year where only a handful of deals were consummated and few investment dollars were directed toward innovative medical devices, a novel interventional device brought down the house by being acquired for a billion dollars and launching a multi-billion dollar marketplace. Privately held **Ardian** (Mountain View, California) was recently acquired by **Medtronic** (Minneapolis) for an approximate $1.25 billion dollars. (*Medical Device Daily,* Jan. 16, 2011). This transaction opened the doors for a huge new market growth opportunity and a race for competing technologies to address this new frontier.

Ardian was able to demonstrate that hypertension – the leading attributable cause of death worldwide, affecting

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Don't miss today's MDD Extra: Orthopedics

INSIDE:

AHC Media

Financings roundup

pSivida to raise $10M in registered direct offering

A *Medical Device Daily* Staff Report

pSivida (Watertown, Massachusetts), a company developing sustained release, drug delivery products for treatment of back-of-the-eye diseases, including the investigational drug Iluvien for the treatment of Diabetic Macular Edema, reported that it has entered into a securities purchase agreement with institutional investors to raise gross proceeds of nearly $10.75 million in a registered direct offering through the sale of a total of 2,150,000 shares of the company's common stock and warrants to purchase 537,500 shares of its common stock. The net proceeds from the sale, after deducting placement agent fees and other estimated offering expenses, will be nearly $9.9 million.

The common stock and warrants will be sold in units, with each unit consisting of one share of common stock and the equivalent of a warrant to purchase 0.25 shares of common stock. Each purchaser will receive warrants to purchase a number of whole shares of common stock equal to 25% of the number of shares of common stock purchased by such purchaser. Each unit will be sold at a negotiated price of $5 per unit.

Each warrant will be exercisable for one share of common stock, has an exercise price of $5 per share and will be exercisable for five years. These securities are being offered through an effective registration statement.

The offering is expected to close on or about Jan. 24, subject to the satisfaction of customary closing conditions. The company intends to use the proceeds from this offering for general corporate purposes. ■

MDD's food for med-tech thought

"Other recommendations for which significant concerns were raised were more challenging to address those issues so we are delaying a decision . . . it doesn't represent that we are necessarily backing down, it does represent that we were listening and are trying to be responsive to what we were hearing."

– Jeffrey Shuren, MD, director of FDA's Center for Devices and Radiological Health, explaining to reporters that the agency has not backed down from tighter regulation of the 510(k) program, "FDA unveils plan to implement 25 changes to 510(k) program," pp. 1, 4.

Patent watch

Acacia Research unit adds new radiation therapy patent

A *Medical Device Daily* Staff Report

Acacia Research (Newport Beach, California) said that a subsidiary has acquired rights to a patent for radiation therapy technology.

"Acacia continues to grow its base of future revenues by adding new patent portfolios," said Paul Ryan, Acacia chairman/CEO. "As our licensing success grows, more patent owners are selecting us as their partner for the licensing of their patented technologies."

Acacia Research's subsidiaries partner with inventors and patent owners, license the patents to corporate users, and share the revenue. Acacia Research's subsidiaries control more than 170 patent portfolios, covering technologies used in a wide variety of industries. ■

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Restructuring roundup

Eigen ready for expansion in urology device market

A *Medical Device Daily* Staff Report

Eigen (Grass Valley, California), a specialty developer of medical imaging systems and software, reported a restructuring plan it says is designed to position the company for "rapid expansion" in the $5 billion urology medical device market. According to Eigen, it has transitioned through a voluntary restructuring process and is now positioned with a "unified management team and strong financial support."

"With Eigen's restructuring complete, the company is now well positioned to seize the promise of our breakthrough technology," said CEO Brian Burr.

According to the company, for the last three decades its name has been synonymous with high-definition imaging systems for cardiology and radiology in many of the world's finest hospitals. In addition, the company says it has built strong relationships with major OEM customers.

Eigen said it has expanded its expertise in imaging technology to urology by providing assistance with the very urgent need of diagnosing prostate cancer. Artemis is the first imaging technology platform to generate true, navigational and quantifiable 3-D prostate images from a standard 2-D ultrasound image, according to Eigen. ■

HIT roundup

Medidata extends budgeting application for trial sponsors

A *Medical Device Daily* Staff Report

Medidata Solutions (New York), a provider of SaaS-based clinical development solutions, said it has extended its Grants Manager web-based budgeting application with a new Contracting module, enabling sites and sponsors to negotiate clinical trial site budgets directly online, eliminating the burden of managing hundreds of email messages and reducing budgeting cycle times. Trial managers will also be able to monitor site negotiation status by study, site or across the portfolio in real-time, bringing unprecedented visibility to the process of site recruitment, the company said.

Sponsors currently rely on Medidata Grants Manager for benchmark cost data to quickly and accurately develop site grant budgets. The new Contracting module provides a natural extension to the budgeting process by offering negotiating, reporting and management of contracting in an integrated, online environment, Medidata noted.

"Grants Manager Contracting represents a significant opportunity to accelerate site recruitment by automating the arduous and manual back-and-forth between sponsors and sites during the clinical trial budget negotiation process, allowing sponsors to move seamlessly from planned budget to finalized site costs in less time," said Lori Shields, VP of Medidata's Data Operations. "In managing to the overall budget, sponsors have been enthused with the visibility to real-time site negotiation data, including signaling the need for intervention if negotiations begin slipping against the project timetable or forecasted budget." ■

Med-Tech Notes

American Scientific's S-1 statement effective

American Scientific Resources (Weston, Florida) reported that its Form S-1 resale registration statement has been declared effective by the Securities and Exchange Commission. The effective registration statement means that the company will commence reporting of its quarterly and annual financial results with the SEC and enable the company to seek to have its common stock quoted on the over-the-counter bulletin board.

The registration statement, while effective, also allows the selling shareholder to freely trade the shares included in the registration statement. The company is not issuing any new share capital and will not receive any proceeds from the sale of the shares by the selling shareholder.

Christopher Tirotta, CEO/chairman of American Scientific Resources, said, "We are pleased that, now that we have completed the SEC review of our registration statement, we will be providing our shareholders with greater disclosure and transparency through regular filings with the SEC including quarterly and annual reports. We will also seek to have our shares quoted on the OTCBB in the near future."

American Scientific Resources makes health and safety products, develops advanced technology and intellectual property and distributes product through established relationships and channels both in-house and through its network of healthcare distributors and retailers.

People in the News

• **Continua Health Alliance** (Beaverton, Oregon) has elected Qualcomm's senior director of market development, Clint McClellan, to president and chairman of the board. McClellan has represented Qualcomm on the board since 2009. Continua Health Alliance is a non-profit organization of healthcare and technology companies.

• **GSI Health** (Philadelphia) reported that Lori Evans Bernstein has joined the company as president. Previously, Evans Bernstein was CEO of a provider solutions division of ActiveHealth Management. GSI Health is a health information solutions provider.

510(k)

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"smarter medical device program that supports innovation, keeps jobs here at home, and brings important, safe, and effective technologies to patients quickly."

In September 2009 the CDRH set up two internal working groups to address concerns relating to the premarket notification process. Industry has argued that the 510(k) process is unpredictable, inconsistent and opaque, while consumers and healthcare professionals have argued that the review process wasn't robust enough to assure the safety and effectiveness of cleared devices. The agency also asked the independent and nonprofit **Institute of Medicine** (IOM; Washington) to study the program. The IOM expects to release its recommendations sometime this summer.

Two FDA working groups issued 55 recommendations in August; however the CDRH only intends to act on 25 of those recommendations at this time. Shuren explained that CDRH is also giving the IOM an opportunity to provide feedback on seven recommendations before making a final decision and is planning for a public meeting in April to seek additional feedback on two other recommendations.

The agency noted that it received 76 written comments to three public dockets from industry members, healthcare professional organizations, consumer groups, patient groups, third-party payers, venture capital groups, agency staff, trial lawyers, foreign regulatory bodies, law firms, individual members of the public, consulting firms and academic institutions.

Shuren explained that in cases where there were significant concerns raised by many parties and the agency had ways to address those concerns it did so. "Other recommendations for which significant concerns were raised were more challenging to address those issues so we are delaying a decision . . . it doesn't represent that we are necessarily backing down, it does represent that we were listening and are trying to be responsive to what we were hearing," he said.

As one reporter from the *Wall Street Journal* put it during the question and answer portion of the call, "these proposed rule changes have papered Washington in the last 20 minutes" with some safety advocacy groups accusing the FDA of backing down under pressure from lobbyists.

Shuren responded to these accusations by noting that the decisions that are being deferred until later have no real impact on patient safety but rather have more to do with providing more clarity for industry on the process itself. "In all of these cases we are deferring the decision; we've not made a decision," he said.

An example of a recommendation that the agency has deferred is one that involves a recommendation for CDRH to develop guidance defining a subset of class II devices that would be called class IIb devices, for which clinical information, manufacturing information, or, potentially, additional evaluation in the post-market setting would typically be necessary to support a substantial equivalence determination. The group suggested that a class IIb guidance would provide greater clarity regarding what submitters would generally be expected to provide for certain 510(k)s. This recommendation was met with strong opposition, however, as many said it would constitute an additional class, not a sub-class, and that CDRH does not have the authority to create an additional class. Others supported the recommendation as long as guidance was provided for such devices.

Stephen Ubl, president/CEO of the **Advanced Medical Technology Association** (AdvaMed; Washington) said the organization is "pleased with FDA's thoughtful analysis of comments by industry and its willingness to listen to views and concerns expressed by members of Congress, patient and physician groups and industry."

"The plan is clearly a good first step that will address some of the major problems with the program, including improving consistency, providing greater reviewer training, and streamlining of the *de novo* process," Ubl said in a statement AdvaMed issued Wednesday soon after the FDA released its recommendations.

"In addition, FDA's plan drops or defers for IOM review many proposals that would have significantly slowed patient access to new diagnostics and treatments and placed significant burdens on industry without corresponding health benefits," Ubl said. "The critical next step is how FDA implements the plan through guidances and regulations. Those details will determine whether today's proposed changes will improve patient access and American competitiveness."

When asked during the media briefing how these changes help to reduce the medical technology gap between the U.S. and Europe, Shuren said that the changes are designed to address the industry's complaints regarding the unpredictability and uncertainty of the 510(k) clearance process. "The U.S. is the leader in medical device innovation," he said. "The greatest threat is uncertainty from FDA. What we're proposing today is to address that uncertainty and to keep us a leader in innovation while at the same time – and this is critical – assuring devices are safe and effective."

Shuren added that one key difference between medical device regulations in the U.S. compared to in Europe is that in the U.S. a device has to be safe and effective. In Europe, a device has to be safe and it has to perform, which is not exactly the same as being effective.

"We also have to remember, let's not throw the baby out with the bathwater," Shuren said. He said there have been cases where a device was approved in Europe but did not meet FDA's safety and effectiveness requirements and was later removed from the European market, making his point that in the U.S. people are not used as guinea pigs. ■

For complete details of the FDA's 510(k) plan go to: http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHReports/ucm239448.htm

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Deals

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atrial appendage closure technology, which is being billed as an alternative to Warfarin, to market in the U.S.

The firm hit a stumbling block in gaining approval, when during an April 2009 meeting, FDA analysts and panel members expressed concern about the "complex" and "unusual" trial design of the PROTECT-AF study, which evaluated the device to the drug. Also problematic were a number of confounding variables, including the use of antiplatelet therapies and whether or not the device could be used in the general population.

"In terms of gaining approval in the U.S., having Boston Scientific's experience to help us navigate the regulatory path, is invaluable," Jim Bullock, president/CEO of Atritech told *Medical Device Daily*.

Bullock, who would not comment on the structure of the deal, said that the 11-year-old company is hoping to have FDA approval for the device sometime in 2013. The company is now just starting its PREVAIL STUDY, which is set to enroll up to 400 patients.

The device already received approval in Europe back in 2009, but doesn't have as strong a sales force as Boston Scientific to get the device into the hands of physicians overseas.

"Boston Scientific has a significant sales marketing force outside the U.S. and we're able to penetrate markets where we have very few representatives," Bullock said.

In the past few months, Boston Scientific has been busy with acquiring med-tech firms, which include the acquisition of **Sadra Medical** (Campbell, California) for $225 million in cash up front, with the potential for up to $225 million more in milestone payments (*Medical Device Daily*, Nov. 22, 2010) and acquiring **Asthmatx** (Sunnyvale, California) for $193 million (*MDD*, Sept. 21, 2010).

"What we're seeing now is Boston Scientific trying to reposition themselves," Larry Haimovitch, president of **Haimovitch Medical Technology Consultants** (Mill Valley, California) and a regular contributor to *MDD* said. "Hence the Asthmatx and Sadra acquisitions. I think in general Boston Scientific is trying to retool [their business]."

In a statement, Boston Scientific President/CEO Ray Elliot, echoed similar comments about strengthening the firm's business portfolio.

"This is an important acquisition in the fast-growing areas of atrial fibrillation and structural heart therapy, both of which are among our Priority Growth Initiatives," said Elliott. "Left atrial appendage closure represents a significant growth opportunity for Boston Scientific. Together with other recent acquisitions, we expect Atritech to play a key role in the realignment of our portfolio."

Attempts were made to get additional comment from Boston Scientific but as of press time, the firm had not responded to phone calls or e-mails.

Haimovitch added that the deal was structured in an interesting way, and gives Boston Scientific an option of playing it safe, should the device not gain FDA approval.

"If this product [Watchman] never gets regulatory approval, Boston Scientific doesn't have to pay most or any of those milestone payments," Haimovitch said. "What Boston Scientific did was hedge their bets. That's a smart move."

He said on one hand if the device is unsuccessful then investors can at least get a good deal of their money back. According to a March 2009 press release issued by Atritech, the company had raised at least $77 million. Haimovitch said on the other hand, that if the device was successful then there was the potential to have a much stronger return on the investment.

Analysts are saying that this deal provides entry into a new market for Boston Scientific.

"Although Atritech is a small deal for Boston Scientific, we believe this is an interesting take on a potentially compelling new market," said Rick Wise, an analyst with Leerink Swann in analysts notes. "That market's potential now is essentially being validated by two large cardiology players (Boston Scientific and **St. Jude Medical** (St. Paul, Minnesota)). St. Jude's recent **AGA** (Plymouth, Minnesota) purchase – whose new product pipeline also includes LAA closure technology – along with Boston Scientific's announcement yesterday could suggest that the LAA closure opportunity is indeed real.

Wise said that the LAA closure market could possibly reach $1 billion – given a large prevalence of AF of greater than 3 million patients in the U.S. and as much as 5.5 million patients worldwide. ■

Med-Tech Notes

DDL increases testing facilities

DDL (Edison, New Jersey), a specialist in package, product and material testing for the lifescience industry, said the DDL laboratory in Edison recently increased its testing capabilities for thermal performance testing and conditioning for thermal testing.

"With the addition of 4 new temperature chambers at the facility, we will be able to better serve the needs of all of our current and new customers for testing projects across the industry," said Peter Johnson, Packaging Engineer at DDL East. "We also added 2 Kaye KL 32 Channel Validators calibrated to 0.25°C and 40 remote data loggers calibrated to 0.25°C which will provide accurate results, with a high degree of sensitivity, when evaluating thermal/temperature controlled packaging."

DDL has also started the processes of becoming an ISTA 7E certified lab. ISTA 7E is a new standard for thermal transport testing and will include new protocols and standardized processes for thermal package design and testing.

Europe

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(600,000 in the U.S.), causing or contributing to 300,000 deaths each year. A PE is caused when a large blood clot obstructs the major blood vessels leading from the heart to the lungs. The victim's heart is suddenly overwhelmed with the task of pushing blood past this obstruction. Symptoms are similar to a heart attack.

About 5% of PEs are massive, resulting in rapid heart failure and shock. Without immediate therapy, death can occur. A large dose of clot-dissolving drug called a thrombolytic, delivered to a vein, was the only approved therapy for these patients; however, unintended bleeding, often fatal itself, is a much feared side-effect. Up to 40% of PE victims have less critical obstructions, often called sub-massive PE, which are currently treated with anti-coagulant medication. These medications do not remove the clot; they simply prevent the clot from growing larger. Recent, studies suggest that failure to remove these sub-massive clots may have long-term adverse events including recurrent PE, chronic pulmonary hypertension, and death. Up to 22% of these patients will die within 90 days. The EKOS EkoSonic System provides a new life-saving therapy for these patients. Until now, drugs were the only approved treatment.

Robert W. Hubert, President/CEO concluded that, "Since 2004, the EKOS system has been cleared for use by the U.S. FDA and European authorities for use in clearing blood clots in the arms and legs. EKOS pursued CE mark for treating PE based on receiving positive results from physicians treating these patients with the EkoSonic system, along with several centers publishing their findings in peer reviewed journals."

EverFlex+ stent system available in Europe

Healthcare products provider **Covidien** (Dublin, Ireland), reported the availability of the EverFlex+ self-expanding peripheral stent system in Europe.

The system is the next generation of EverFlex stent technology for the treatment of peripheral arterial disease. The company said the system strengthens its portfolio of stents used for treating the superficial femoral artery (SFA) and proximal popliteal lesions.

The new EverFlex+ system is designed to reduce the risk of fracture when elongated, improving clinical outcomes for patients. The next generation system offers the same customized technology as the current EverFlex system, retaining similar radial strength and flexibility, but adds even more durability. The EverFlex family of products is engineered to provide unmatched durability in a highly flexible platform, representing a significant advance in nitinol self-expanding stent technology.

EverFlex was launched worldwide in March 2006 as the first of the "long stents" for peripheral arterial disease and stenting for the SFA.

BSD reports first European sale of MicroThermX

BSD Medical (Salt Lake City), a provider of medical systems that utilize heat therapy to treat cancer, reported the sale and shipment of the MicroThermX microwave system to **Med-Italia Biomedica**, one of the largest interventional radiology/oncology distributors in Italy. This is the first European sale of BSD's MicroThermX microwave system.

BSD personnel will be attending the premiere of the European clinical use of the system, which will involve the treatment of a patient with a large hepatic tumor. The treatment will be carried out by a physician in Torino, Italy.

Med-Italia is a distributor and manufacturer of products designed for the interventional radiology and oncology market in Italy. They are an exclusive distributor in Italy for a number of large medical companies, selling strategically adjacent products to the same clinicians and market that will be targeted for the MicroThermX system.

BSD is in the final process of establishing both domestic and international distribution networks dedicated to selling its new microwave ablation product line. The company has elected to pursue the strategy of utilizing a network of leading specialty distribution firms who are focused on selling products in the field of interventional radiology, the target market for its ablation product line. To support the global distribution network for the MicroThermX product line, the company is increasing its marketing and sales staff. ■

Agreements roundup

Premier awards firestop products to 3M Building

A *Medical Device Daily* Staff Report

The **Premier** (Charlotte, North Carolina) healthcare alliance reported that a new agreement for firestop products has been awarded to the **3M Building and Commercial Services Division** (St. Paul, Minnesota).

The agreement is available to acute care and continuum of care members of the Premier healthcare alliance.

Premier is a performance improvement alliance of more than 2,400 U.S. hospitals and 72,000-plus other healthcare sites using the power of collaboration to lead the transformation to high quality, cost-effective care. ■

Hypertension

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roughly 1.2 billion people – can also be treated interventionally. Ardian's Simplicity catheter system uses an interventional catheter that ablates the nerves lying on the renal artery. Currently, and until Ardian/Medtronic's Simplicity catheter system is FDA cleared, drugs are the only treatment for hypertension. However, hypertension for millions of patients cannot be adequately controlled with drugs, even when they are taking up to five different blood pressure medications. Ardian's clinical trial presented at the **American Heart Association** (Dallas) meeting last November (*MDD*, Nov. 18, 2010) studied only patients whose blood pressure could not be controlled using five different drugs. In Ardian's clinical trial, 85% of drug resistant patients blood pressure dropped an average of 33/12 mg Hg. These results spurred not only a big acquisition in the industry but also opened the doors for the first new growth market opportunity since stents to dramatically improve patients' lives.

About 74 million people in the U.S. and more than 1 billion people worldwide are affected by hypertension and these numbers are increasing as the population ages and obesity accelerates. Of the 74 million hypertensive patients, about 35% are going untreated. Of the remaining 65% that are receiving treatment, only half have their hypertension under control. (*See Table 1*) The other half remain uncontrolled, largely because they are refractory to medical therapy (so-called drug-resistant hypertension [DRH]), which usually consists of a combination of several types of drugs including ACE inhibitors, angiotensin receptors, calcium channel and beta-blockers, and diuretics. In addition, there is also a significant non-compliance with medical regimens, either because of the number of pills a patient is taking or the side effects they produce (most commonly a loss of energy or sense of fatigue). This large patient population is ripe for an alternative therapy – and Ardian, along with other competitors, is ready to serve them.

The economic burden of the disease in the U.S. alone is projected at $76.6 billion this year according to the American Heart Association. In addition, DRH is on the rise, now affecting about 15% of U.S. patients and representing almost 11 million Americans – translating into an even higher cost burden. The cost of the antihypertensive drugs alone represent the single largest therapeutic category in the cardiovascular drug arena and in 2009 was valued at $37 billion. Besides the economic cost, for patients with refractory hypertension there is an associated high cardiovascular risk, including heart failure, diabetes, stroke, renal disease, chronic renal failure and acute myocardial infarction. (*See Table 2*)

The fact that a device may be able to disrupt the drug market currently in place represents a major revenue opportunity for both big cardiovascular companies currently facing slow growth as well as start-ups with other technologies that can produce similar results. With the average selling price for the Ardian catheter system projected to be about $5,000 per disposable, and if only the estimated 11 million refractive patients were targeted, this could be a potential $55 billion market opportunity. It is not surprising that multiple device companies are on the

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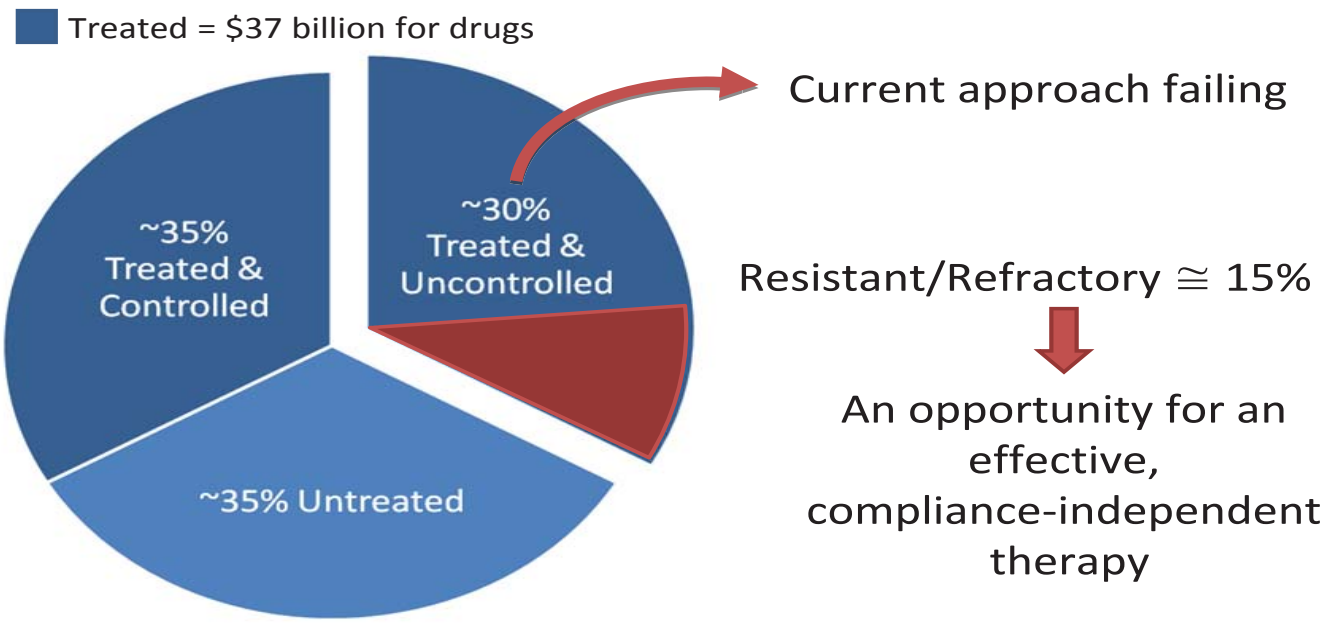
Table 1: Hypertension: The Unmet Need



Source: CryoMend

Hypertension

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horizon to also participate in this technological breakthrough including **CryoMend** (San Diego), **Mercator Medsystems** (San Leandro, California), **CVRx** (Minneapolis), along with some of the big boys such as **Boston Scientific** (Natick, Massachusetts) and **Johnson & Johnson** (New Brunswick, New Jersey).

The Ardian/Medtronic Simplicity system uses a catheter-based low-power radio frequency (RF) renal denervation device that ablates parts of the sympathetic nerves on the renal arteries. Although Ardian had planned to enroll 300 patients in its U.S. trial with a six month follow-up period, it has been reported that Medtronic may decide to increase the number of patients and length of trial with a possible U.S. launch sometime in 2013 or 2014. Ardian's device is currently approved for selling in Australia and has the CE mark for European sales. Professor Murray Esler, Principal Investigator for the Ardian Simplicity clinical trial, feels that most physicians who are already performing interventional procedures could learn this denervation procedure after watching 5-10 procedures. He also thought that it was possible for about 10,000 procedures to be performed in Europe in 2011. At approximately $5,000 per procedure, this represents a $50 million revenue opportunity for Medtronic in 2011.

CryoMend is a development stage device company with the exclusive worldwide rights to CryoMedix's patented cryoablation technology. CryoMend is developing a proprietary novel catheter-based system using a single-phase liquid coolant to reach the very cold temperatures (-80° C) required to ablate the renal nerve. Their closed system is compact, portable and does not require gas tanks. The system is similar in concept to Ardian's except they use very cold temperatures to achieve renal denervation instead of the heat generated by RF energy. The theory is that not only is it safer, but there should be much less pain for the patient due to the analgesic effect cooling contributes.

Boston Scientifics' Cardiology, Rhythm and Vascular division said that interventional hypertension is one of their key focuses for growth and development. Ray Elliott, CEO, in his last analyst meeting said, "Interventional hypertension: expect a $1 billion market in 2015 growing to over $5 billion in 2020. This is for medically refractory patients and we see it as a technology fit for Boston Scientific with its catheter, ablation and stimulation technologies." In addition to their RF catheter technology, Boston Scientific has in the past purchased **Cryocor** (San Diego) and **CryoVascular** (Los Gatos, California) and may be attempting to leverage those technologies into a hypertension catheter using cryoablation. Cryocor's freezing technology was incorporated into their internally developed cryo-therapy balloon used in the treatment of atrial fibrillation. Cryovascular had a peripheral dilatation system that utilized liquid nitrous oxide to provide precise cooling of the diseased artery during balloon angioplasty. However, both of these cooling technologies utilize nitrous oxide that may not be able to achieve the very low required temperatures.

Mercator is a medical technology company focused on the treatment of hypertension utilizing its catheter-guided, microfluid injection systems for site-specific, non-systemic delivery of therapeutic agents directly across any blood vessel. Their micro-infusion catheter delivers a drug in the adventitia of the renal artery wall that creates an effective cylindrical treatment zone to reduce the nerve signals. Human investigational trials are anticipated to begin soon with commercialization expected in 2013-2014.

CRVx has developed the Rheos system using Baroreflex

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Table 2: Impact of Reducing Blood Pressure

– A **5mm** reduction in blood pressure results in
- a 14% decrease in stroke
- a 9% decrease in heart disease
- a 7% decrease in death

– A **20mm** reduction in blood pressure results in
- a 50% decrease in heart disease-related death

Sources: American Heart Association, CryoMend

Product Briefs

• **ARUP Laboratories** (Salt Lake City) reported the availability of a new laboratory developed test designed to classify breast cancer into clinically significant molecular subtypes that are important for the management of the disease. The new test is a RT-qPCR assay that measures the expression of 50 classifier genes and five control genes to identify the intrinsic subtypes known as Luminal A, Luminal B, HER2-enriched and Basal-like. Along with a categorical classification of breast cancer subtype, it also provides quantitative values for proliferation, luminal gene expression, ESR1, PGR and ERBB2. The test is listed in ARUP Laboratories Laboratory Test Directory (LTD) as the PAM50 Breast Cancer Intrinsic Classifier. The PAM50 test offered by ARUP is the first clinical iteration of this gene expression signature, which has already been extensively validated in the research setting.

• **CAS Medical Systems** (Branford, Connecticut) reported FDA clearance for expanded labeling of its Fore-Sight Absolute Tissue Oximeter to monitor skeletal muscle of infants, children and adolescents weighing between 5 and 50 kg. The Fore-Sight Absolute Tissue Oximeter is used for the continuous, non-invasive monitoring of oxygen saturation of blood in the brain of patients in critical situations. Fore-Sight provides absolute measurement of oxygenation levels which allows clinicians to take immediate corrective action when those levels become dangerously low. With this FDA cleared indication, Fore-Sight can now be clinically utilized for use on both brain and skeletal muscle.

• **GE Healthcare** (Princeton, New Jersey) said the FDA has approved DaTscan (Ioflupane I 123 Injection), a radiopharmaceutical agent intended for use with single photon emission computed tomography (SPECT) imaging, for the detection of dopamine transporters (DaT) in the brains of adult patients with suspected Parkinsonian syndromes (PS). The first FDA-approved diagnostic imaging agent to help physicians evaluate neurodegenerative movement disorders, such as idiopathic (of unknown cause) Parkinson's disease (PD), DaTscan may be used as an adjunct to other diagnostic evaluations to help differentiate essential tremor (an involuntary shaking of the hands, head, and face2) from tremor due to PS. DaTscan cannot differentiate between the different types of PS.

• **PositiveID** (Delray Beach, Florida) has completed the development of its temperature-sensing microchip in conjunction with development partner **RFID Solutions** (Malaga, Spain). The microchip, which uses radio frequency identification (RFID) technology, is able to measure internal temperature within the body and communicate that temperature wirelessly to an external reader. The company plans to integrate the temperature-sensing microchip with its Wireless Body platform. The company expects its Wireless Body platform will continue to evolve with the addition of other bio-sensing capabilities, including glucose-sensing through its GlucoChip, which is currently under development.

• **Z-Medica** (Wallingford, Connecticut) has developed QuikClot Combat Gauze LE, a new version of its QuikClot Combat Gauze dressing specially designed and packaged for use by law enforcement and first responders. Similar to the QuikClot Combat Gauze which is carried by every warfighter currently serving in all branches of the U.S. military and many U.S. allied militaries, QuikClot Combat Gauze LE is a soft, white, sterile, nonwoven 3" by 12 feet z-folded gauze impregnated with kaolin, an inert mineral with no known contraindications. Each QuikClot Combat Gauze LE unit is individually wrapped in an easy rip, sterile pouch. Rather than a standard roll, Z-Medica uses a z-fold design which allows for a quicker release from the package and more sanitary application process in a trauma situation. Indicated for temporary external use to control traumatic bleeding, QuikClot Gauze is flexible and pliable and contours to all wounds, and can achieve hemostasis in traumatic bleeding situations in as little as three minutes, the company said.

• **Zyga Technology** (Minneapolis) said the FDA has granted the company 510(k) clearance to market the SImmetry Sacroiliac Joint Fusion System. The system is intended for treating conditions including degenerative sacroiliitis and sacroiliac joint disruptions. The SImmetry consists of a range of threaded, cannulated implants and associated instrumentation. The implants are designed to transfix the sacrum and ilium, providing stability for bony fusion. Sacroiliac joint dysfunction has been shown to be the source of pain for up to 30% of patients suffering from low back pain. Sacroiliac joint dysfunction can cause SI joint pain and is typically characterized by sacroiliac ligament pain, lower back pain, buttock pain, or pain in one or both legs.

Hypertension

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Activation Therapy (BAT). The Rheos system works by electrically activating the baroreceptors, located on the carotid artery, that regulate cardiovascular function. This system includes three components: a small device that is implanted under the collar bone, two thin lead wires that are implanted at the left and right carotid arteries, and the Rheos programmer system, an external device used by doctors to noninvasively regulate the activation energy therapy from the device to the leads. The Rheos system is CE-marked and approved for sale for hypertension patients in Europe. **Johnson & Johnson Development Company** has an investment in CRVx.

While Medtronic's recent acquisition of Ardian represents the first medical device for the treatment of hypertension, it is expected that some of the above companies represent additional opportunities in the new multi-billion hypertension market. ■

MDD's Ortho Extra

Additional Developments in One of Med-Tech's Key Sectors

Thursday, January 20, 2011

Keeping you up to date on recent developments in orthopedics

Routine osteoporosis screening recommended for all women over age 65 . . . In an update to its 2002 recommendation, the U.S. Preventive Services Task Force (USPSTF) now recommends that all women ages 65 and older be routinely screened for osteoporosis. This is the first final recommendation statement to be published since the USPSTF implemented a new process in July 2010 in which all of its draft recommendation statements are posted for public comment on the USPSTF website prior to being issued in final form. The draft recommendation statement on screening for osteoporosis was posted for public comment from July 6 to Aug. 3, 2010. The USPSTF also recommends that younger women with increased risk factors for osteoporosis be screened if their fracture risk is equal to or greater than that of a 65-year-old white woman who has no additional risk factors. White women are used as the benchmark because they have a markedly higher rate of osteoporosis and fractures than other ethnic groups. Risk factors for osteoporosis include tobacco use, alcohol use, low body mass and parental history of fractures. The USPSTF did not indicate a specific age limit at which screening should no longer be offered because the risk for fractures continues to increase with age and the evidence indicates that benefits can be realized within 18 to 24 months after starting treatment. The USPSTF also looked at whether to recommend screening men for osteoporosis but found insufficient evidence to make a recommendation at this time. This new final recommendation will become effective when it appears in the January 18 online issue of Annals of Internal Medicine and will also be available on the USPSTF website. "As the number of people over the age of 65 in the United States increases, osteoporosis screening continues to be important in detecting women at risk who will benefit from treatment to prevent fractures," said Task Force Chair Ned Calonge, MD, who is also the president and CEO of The Colorado Trust. "Clinicians also should talk to their younger patients to learn if they have risk factors that mean they should be screened." Osteoporosis screening involves a measurement of bone density, which is currently covered by Medicare. The most commonly used bone density measurement tests are dual-energy X-ray absorptiometry (DXA) of the hip and lumbar spine, as well as quantitative ultrasound of the heel, although current diagnostic and treatment criteria are based on DXA tests alone. The USPSTF noted that there is a lack of evidence about how often screening should be repeated in women whose first test is negative. In postmenopausal women who have no prior fractures caused by osteoporosis, the USPSTF found convincing evidence that drug therapies (including bisphosphonates, parathyroid hormone, raloxifene and estrogen) reduce the risk for osteoporosis-related fractures. Osteoporosis, a condition that occurs when bone tissue thins or develops small holes, can cause pain, broken bones and loss of body height. Osteoporosis is more common in women than men and is more common in whites than any other racial group. For all demographic groups, the rates of osteoporosis rise with increasing age.

New treatment unlocks curled fingers . . . Loyola University Health System (Chicago) is among the first centers to offer a new, nonsurgical treatment for Dupuytren's contracture, a debilitating condition that curls fingers toward the palm. Dupuytren's contracture affects one or more fingers, usually the little finger and ring finger. Growth of a cord of tissue under the skin causes the finger to bend inward so that the finger can not be straightened. The traditional treatment is outpatient surgery to remove the tissue, said Loyola hand surgeon Randy Bindra, MD. The patient has stitches for 10 to 14 days and needs to do physical therapy. It takes one to three months before the fingers become fully flexible. The new drug is Xiaflex (collagenase clostridium histolyticum). In an outpatient clinic, a doctor injects the drug into a Dupuytren's cord that is causing the finger to bend. The drug contains enzymes that break down collagen, one of the main components of the cord. The patient returns to the clinic the next day, and the physician gently extends the finger to break the cord. "The patient feels a pop and the finger opens up," Bindra said. No physical therapy is needed. A study of 306 Dupuytren's contracture patients found that 64% had a straight or nearly straight hand after one to three injections of the drug, compared with 7% who received a placebo. The FDA, which approved the drug, called it "an important advance in the management

of this disabling condition." Bindra said the injections must be carefully administered, because the drug can dissolve collagen in healthy skin and tendons. If injected in the wrong spot, the drug can snap a tendon and leave the patient unable to close the finger. As a hand surgeon who has done more than 100 surgeries for Dupuytren's contracture, Bindra knows exactly where to inject the drug. The FDA said the drug should be administered only by a health care professional experienced with the anatomy of the hand, because tendon ruptures can occur. The most common adverse reactions to the drug are fluid build-up, swelling, bleeding and pain in the injected area, the FDA said. Bindra said the drug does not necessarily cure the condition. In some patients, the abnormal tissue grows back and curls the finger, requiring further treatment. Dupuytren's contracture often runs in families. It is more common in men, especially in the case of Northern European descent. Other risk factors include increasing age and certain medical conditions, such as diabetes and seizures.

Columbia University uses technological innovation to study bone structure . . .

A team of researchers at Columbia Engineering and **Columbia University Medical Center** (New York) reported the results of the first study comparing bone structure in Chinese-American women to Caucasian women. The report, just presented at the **Orthopaedic Research Society**'s (Rosemont, Illinois) annual meeting at Long Beach, California, found that pre-menopausal Chinese-American women have far greater bone strength than their Caucasian counterparts, as determined by a breakthrough technological advance. The Columbia team was led by X. Edward Guo, Professor of Biomedical Engineering at Columbia University's School of Engineering and Applied Science, and, from Columbia University Medical Center, John P. Bilezikian, Professor of Medicine and Pharmacology, Marcella Walker, Assistant Professor of Medicine, and X. Sherry Liu, Associate Research Scientist. The team used a groundbreaking analytical technique developed at Columbia Engineering - Individual Trabeculae Segmentation (ITS) - to analyze the microstructure and strength of the trabecular, or spongy bone, one of the two types of tissue that form bone (the other is cortical, or compact bone). Trabecular bone is the most important site of osteoporosis-related fractures. Critical to the research was the use of ITS, an advanced 3-D imaging analysis technique that was conceived and developed in Guo's Bone Bioengineering Laboratory, and has a unique ability " using high-resolution computed tomography images - to quantify the plate and rod microstructure crucial to bone strength and osteoporotic fracture of bone. The Columbia group is the first to apply ITS to clinical studies; this is the first time they have applied ITS to ethnic studies of bone health. A total of 95 women were included in the study - 49 Caucasian and 46 Chinese-American. There were no significant age differences between the two groups. "We found in this research that Chinese-American women do not have the same risk of fracture as Caucasian women due to the plate-like structure of their bone, which offers mechanical advantages over the rod-like structure found in the bones of Caucasian women," Guo explained. "If you look at a building made of walls, you can see that it is much stronger than a building made only of columns. Columbia Engineering's ITS is the only established technique that can distinguish plate vs. rod and it clearly revealed in this study the striking magnitude of the differences between the bone structure of the Chinese-American and Caucasian women." Drs. Bilezikian and Marcella Walker led the clinical aspect of the study and quantified the microstructures in the distal radius and the tibia. "These are the two areas that the instrument can measure," Bilezikian said. "But we believe the data that come from these sites can be applied to other sites such as the hip." The researchers also found that Chinese-American women had better cortical bone quality than Caucasian women. The study has not yet explored potential explanations for these differences.

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