MEDICAL DEVICE DAILY™

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COMPANY RAISES $18.1M

Corus coronary artery disease test from Cardiodx fares well in PROMISE trial

By Omar Ford, Staff Writer

Cardiovascular genomic's specialist Cardiodx Inc.'s test to detect obstructive coronary artery disease (CAD) received long-term validation from a study published in this month's *American Heart Journal*. The Corus CAD test was evaluated in a genomic sub study of the Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE), which was sponsored by the National Heart, Lung and Blood Institute.

PROMISE results come shortly after the Redwood City, Calif.-based company raised $18.1 million in equity financing from a total offering amount of $41.8 million, last month.

The 2,370-patient study showed that individuals with low Corus CAD test scores had a lower likelihood of obstructive CAD in the arteries and the opposite is true for higher

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Researchers test brain tumor imaging for faster diagnosis than lab

By Stacy Lawrence, Staff Writer

University of Michigan researchers are working to establish a new technology to process images that's known as stimulated Raman histology (SRH). It enables cellular-level imaging during brain tumor surgery with results within a few minutes that could obviate the need to send slides out to a pathology lab for diagnosis.

The technology was initially developed as a potential aid for image-guided

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REPORT FROM ISRAEL

Rigid Chinese currency restrictions slowing Israeli med-tech investments

By Merrill Weber, Staff Writer

JERUSALEM – New Chinese currency transfer regulations are lengthening the process of Chinese investment deals in Israeli medical device companies, but Israeli entrepreneurs and their attorneys are confident that Chinese investment will continue.

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ALTERNATIVE TO CPAP

Australian newcomer Oventus oral device a potential disrupter in sleep apnea market

By Tamra Sami, Staff Writer

PERTH, Australia – New clinical data show that an oral sleep apnea device developed by Indooroopilly-based Oventus Medical Ltd. could be as effective as a CPAP device. And it could potentially replace the CPAP altogether.

Oventus Founder and Clinical Director Chris Hart told *Medical Device Daily* that he originally invented the oral appliance to manage his own snoring. He said he had chronic nasal congestion and couldn't tolerate a continuous positive airway pressure (CPAP) device.

Trained as a dentist, he sold his dental practice about three years ago to private equity investors to fund development of his invention, the O2vent T.

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APPOINTMENTS AND ADVANCEMENTS

Dynarex Inc., of Orangeburg, N.Y., reported several executive promotions and new hires as the company continues to grow, introduce new products and launch into new industry market segments. John Burns has been promoted to vice president of marketing after serving as director of marketing and new product development since joining the company in 2011. Igal Hodorov has been appointed director of new product development and brings more than 15 years of product development experience to Dynarex. Marc Somelofski, has been appointed director of regulatory and quality. Raymond Gillis will serve as the new account manager in Canada. Gillis has 16 years of experience in medical sales throughout Canada.

Endologix Inc., Irvine, Calif.-based developer of treatments for aortic disorders, said its board of directors has elected to separate the positions of chairman of the board and CEO, effective today. Dan Lemaitre, lead independent director, has been appointed chairman, and John McDermott will continue to serve as CEO and director.

Glaukos Corp., a San Clemente, Calif.-based company that develops products and procedures for the treatment of glaucoma, reported that Joseph Gilliam will join the company as chief financial officer and senior vice president of corporate development in May 2017. Gilliam will replace the company's current CFO Richard Harrison, who is retiring later in 2017. Gilliam joins Glaukos from J.P. Morgan, where he was managing director in the Healthcare Investment Banking Group and focused on the life sciences industry, including the medical technology, diagnostics and biotechnology sectors.

Stereotaxis Inc., a St. Louis-based company specializing in robotic technologies for the treatment of cardiac arrhythmias, reported a senior management transition. The company's board of directors has unanimously appointed David Fischel as acting CEO and chairman, effective immediately. Fischel replaces William Mills, who has resigned from his position as CEO and from the board. Fischel has served as a director of Stereotaxis since orchestrating the equity investment and positive strategic initiatives announced in September 2016. The company also announced the appointment of Nathan Fischel, CEO and founder of DAFNA Capital Management LLC, as a director.

DAILY M&A

Merit Medical Systems Inc., of South Jordan, Utah, has acquired product lines from both Athens, Texas-based **Argon Medical Devices Inc**. and Salt Lake City-based **Catheter Connections Inc**. for about $48 million. The combined revenues of the two acquired product lines were about $46 million in 2016, and the acquisitions were financed with a combination of cash and existing credit facilities

FINANCINGS

Promis Neurosciences Inc., of Mississauga, Ontario, is offering, on a private placement basis, up to 14 million units at a price of CDN$0.145 per unit for proceeds of up to approximately C$2.03 million (US$1.55 million). Each unit will consist of one common share of the company and one-half of a common share purchase warrant, with each whole warrant exercisable into one common share at a price of $0.20 per share for 36 months. The net proceeds of the offering will be used to further advance the company's Alzheimer disease portfolio, including development of its lead product PMN 310.

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BUSINESS OFFICE

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Cardiodx

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scores. The private company launched Corus CAD on the market in 2009.

Mark Monane, Cardiodx's CMO, said PROMISE tested a larger population than both PREDICT and COMPASS, two validation trials that evaluated the Corus CAD test. Monane said PROMISE addresses provider concerns over seeing the test evaluated on a larger patient population.

"The study helped confirm and extend previous information that the test is valid and that it measures what we want it to measure, which is the likelihood of obstructive CAD," Monane, told *Medical Device Daily*. "The trial gave us independent confirmation [of Corus CAD] with a large patient size."

The primary analysis found that the clinical event rate was lower in patients with low Corus CAD test scores as compared to patients with higher Corus CAD test scores. Additionally, the clinical event rate for patients with low Corus CAD test scores compared to noninvasive cardiac testing was low and no different from a negative or normal cardiac stress test or CT-angiography at 25-month median follow-up.

Nearly half of the patients in the sub-study were randomized to the coronary CT-angiography arm. In this group, 10.1 percent of patients were found to have obstructive CAD.

The relationship between Corus CAD test scores and clinical event rates remained significant even after adjusting for common clinical risk factors using the Framingham Risk Score. When the Corus CAD test was added to functional or anatomical testing, the Corus CAD test score provided independent and incremental information beyond that of noninvasive diagnostic imaging and helped to accurately reclassify patients to their appropriate risk levels. The increased risk of clinical events seen with elevated Corus CAD test scores were largely driven by a higher rate of revascularization procedures in this group, thus reaffirming that the likelihood of obstructive CAD increased with higher Corus CAD test scores, the company said.

Monane said that right now there are a number of blood tests that help tell the clinician about the future risk of a heart attack or a major adverse cardiovascular outcome. However, Corus CAD is different because it "focuses on the current likelihood" of a patient having obstructive CAD.

Corus CAD has been developed to be used in the early diagnostic setting, or primary care – before patients get to a cardiologist. It relies on a score, which clinicians use, along with other clinical information, to determine whether further cardiac testing is necessary, which can help patients avoid unnecessary exposure to radiation associated with medical imaging testing, as well as possible reactions to imaging dyes and/or potential complications from invasive cardiac tests requiring catheterization. The Corus CAD test is sex-specific to account for cardiovascular differences between men and women.

"I want to be perfectly clear, our test is not meant to substitute for other tests, but our test is meant to be used early in the diagnostic process," Monane said. "For some patients, the test will be helpful to rule out a cardiac cause." //

FINANCINGS

Second Sight Medical Products Inc., the Sylmar, Calif.-based producer of implantable visual prosthetics to provide some useful vision to blind patients, reported it has set 5 p.m. Eastern Time on Feb, 10, 2017 as the record date for its upcoming rights offering. Second Sight intends to issue non-transferable subscription rights to purchase units, composed of a share of Second Sight common stock and a five-year warrant to purchase an additional share of common stock, to holders of Second Sight's common stock on the record date. Under the rights offering, Second Sight will distribute one nontransferable subscription right for each share of common stock held on the record date. Each right will entitle the holder to invest $0.47 toward the purchase of units, each such unit, composed of one share of common stock and a warrant to purchase common stock, at a subscription price that is the lesser of $2 or the closing price per share of our common stock on Nasdaq on March 6, 2017, the close of the subscription period.

Veryan Medical Ltd., of Horsham, U.K., said it received a further £13.5 million (US$16.8 million) of funding in the form of both equity and debt. The new equity funding has been secured from its existing investors, including Touchstone Innovations, Invesco Perpetual and Seroba Life Sciences. The debt element of the round has been provided by Silicon Valley Bank in the form of a €5 million (US$6.2 million) capital term loan. Veryan's Biomimics 3-D stent technology involves adapting traditional straight stent designs to a patented three-dimensional helical shape, which more closely mimics the natural geometry of the human vascular system.

PRODUCT BRIEFS

Aura Biosciences Inc., of Cambridge, Mass., has cleared the investigational new drug application for the company's lead program, light-activated AU-011 in ocular melanoma (OM). This active IND enables Aura to begin initial clinical testing of AU-011, a targeted therapy that could transform the primary treatment of patients with OM, a rare and life-threatening disease.

Brain imaging

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surgery, but its level of accuracy spurred researchers to explore this application. SRH achieved comparable diagnostic results from neuropathologists as compared to a traditional process that requires 30 to 40 minutes, according to a new paper in *Nature Biomedical Engineering*.

Up next, through Santa Clara, Calif.-based start-up Invenio Imaging Inc., the researchers plan a large clinical trial to demonstrate that SRH-created virtual slides are equivalent to standard pathology techniques using processed tissue in making diagnoses. They are also working to integrate and advance machine learning to analyze these images, which they've already found to be useful.

"The expectation is that the time from when the tissue gets cut out of the patient to diagnosis is going to be cut dramatically. It could be an iterative, real-time process with the algorithm. It could pop up automatically with a predicted diagnosis," said Daniel Orringer, an assistant professor of neurosurgery at the University of Michigan Medical School who was the lead author on the latest study and is on the Invenio board.

SEEING CELLS AND CHEMICAL REACTIONS

The SRH technology is used to make virtual haematoxylin-and-eosin-stained slides that highlight necessary diagnostic cellular structures and architectural features. It introduces color to the images to highlight key features in brain tumors. The images resemble traditional stained tissue slides.

SRH builds upon stimulated Raman scattering (SRS) microscopy, which is used to create the underlying images from unprocessed specimens via a portable fiber-laser based microscope. In 2008, an initial paper was published on SRS by Christian Freudiger, a Harvard University professor in the department of physics as well as the department of chemistry and chemical biology.

"That was a big breakthrough; it amplified microscopic signal by 1,000 fold, enough to create very high resolution images. The practical implication was the ability to create very high-resolution, chemically based images without having to section stain or process the tissue," said Orringer

Invenio was founded by Sunney Xie of the department of chemistry and chemical biology at Cambridge-Mass. based Harvard University, who was the lead author on the original paper. Orringer met Xie at an industry conference, and they started to work together on how the technology might be applied to neurosurgery. They spent a year in the lab and then published early proof-of-concept data in 2013, just after founding Invenio. The effort then was devoted to translating the technology for human use, and conducting the newly reported study.

To test the SRH technology, University of Michigan researchers took 30 specimen samples that looked similar but were treated either with SRS/SRH imaging or traditional pathology methods and then presented them to a panel of neuropathologists.

This simulation found that the method accurately predicted diagnosis about 92 percent of the time. In addition, pathologists had 98 percent accuracy in determining if tissue was lesional or non-lesional and 100 percent accuracy in telling glial from non-glial tumors.

The researchers also used a machine-learning approach to analyzing the SRH images. By inputting quantified images, they were able to develop an artificial intelligence-based system that can predict brain tumor sub-type with 90 percent accuracy.

"We are not aiming to replace pathologists and radiologists through machine learning. Probably, medical decision-making will be much more based on these machine learning algorithms. They will be viewed as valuable tools," said Orringer.

The newly published research was backed by several programs that are part of the U.S. National Institutes of Health, including the National Institute of Biomedical Imaging and Bioengineering, the National Institute of Neurologic Disorders and Stroke, the Health Director's Transformative Research Award Program and the National Cancer Institute.

Orringer said he expects the NIH may step in to support the upcoming clinical trial as well, which is slated to start in early 2018. The company has received about $1 million in venture backing, according to SEC filings, and is in the midst of working to attract more.

The trial is expected to take a tissue specimen from the operating room that is cut in half with analysis by traditional means or the SRH system applied to each segment. The information won't be used for clinical decision-making, but researchers will compare the diagnoses and time spent with each method. The prospective, randomized clinical trial is expected to run in at least two institutions with tissue from about 200 patients.

Invenio has already had initial conversations with the FDA about the technology. "No regulatory barriers exist to the implementation of our existing microscope," Orringer said, adding, "We are very optimistic about our regulatory position."

REMOTE ASSESSMENT AND BEYOND THE BRAIN

This new approach to imaging and diagnostics could be significant for surgeons in hospitals that are lacking specialist diagnostic capabilities. There are less than 800 board-certified neuropathologists in the U.S., but about 1,400 institutions in the country that are licensed to perform brain surgery.

"In Michigan, we are operating in a resource-rich environment. But the places where most brain tumors are taken out, in the U.S. and certainly globally, are typically in resource-poor environments. The role for this technology, specifically the diagnostic capabilities, is much greater there," said Orringer. "In a lot of centers, a general pathologist or even the surgeons themselves make a diagnosis when they take a look at the tissue." He noted that the on-the-spot guidance during surgery can help to prevent unnecessary surgery, since some types of tumors are better treated with just chemotherapy.

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China

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"There's definitely a slowdown. We feel the slowdown," said Simon Weintraub. Weintraub and Daniel Green, partners at the Israeli law firm Yigal Arnon & Co., co-chair the firm's China Practice Group.

Chinese authorities are restricting overseas investments by Chinese companies unless there is corresponding inflow of funds. Specifically, banks in China have been required to "import" renminbi when money is transferred out of China. While this requirement has been in place before 2017, the ratios have since tightened. Banks in Shanghai are now required to import 100 yuan for every 100 yuan they allow a customer to transfer out of China, and banks in Beijing are required to import 100 yuan for every 80 yuan they transfer out.

"We had a much bigger potential pipeline before the currency transfer restrictions were enacted," said Weintraub. "Even [in the case of] deals that are in later stages, it is hard to get money out of China."

He added that even obtaining Chinese government approval for small deals, which used to take only a couple of weeks, now takes a couple of months. Nevertheless, he is confident that some smaller deals will be consummated.

In confirmation of Weintraub's analysis, on Jan. 30, Inovytec Medical Solutions Ltd., an Israeli medical device company, announced that it had received a $3 million investment from Vincent Medical Holdings, a Chinese medical device company listed on the Hong Kong Stock Exchange. Inovytec makes noninvasive respiratory devices for outpatient emergencies, including a device that has been cleared for sale in the U.S. by the FDA. Vincent Choi, founder of Vincent Medical, described Inovytec as a strategic investment that will enable Vincent Medical to expand its portfolio of products.

However, Bio Light Israeli Life Sciences Investments Ltd., an Israeli company developing ophthalmic diagnostics, devices and pharmaceuticals, reported that a Chinese investment fund had withdrawn its offer to purchase the company's public stock; it blamed the new currency rules for the decision. The agreement had been announced to the public on Dec. 29, 2016.

Green of Yigal Arnon & Co. noted that Chinese investments in Israeli medical device companies are smaller than the multibillion dollar deals that attract the attention of Chinese regulators and are in the several million dollar range. He also pointed out that Chinese investments in Israeli medical device companies generally include commercial as well as purely financial terms, and that manufacturing is often transferred to China as part of the agreement. A key component of the Chinese government's "Made in China 2025" initiative to upgrade China's industrial sector involves bringing additional manufacturing to China. As a result, the Chinese government may not find it to be in the country's interest to oppose this type of arrangement, said Green.

Zvi Shalgo, founder of PTL Group, an Israeli company that promotes Israeli businesses in China, says that his company has dealt with two Chinese companies that were unable to transfer money out of China. He said that his organization was able to help those companies transfer the funds "in cooperation with the government."

Hong Kong venture capital funds and family offices with large deposits of U.S. dollars or other Western currencies have been looking at Israeli technology opportunities over the past year. "Offshore money is not affected. Many of the larger Chinese players have funds offshore," said Green.

Eliezer Manor of Israel's venture capital industry speculated that the new currency transfer restrictions are likely to have a greater impact on venture funds than on operating companies, since operating companies are more likely to have funds deposited outside of China. However, the new regulations are intended to be of greatest impact on investment funds because investments by companies that are not located in China do not benefit the Chinese economy.

On the other hand, because the Chinese government is trying to slow the outflow of the Chinese currency, manufacturing facilities to be built in China and funds to be expended in the country might have an easier path in the regulatory process. Experts say that Chinese investments in Israel will continue; only the dialogue will change somewhat. Israel's medical technology is still very strategic for the China market, according to experts.

Both Weintraub and Green expect the number of Chinese-Israeli business deals to be in high double digits this year.

At present, Yigal Arnon & Co. is involved with two deals, one of which is valued at tens of millions of dollars. The law firm is one of many that handle Chinese-Israeli cross-border transactions. While the timeline to get all necessary approvals will be lengthened, Weintraub still expects the deals to be consummated.

"It's going to be a long process, but it will continue," he said. //

OTHER NEWS TO NOTE

Arbor Assays Inc., of Ann Arbor, Mich., reported that on Jan. 1, 2017, it became the first employee-owned life sciences company through the use of a perpetual trust. The owners sold their interests to the employee trust and provided seller financing. This method of employee ownership maintains the company perpetually for the benefit of its employees. Founded in 2007 by Russell Hart, Nancy Schmidt and Barbara Scheuer, Arbor Assays develops and manufactures detection and immunoassay products for research biomolecules. Bobbi O'Hara, R&D project manager at Arbor Assays, led the employee group through the transaction as the employee representative. Hart, Scheuer and O'Hara are directors of the perpetual trust that now owns the stock of the company.

Oventus

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The original prototype was made out of wax, but it wasn't very durable, so Hart teamed up with Neal Anderson, the current CEO of the company, to help develop a commercially viable product. They took the concept to the Commonwealth Science and Industrial Research Organization (CSIRO), which helped them develop the product for the market.

It only took about nine months to optimize the device, and by November 2014 they had registered the class I device with Australia's Therapeutic Goods Administration.

The O2vent T is an oral mandibular appliance about the size of an orthodontic retainer. It works by stabilizing the jaw position to bring the tongue forward to reduce airway collapse, which causes snoring.

What sets it apart from similar oral mandibular devices is an airway embedded within the device that protrudes like a small duckbill, giving the patient a "second nose." The airway delivers air to the back of the mouth bypassing obstructions from the nose, soft palate and tongue.

Although the original invention was intended for patients with high levels of nasal congestion, the O2vent is also effective in patients with severe sleep apnea. The CPAP is generally the first line of treatment for patients with obstructive sleep apnea; however, many patients have difficulty tolerating the devices, and oral appliances have emerged as an alternative treatment.

MOUNTING CLINICAL EVIDENCE

Results from a pilot study show that when used as a stand-alone device, the O2Vent T reduced the number of respiratory events by roughly 78 percent.

When the external airway of the O2vent was used as a CPAP interface, the pressure requirement dropped by two-thirds to about 2.3 centimeters of water. CPAPs typically require about 5 centimeters to 20 centimeters of water. The design of the CPAP connection enabled simultaneous nasal CPAP delivery, while patients continued to breathe through the device airway without a mask.

The reduced pressure requirement allows the company to develop a miniature CPAP that could be portable, even wearable, but with no mask or straps, Hart said.

The company is now engineering a CPAP that would be an add-on product to work with the existing device, attaching to the front of the duckbill-like protrusion.

Oventus is running three additional trials to gather more clinical evidence to validate the O2vent T as a viable alternative to CPAPs. It plans to run a head-to-head trial against a CPAP device this year. Data is expected by mid-year.

The goal is to capture all of the sleep apnea market, Hart said, noting that appliance therapy is often seen as a secondary treatment to CPAP, but "we hope to change that to go to combination therapy to treat the entire patient population."

"It's an absolute paradigm shift in how sleep apnea can be treated," Hart said, noting that the device "could wipe out all other treatments and be a major disrupter."

"As the clinical evidence builds, there will be no choice but for clinicians to start to incorporate the O2 technology into their treatment modalities. There are millions of patients outside of care who cannot tolerate current treatment so it's changing the lives of those patients."

The device is registered in Australia as a class I device, and it received 510(k) clearance from the U.S. FDA.

Oventus just launched the device in the San Francisco Bay area on Jan. 21, and it's being rolled out in four other beta sites in Los Angeles, Boston, Kansas and Delaware. Clinical partners in San Francisco have already delivered the O2vent T device to the first group of patients.

The company is in discussions about a China FDA application for mainland China and Hong Kong. Hart said it's not yet clear whether a Chinese trial will be required. Oventus hopes to also launch the device in Southeast Asia, Canada and Europe.

3-D PRINTING DELIVERS LIGHTNING SPEED DEVELOPMENT

The O2vent is custom made for each patient and is fitted and delivered under the supervision of a dentist. Using CAD software to create a 3-D drawing of the patient's mouth and bite, Oventus then uses 3-D printing technology to manufacture a custom-made medical-grade mouthguard from titanium.

Oventus opened the 3-D printing facility at CSIRO's Clayton site in Victoria in December 2016, and Health Minister Greg Hunt praised Oventus and CSIRO as a prime example of how Australian innovator firms can help reshape the country's economy.

"The partnership between Oventus and CSIRO is an example of collaboration between private sector and public research, creating businesses opportunities and new jobs – a key aim of the National Innovation and Science Agenda," Hunt said.

CEO Neil Anderson said the addition of the 3-D printing plant also adds value to the Australian supply chain as it will improve quality and reduce costs because the company can buy Australian titanium at Australian rates.

Oventus underwent a medical device single-audit program (MDSAP), which allows it to market in the U.S., Europe, Canada, Brazil, Japan and parts of Asia.

It also received ISO 13485 certification in January. The global certification verifies that the company's quality management system complies with the requirements of ISO 13485:20121 for the design, development and manufacture of oral appliances. The certification was issued by TÜV SÜD, an independent notified body.

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Brain imaging

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Orringer anticipates that the technology will be useful in cancer surgery in other parts of the body, particularly those in tricky areas to ensure clean margins such as in head and neck cancers.

"There are at least two million surgeries for cancer in the U.S. per year; most of those probably rely upon an intraoperative diagnosis. There is nothing unique about the brain. We are hoping to branch into other areas where diagnosis is essential," Orringer said.

He added that, ultimately, the aim is to incorporate data from molecular and genetic testing. These elements are part of a final diagnosis that Orringer expect will need to be incorporated, with certain molecular features accessed via these imaging techniques. //

Oventus

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Oventus listed on the Australian Stock Exchange in July 2016 (ASX:OVN) following an IPO that raised $12 million. The company's market cap is about A$50 million, and Hart anticipates being cash positive in the next year or two.

"We've had a very rapid take off and development phase. We're starting to get some real clinical data. We think we have the ability to redefine how sleep apnea is treated," Hart said, adding, "this is the first real innovation in the field for decades." //

OTHER NEWS TO NOTE

Biomerics, of Salt Lake City, reported the creation of its new Biomerics Advanced Laser division. Biomerics Advanced Laser will specialize in laser welding, cutting, ablating, and marking metal and plastic materials within the precision medical device market. The new division will be led by Mark Dustrude.

Cytori Therapeutics Inc., of San Diego, said the U.S. **FDA** Division of Industry and Consumer Education has granted small business status to Cytori for fiscal year 2017. The small business status allows Cytori to receive significant financial incentives, fee reductions and fee waivers for selective FDA medical device regulatory filings. Such designation makes the company eligible for a one-time waiver of the user fee for its first premarket approval application, potentially occurring later in 2017.

Exosome Diagnostics Inc., of Cambridge, Mass., has entered into an agreement with **Merck KGaA**, of Darmstadt, Germany, to help further the company's drug development efforts in oncology and other therapeutic areas, utilizing Exosome Diagnostics' proprietary technology platforms. The platforms span across both nucleic acid and protein, including Shahky, Exosome Diagnostics' exosomal protein capture and quantitative analysis instrument. This agreement represents the first publicly announced partnership that grants access to Exosome Diagnostics' recently unveiled point-of-care protein detection instrument.

Gamma Medica Inc., a Salem, N.H.-based company developing molecular breast imaging (MBI) technology, said it has partnered with **Medical Imaging Inc.** and **Capital X-Ray Inc.**, providers of medical imaging equipment, to give women in Georgia, Louisiana, Alabama, Mississippi, Idaho and parts of Oregon, Montana, Wyoming and Washington State access to Gamma Medica's Lumagem MBI system.

Maquet Cardiovascular LLC, of Wayne, N.J., filed an amended complaint against West Bridgewater, Mass.-based **Saphena Medical Inc.** and Albert Chin, who was once employed by Maquet, on Feb. 6, 2017. Maquet's amended complaint expands its patent infringement lawsuit, originally filed on Dec. 16, 2016 in the U.S. District Court for the Northern District of California, by adding two claims relating to specific actions taken by Chin and Saphena. The amended complaint seeks an injunction, Saphena's profits and costs of suit to remedy the alleged false advertising.

Dublin-based **Medtronic plc**, reported Medtronic Care Management Services (MCMS) is one of four vendors awarded a national contract from the U.S. Department of Veterans Affairs (VA) for Home Telehealth Technologies. MCMS has supplied the VA with telehealth solutions since 2011, and the new contract enables MCMS to continue supplying the VA with remote patient monitoring technology for one year, followed by four optional one-year periods exercised at the discretion of the VA.

Mimedx Group Inc., a regenerative medicine company based in Marietta, Ga., reported the decision of its board to authorize an increase of $10 million to the company's share repurchase program. This action brings the total authorized to $76 million since the share repurchase program began in May 2014. Mimedx reported that in light of the prevailing market conditions, the company's available resources and other factors, the board believes the stock repurchases are a favorable investment for the company. The board agreed to review this program again at its scheduled meeting on Feb. 22 and to consider a substantial additional commitment to this beneficial program.

Sectra AB, a Linköping, Sweden-based medical imaging IT and cybersecurity company, reported that **Cascade Medical Imaging LLC** (CMI), of Bend, Ore., has purchased Sectra Enterprise Imaging for Radiology. This solution will offer scalability for growth and provide a single platform for all clinicians to access patient images and information. The multiyear contract includes Sectra Pacs for diagnostic radiology, Sectra Breast Imaging Pacs for mammography workflow; and Sectra Business Analytics for measuring and improving the performance of radiology operations.

CARDIOLOGY EXTRA

Keeping you up to date on recent developments in cardiology

By Andrea Gonzalez, Production Editor

Researchers find better way to predict blood clots in the left ventricle

In research reported in the *International Journal of Cardiology*, scientists from Johns Hopkins University and Ohio State University presented a new method for predicting those most at risk for thrombus, or blood clots, in the heart. The critical factor, the researchers found, is the degree to which the mitral jet penetrates into the left ventricle of the heart. If the jet doesn't travel deep enough into the ventricle, it can prevent the heart from properly flushing blood from the chamber, potentially leading to clots, strokes and other dangerous consequences. The findings were based on simulations performed using the Stampede supercomputer at the Texas Advanced Computing Center and validated using data from patients who both did and did not experience post-heart attack blood clots. The work was supported by a grant from the National Science Foundation. The metric that characterizes the jet penetration, which the researchers dub the E-wave propagation index (EPI), can be ascertained using standard diagnostic tools and clinical procedures that are currently used to assess patient risk of clot formation, but is much more accurate than current methods. "We showed very clearly that the ejection fraction is not able to differentiate a large fraction of these patient and stratify risk, whereas this E-wave propagation index can very accurately stratify who will get a clot and who will not," said Rajat Mittal, a professor of mechanical engineering at Johns Hopkins University and one of the principal investigators on the research. The results were the culmination of many years of investigation by Mittal and his collaborators into the fundamental relationship between the structure and function of the heart. To arrive at their hypothesis, the researchers captured detailed measurements from 13 patients and used those to construct high-fidelity, patient-specific models of the heart that take into account fluid flow, physical structures and biochemistry. These models led, in turn, to new insights into the factors that correlate most closely to stagnation in the left ventricle, chief among them, mitral jet penetration. Working in collaboration with clinicians, including lead author, Thura Harfi of Ohio State University, the team tested their hypothesis using data from 75 individual – 25 healthy patients, 25 patients who experienced clots in their left ventricle and 25 patients who had a compromised heart but who didn't have any clots. Pending validation in a larger cohort of patients, the researchers found that based on the EPI measurement, one in every five patients with severe cardiomyopathy who are currently not being treated with anticoagulation, would be at risk of a left ventricular clot and would benefit from anticoagulation. The team plans to continue to test their hypothesis, applying the EPI metric to a larger dataset. They hope in the future to run a clinical study with prospective, rather than retrospective, analysis.

Cobra Pzf stent successful in SHIELD trial

Celonova Biosciences Inc., of San Antonio, reported the publication of primary endpoint results from its global, multicenter Pzf SHIELD clinical trial evaluating the first-in-class Cobra Pzf Nanocoated Coronary Stent. The nine-month findings were published in the *Journal of the American College of Cardiology* (*JACC*): *Cardiovascular Interventions*. In the study, the Cobra Pzf stent met prespecified performance goals for both the primary endpoint of target vessel failure and the secondary endpoint of angiographic late lumen loss at nine-months post-intervention. The trial was conducted under an investigational device exemption from the U.S. FDA. As the first nanocoated stent to be evaluated in clinical trials in the U.S., the Cobra Pzf stent combines a highly deliverable cobalt chromium platform design with a biocompatible Polyzene-F nano-thin polymer. A total of 296 patients from 35 centers in the U.S. and abroad with symptomatic ischemic heart disease received treatment with the Cobra Pzf stent in the single-arm, nonrandomized trial, many of whom had comorbidities including diabetes (33.7 percent), prior percutaneous coronary intervention (30.4 percent) and atrial fibrillation (12.2 percent). Currently, the company is further studying the Cobra Pzf stent in the COBRA REDUCE trial. This randomized controlled trial will evaluate the safety and efficacy of the Cobra Pzf stent to reduce the need for long-term dual antiplatelet therapy in patients to 14 days who are at high-risk for bleeding and require treatment for coronary artery disease.

Chest pain cardiac monitoring rule verified

Ottawa researchers have validated a rule that could safely take a third of chest pain patients in the emergency department off of heart monitors, according to a study published in the *Canadian Medical Association Journal*. Implementing this made-in-Ottawa rule could free up these monitored beds for sicker patients and reduce wait times. About 70 percent of chest pain patients who come to the emergency department are put in beds with heart monitors in order to detect a potentially dangerous condition called arrhythmia, or irregular heartbeat. However, previous studies have shown that this condition is rare, with less than two percent of chest pain patients experiencing it during their stay. This is why Ottawa researchers had previously developed a simple, highly sensitive tool to identify those patients who can be safely removed from heart monitors. According to the Ottawa Chest Pain Cardiac Monitoring Rule, patients can be removed if they have no

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current chest pain and there are no significant abnormalities in the electrocardiogram reading. Patients are normally taken off the monitor after about eight hours, when they are discharged home. Applying this rule will allow patients to be taken off monitors much sooner. If implemented when they first arrive, the rule will allow them to be redirected to a non-monitored area of the emergency department. To verify the rule, researchers observed chest pain patients in the emergency department. Then they tested whether the tool could accurately predict which patients had needed to stay on heart monitors because of irregular heartbeat. They found that 15 of the 1,125 patients admitted to The Ottawa Hospital emergency departments for chest pain between November 2013 and April 2015 experienced irregular heartbeat during their eight-hour stay. The rule was able to predict with 100 percent accuracy the 15 patients who needed to stay on heart monitors. It also indicated that 36 percent of the 796 patients who were monitored during the study could have been safely removed from the monitors.

Vitamin C supplementation may decrease the risk of AF after cardiac surgery

Harri Hemilä from the University of Helsinki, Finland, and Timo Suonsyrjä from the Helsinki University Central Hospital carried out a systematic review of vitamin C for preventing atrial fibrillation (AF) in high risk patients. They identified 14 randomized trials totaling 2,006 patients who had undergone cardiac surgery and one trial with 44 patients that had investigated the recurrence of AF after a successful cardioversion. There was substantial heterogeneity between the 14 cardiac surgery trials, but the heterogeneity was explained by the division of them between five trials carried out in the U.S. and nine trials conducted outside of the U.S. The five cardiac surgery trials carried out in the U.S. uniformly found no effect of vitamin C against post-operative AF. In contrast, the nine cardiac surgery trials conducted outside of the U.S. found a mean reduction of 44 percent in the incidence of post-operative AF and there was no heterogeneity between these nine trials. Five of the latter trials were carried out in Iran, two in Greece, one in Slovenia and one in Russia. The single study on the recurrence of AF after a successful cardioversion, which was carried out in Greece, found that vitamin C decreased the risk of AF recurrence by 87 percent. In the non-U.S. cardiac surgery trials, vitamin C decreased the length of hospital stay by 12.6 percent and intensive care unit stay by 8.0 percent. Some of the surgery patients in the non-U.S. studies were administered vitamin C orally, whereas in others vitamin C was administered intravenously. The latter route leads to substantially higher levels of vitamin C in the blood, thus the effects of the two administration methods might differ. Oral administration of vitamin C decreased the occurrence of post-operative AF by 73 percent, whereas intravenous administration decreased it by 36 percent. On the other hand, oral administration shortened the length of hospital stay by only 7 percent (0.4 days), whereas intravenous administration decreased it by 16 percent (1.5 days). Thus, the effect of intravenous vitamin C administration was greater for the length of hospital stay, but less for the occurrence of post-operative AF. According to the authors, "Vitamin C is a safe low-cost essential nutrient. Given the consistent evidence from the less wealthy countries, vitamin C might be administered to cardiac surgery patients, although further studies are needed to find out optimal protocols for its administration. However, there seems to be no rationale for further study of unselected patients in wealthy countries, but the effects of vitamin C for patients who have a particularly low documented level of vitamin C might still be worthwhile."

Discovery of 100+ new blood pressure genes could provide targets for treating hypertension

Scientists have found 107 new gene regions associated with high blood pressure, potentially enabling doctors to identify at-risk patients and target treatments. The study, led by Queen Mary University of London and Imperial College London, suggests that by using genetic testing, doctors could target medication to certain high blood pressure (hypertension) patients and advise on appropriate lifestyle changes to reduce a risk of heart disease and stroke. The findings are published in *Nature Genetics*. The researchers tested 9.8 million genetic variants from 420,000 U.K. Biobank participants and cross-referenced these with their blood pressure data. Of the 107 new gene regions, many were expressed in high levels in blood vessels and cardiovascular tissue, and could be potential new drug targets for hypertension treatments. The team also developed a genetic risk score by linking health and hospital data from U.K. Biobank participants with their blood pressure genetics. They showed that the score could be used to predict increased risk of stroke and coronary heart disease. The higher a patient's risk score, the more likely they were to have high blood pressure by the age of 50. Those on the top end of the risk scale were likely to have 10 millimeters of mercury (mmHg) higher blood pressure than patients with lower risk scores. For every 10 mmHg a person's blood pressure is above normal, the risk of heart disease and stroke is increased by around 50 percent or more. If such a genetic risk score could be measured in early life, it might be possible to take a personalized medicine approach to offset a person's high risk of stroke and heart disease. This could involve lifestyle interventions such as changing sodium and potassium intake, weight management, reducing alcohol consumption and increasing exercise.