MEDICAL DEVICE DAILY™

THE DAILY MEDICAL TECHNOLOGY NEWS SOURCE

THURSDAY, MARCH 23, 2017 VOLUME 21, NO. 56

INTERIM RESULTS COULD COME IN 4Q17

Trial serves as 'GENESIS' of Origin's path in obtaining approval for DFU therapy

By Omar Ford, Staff Writer

Treatment has begun on the first patients in Origin Inc.'s U.S. dose-ranging GENESIS trial. The Princeton, N.J.-based company has developed a technology to produce and deliver plasma-generated nitric oxide for the treatment of chronic diabetic foot ulcers (DFU).

Origin, which was formed in 2010 and was formerly called Advanced Plasma Therapies Inc., has developed a device with a hand-held, computer-guided system that generates nitric oxide from ambient room air within a defined plasma stream. From there, nitric oxide is generated and targeted toward the patients wound for about six to 12 minutes.

See Origin, page 3

OFFERS 360° ABLATION EVALUATION

Medlumics raises $37.2M to back optical wave, cardiac imaging to guide ablation

By Stacy Lawrence, Staff Writer

Cardiac ablation is increasingly common as a treatment for atrial fibrillation and other arrhythmias. Madrid-based start up Medlumics SL aims to make those procedures more precise via its Ablaview catheter that's intended to better guide ablation procedures and to detect to

See Medlumics, page 4

REGULATORY

FDA says lack of data a driver of lagging neuro *de novo* filings

By Mark McCarty, Regulatory Editor

The FDA webinar regarding *de novo* applications for neurological devices plowed little new regulatory ground, but one agency employee advised device makers that lack of information in pre-submission documents often triggers a need for further

See FDA, page 5

MUCH OF POPULATION LIVING IN POVERTY

Sub-Saharan Africa's med-tech sector to grow despite massive challenges

By Carmen Ho, Staff Writer

Sub-Saharan Africa (SSA) may be the least attractive region in the world in which to commercialize a medical device for the time being, but the market has high potential for development despite significant obstacles, say analysts.

According to a recent report by BMI Research, SSA medical device markets come with significant regulatory and operational risks that make them less attractive to med-tech companies. In addition to security threats and economic and political risks, the governments also allocate very few resources towards health care, making it difficult for both domestic firms and multinationals to grow in the sector. As a result, SSA continues to be the smallest medical device market in the

See Africa, page 6

IN THIS ISSUE

ORTHOPEDICS EXTRA

Executive Editor Holland Johnson on one of med-tech's key sectors

Read this week's Thursday Special

DAILY M&A

Dynatronics Corp., of Cotton Heights, Utah, said it will acquire substantially all of the assets of **Hausmann Industries Inc**., of Northvale, N.J. The purchase price is about $10 million in cash, subject to adjustments. Hausmann manufactures laminated treatment tables and wood products which complement Dynatronics' existing line of solid wood and custom design treatment tables.

Hologic Inc., of Bedford, Mass., has completed the acquisition of **Cynosure Inc.**, of Westford, Mass., a specialist in medical aesthetics systems and technologies, for $1.65 billion. Hologic first disclosed it would acquire Cynosure last month. (See *Medical Device Daily*, Feb. 15, 2017.)

FINANCINGS

Ben Franklin Technology Partners of Southeastern Pennsylvania; **Independence Health Group**, and **Safeguard Scientifics Inc.,** of Wayne Pa., said **Vitaltrax LLC,** of Philadelphia, received $150,000 in seed financing. Vialtrax is the first company to receive funds from the group's $6 million digital health funding initiative, which was announced in December 2016. Founded in 2016 by serial entrepreneur, Zikria Syed, Vitaltrax delivers a complete clinical trial data collection and patient engagement solution built on a cloud-based enterprise platform and a mobile application for patients.

APPOINTMENTS AND ADVANCEMENTS

The Washington-based Advanced Medical Technology Association (AdvaMed) reported that **CVRx Inc.** president and CEO Nadim Yared has been named chairman of the AdvaMed board for a two-year term. Yared has served on the AdvaMed board since 2011 and on the board of AdvaMed Accel (the division within the association focused on the needs of emerging growth companies) since its inception in 2012. As past chairman of AdvaMed Accel, Yared was instrumental in increasing engagement of small companies in AdvaMed's advocacy work. Yared succeeds BD chairman, CEO and president Vincent Forlenza.

Woodridge, Ill.-based **Endotronix Inc.**, a digital health med-tech company providing solutions for patients who suffer from advanced heart failure, reported the expansion of its management team. Recent hires include Katrin Leadley, chief medical officer (CMO), Richard Powers, chief information officer, and Mike Dilworth, vice president of manufacturing and operations. Leadley held CMO roles at Heartware and Jenavalve Technology as well as senior level clinical positions at Boston Scientific and Advanced Stent Technologies. Powers joins the Endotronix team after a tenure at Cardiomems, culminating as chief information officer. Dilworth was most recently senior vice president manufacturing operations at Nanosphere

MEDICAL DEVICE DAILY

Medical Device Daily™ (ISSN# 1541-0617) is published every business day by Clarivate Analytics, formerly the IP & Science business of Thomson Reuters. Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. All Rights Reserved. No part of this publication may be reproduced without the written consent of Thomson Reuters (GST Registration Number R128870672).

CONTACT US

newsdesk@medicaldevicedaily.com

Donald R. Johnston, (770) 810-3118 // Holland Johnson, (770) 810-3122 // Omar Ford, (770) 810-3125 // Mark McCarty, (703) 966-3694 // Andrea Gonzalez, (770) 810-3049 // Penney Holland, (770) 810-3047 // Lynn Yoffee, (770) 810-3123

OUR NEWSROOM

Lynn Yoffee (News Director), Holland Johnson (Executive Editor), Mark McCarty (Regulatory Editor), Andrea Gonzalez (Production Editor) Staff writers: Omar Ford, Bernard Banga, John Brosky, David Godkin, Larry Haimovitch, Sergio Held, Stacy Lawrence, Alfred Romann, Tamra Sami, Melody Watson

PRACTICAL INFORMATION

For Sales Inquiries: http://ip-science.interest.thomsonreuters.com/Bioworld_Sales_Inquiry. NORTH AMERICA, Tel: (855) 260-5607. Outside of the U.S. and Canada, Tel. +44.203.684.1797. For Customer Service Inquiries, NORTH AMERICA, Tel: (800) 336-4474. Outside of the U.S. and Canada, Tel. +44-203-684-1796. Or email bioworld.support@thomsonreuters.com. Copyright ©Thomson Reuters. Reproduction is strictly prohibited. Visit our website at www.medicaldevicedaily.com.

For ad rates and information, please contact Chris Venezia toll free at (855) 260-5607; outside the U.S. and Canada, call (646) 522-6243 or by email at christopher.venezia@thomsonreuters.com.

For photocopy rights or reprints, please contact Chris Venezia toll free at (855) 260-5607; outside the U.S. and Canada, call (646) 522-6243 or by email at christopher.venezia@thomsonreuters.com.

Send all press releases and related information to newsdesk@medicaldevicedaily.com.

BUSINESS OFFICE

Donald R. Johnston (Senior Director, Current Awareness), Penney Holland (Web Production Manager)

Origin

Continued from page 1

"From an external source, we're able to deliver a critical mechanism to the body, to allow healing to begin," Betsy Hanna, chief operating officer of Origin, told *Medical Device Daily*.

In the GENESIS study, the company will recruit up to 100 patients across 15 clinical sites in the U.S. After a two-week run-in period, patients will be randomized into one of four different dosing regimens or a standard of care treatment arm to assess efficacy and safety. Patients will be treated over 12 weeks and monitored for 12 weeks post treatment.

Standard for care treatment for chronic wounds includes dressing changes, wound cleansing, pressure relief (off-loading) and wound debridement.

Effectiveness will be measured by wound closure rate and wound closure percentage. Safety will be measured by wound-related adverse events, which include adverse events of all causes that affect the wound. The company said it would provide an update and initial readout of the interim results in 4Q17.

"We're going to do an analysis of the data at the mid-point of the trial to see the differences of the arms and the efficacy vs. the standard of care," Hanna said. "That data will [determine] the time in which we file for a new IDE for a pivotal trial."

Because of the nitric oxide component, the technology is being treated like a combination product by the FDA.

"The FDA has put us in the device division," Hanna said. "But because of the mode of action of nitric oxide, we do have in our review process and our regulatory process members from the [Center of Drug Evaluation and Research] are also involved in the discussions of the safety and efficacy of the therapy."

Plans eventually call for the company to seek approval in Europe.

"Our target initially is going to be looking at wounds that have failed the standard of care," Hanna said. "There are a number of different products out ... [but] nothing with an overwhelming clinical success in treating these kinds of ulcers. You've got a market out there for advanced wound treatment products and the market is more than $13 billion."

She added, "We see this as a wide open opportunity, and our job is to get the first use and indication approved for our device, to demonstrate we can make a difference in that healing."

Origin isn't alone in its goal to get secure FDA approval for a diabetic foot ulcer technology.

One of the most notable companies in the space is Sanuwave Inc. The Alpharetta, Ga.-based firm has been vying to gain FDA approval for its Dermapace technology for a number of years. The device has CE mark approval and uses a noninvasive, biological response for the repair and regeneration of skin, musculoskeletal tissue and vascular structures.

Sanuwave initially hit a major snag in its plans to bring the device to market back in 2011, after it was revealed in the 206-patient trial that there was no statistically significant difference regarding wound closure after 12 weeks between the sham treatment and the treatment with Dermapace. Sanuwave has been notably quiet with its progress in the U.S., but last month it launched a blog on its website to update key developments with its product line.

Integra Lifesciences Holdings Corp. also has applications in soft tissue repair and regeneration applications. The Plainsboro, N.J.-based company broadened its strength in the space when it acquired Tei Biosciences and Tei Medical for $312 million. (See *Medical Device Daily*, June 30, 2015.) //

OTHER NEWS TO NOTE

Brightree LLC, of Lawrenceville, Ga., said its home medical equipment billing and business management module has enhanced integration capabilities with Airview and Myair, Resmed's cloud-based sleep and respiratory care patient management and patient engagement platforms. The latest enhancements integrate within Brightree's Document Management module. This connection enables HME providers to efficiently perform regular compliance/therapy adherence checks and maintain audit compliance. San Diego-based Resmed acquired Brightree in 2016. (See *Medical Device Daily*, February 24, 2016)

Nexstim plc, of Helsinki, Finland, said its wholly owned subsidiary Nexstim Inc. has signed a new independent selling representative agreement in the U.S. with **Jtec Surgical Inc.** to represent the Nexstim Brain Mapping (NBS) system. Jtec Surgical will cover the Southern California region. The NBS system is used for the presurgical mapping of the speech and motor cortices of the brain.

Nuance Communications Inc., of Burlington, Mass., and **Epic Systems Corp.**, of Verona, Wisc., reported a partnership to deliver computer-assisted physician documentation (CAPD) capabilities embedded within Epic. The Epic Notereader CDI solution leverages artificial intelligence capabilities found in Nuance CAPD technology to automatically provide real-time clinical documentation improvement (CDI) feedback to physicians at the point of care. This improves severity-adjusted quality scores and captures appropriate reimbursement and risk adjustment factors that are critical to proper care and management of patients.

Transenterix Inc., of Morrisville, N.C., reported it has expanded the clinical adoption of its Senhance Robotic Surgical System to include a full range of hernia repair surgeries. St. Marien-Krankenhaus Siegen in Germany was the first site to begin using the Senhance for unilateral and bilateral inguinal hernia repairs as well as ventral hernia repairs. Doctors performed up to three robotic hernia surgeries per day with the Senhance during the first weeks of its clinical use at the hospital. The Senhance Surgical Robotic System has been granted a CE mark but is not currently available for sale in the U.S.

Medlumics

Continued from page 1

what extent these have achieved their aims.

Medlumics has raised a €34.4 million (US$37.2 million) series B round to further refine Ablaview to take it into the clinic, as well as to do EU clinical testing, start marketing in Europe and to conduct a pivotal U.S. trial.

TISSUE VIA OPTICAL WAVES

The device is based on optical coherence tomography (OCT), a light-based imaging technique that provides high-resolution sectional tissue information by using optical waves that can be used to guide ablation procedures and for diagnostic purposes.

"Ablaview is incorporating tissue evaluation technology. We use our technology platform to sense tissue properties in the environment to sense, first, where there's contact; whether that contact is stable; and, during ablation, to detect when a lesion has been created," Medlumics CEO Eduardo Margallo told *Medical Device Daily*.

"It can discriminate between healthy and necrotic tissue. You can spot treatment gaps and treat again. That's what it brings, information about the ablation environment and lesion detection and assessment," he explained.

The Ablaview previously had forward imaging only, but the clinical iteration of the device that's in process is expected to offer a 360-degree, real-time evaluation of the ablation procedure, as well as a means to evaluate if it has achieved its aims.

"The new device incorporates technology that allows us to sample tissue in all possible directions around the catheter, we are now in the process of finalizing this development," said Margallo. "It's our plan to start a safety study toward the end of this year or toward the beginning of next year." Prior to that, once the new iteration of the device is complete, Medlumics anticipates a first-in-human study that will start in the next few months.

Medlumics initial aim is to gain a CE mark and to start marketing in Europe, after that it is planning a pivotal U.S. trial that could serve as the basis for a PMA submission.

THE COMPETITIVE FIELD

The innovation around cardiac ablation is evolving rapidly with various guidance, imaging and diagnostic options related to this sort of procedure including standard fluoroscopy, coordinate-based navigation tools and sensor-based catheters.

"Electrophysiologists have an array of tools at their disposal to help guide the procedure today. Of course, there's fluoroscopy so they can get a prediction of where the catheter is. But that's just a prediction, it's not establishing the position of the guide. And it's impossible to distinguish healthy tissue and treated tissue from lesions that have been created," said Margallo.

He continued, "There are some navigation tools that give 3-D coordinates of the catheter within the heart; they have some limitations in terms of accuracy, but they are certainly useful to move the catheter around and to move it to the area you want to ablate."

As for the sensor-based catheters, Margallo argued that these offer a useful indication of contact with the heart wall and force readings, but he suggested that stability, rather than force, is increasingly viewed as defining a successful procedure.

Margallo summed up, "All these tools aren't able to say anything about the lesion that has been formed. If there's a spot where the ablation has been unsuccessful, the doctor has no way to know it until recurrence might appear again. Incomplete ablation is probably the most common source of recurrence in atrial fibrillation treatment."

The company estimated, based on broad registry data, that up to 60 percent of patients who have had atrial fibrillation treatment via catheter ablation show recurrence at one-year after an initial procedure. This is believed to be because of pulmonary vein reconnection after ineffective lesion formation. Recurrence can mean subjecting the patient to a further ablation procedure, sometimes repeatedly.

HOW IT WORKS

Medlumics' Ablaview is designed to offer real-time information on lesion formation in the tissue around the radiofrequency electrode during the catheter-based ablation process. The small optical sensor generates 15 beams of light directed into the tissue and blood around the catheter. It is slated to work with a number of existing ablation tools, Margallo said.

Ablaview includes the catheter, a visualization unit and a console where the information is represented in a simple display. On the left, physicians can see contact information and on the right, they can view information on the persistence of the lesion. The latter is intended to enable physicians to more effectively deliver ablation, potentially preventing imprecise or over-treatment.

The latter can be particularly problematic for patients.

"When doctors overtreat patients, which they tend to do to make sure that the lesion's there, there's a high risk of perforation or of bubbles forming in tissue and bursting when the temperature goes really high. And there's also a risk of damaging the delicate structures of the heart, which can have very serious implications," Margallo said.

He anticipates that the Ablaview, therefore, may not just have an impact on ablation efficacy but also potentially on patient safety as well.

REFOCUSED AFTER SPINOUT

Medlumics was co-founded in 2009 by Margallo and Jose Luis Rubio, who had been doctoral students together at the Polytechnic University of Madrid and based the company on their research. It brought in a €3.5 million (US$4.7 million)

See Medlumics, page 7

FDA

Continued from page 1

correspondence, and that "this ends up extending the length of the pre-submission review."

The webinar for *de novo* filings for neurological devices is the second in a series, which is part of an outreach to device makers for devices targeting neurological conditions, such as Parkinson's disease.

The first webinar addressed investigational device exemptions, and Carlos Peña, director of the division of neurological devices at the Office of Device Evaluation, said, "We're trying to make sure – as this is an up-and-coming technology area – that the regulatory landscape for these products is as transparent and clear as possible."

Peña said the agency will hold a webinar for neurological devices addressing PMA filings sometime over the next six months. The agency's emphasis on this technological area is part of the Obama administration's Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, part of which is an article appearing in the Dec. 7, 2016, issue of *Neuro*.

Patrick Antkowiak, a biomedical engineer at the division of neurological devices at the Office of Device Evaluation, said sponsors' pre-submission filings often trip up on some of the basics. "The one common issue … is having them in the correct e-copy format," Antkowiak said, noting that any such filings "will not be logged in and will not be reviewed" until the submitter corrects the e-copy problem.

Pre-submissions should not include data from clinical studies, Antkowiak said, but should include "a discussion of existing device regulations and why your device should fall into that" device class. He said such filings should include intended use information along with key design aspects.

"When it comes to background information, we prefer to err toward more is better," Antkowiak continued, although he remarked, "there is such a thing as providing us with too much information."

Among the materials that would fall into this category are source code for algorithms, and the agency will not answer questions about subjects such as which animal model is appropriate for preclinical testing. The FDA cannot answer data review questions, either, in the pre-sub phase.

Regarding nonsignificant risk devices, Antkowiak urged sponsors to contact the agency with a pre-submission "that asks specific questions" regarding trial design, endpoints and study populations. "If [those studies] aren't done appropriately, it could result in us asking you to perform a new clinical trial," he advised. "Even if you're not entirely sure about your device design … we can still give you feedback," Antkowiak promised, adding, "we might be able to give you tips about what we want to see from a design standpoint."

Avena Russell, assistant director of program operations at the neurological devices division, said the expedited access program has been tweaked thanks to the 21st Century Cures Act, and that the FDA no longer requires that sponsors provide a draft data development plan to participate in the EAP program. Sponsors that do provide such information should spell out a timeline for marketing activities and post-market data collection, however.

Peña closed the webinar with the usual FDA message about "early and often." He said, "If you think it's too early to contact us, that is the right time to contact us. I think you'll be pleasantly surprised at your engagement with FDA," he vowed.

PANEL URGES MORE CLARITY FOR PEROXIDE SOLUTIONS

Hydrogen peroxide-based contact lens solutions offer distinct benefits, but have been associated with hundreds of medical device reports (MDRs), and a March 17 FDA advisory panel concluded with a series of recommendations that may force sponsors to change labels and packages in an effort to thwart these adverse events.

The FDA said it had identified 370 MDRs in connection with peroxide-based contact lens solutions in the 10 years ending in mid-December 2016. Nearly 120 of those MDRs surfaced in 2015, although the agency noted that the spike in reports for that year may have been driven at least in part by an advocacy group's submission of 74 reports "on behalf of consumers."

More than 45 percent of the MDRs were classified as entailing "accidental use," a category that includes instances in which fingers were contaminated with the peroxide upon placement of the lens in the eye. Other events included user confusion between the peroxide solution container with that of a saline or multipurpose solution. Another 29 percent of the events were associated with failures to neutralize the peroxide solution with another solution, said to the single most common type of peroxide fluid misuse. Erroneous purchases accounted for nearly 11 percent of the reports.

Peroxide solution bottles already feature a red cap to distinguish them from other lens care solutions, but the panel indicated that further measures, such as the use of large icons on bottle labels, might be necessary to warn the user as to the hazards associated with improper use. The text on these labels were said to be "too busy" and "too small" to exert the desired effect. Simplicity, clear messaging and standardization of labels were among the suggested remedies.

Product cartons and boxes may have to be redesigned so as to feature colors and font sizes that would distinguish them from cartons and boxes used for other lens care products, given the panelists' remarks. As for efforts to widen general awareness of the risks associated with peroxide solutions, the panel suggested the FDA consider working with retailers and optometrists via social media and other channels to "improve adherence and reduce human error." //

Africa

Continued from page 1

world, despite having a combined population of more than 300 million.

"SSA poses high risks. Access to health care is very poor, particularly in rural areas. Health care resources are low, including shortages in hospital beds. The regulatory framework is underdeveloped and the low level of health insurance means reimbursement is also low," said BMI.

While there is a growing middle class who can afford inexpensive health care, the region's population is still mostly living in poverty in underdeveloped areas.

Of the countries in the region, South Africa has the highest potential, while Nigeria sits at the bottom.

BMI forecasts that the South African market will register a 2015-2020 compound annual growth rate (CAGR) of 8.6 percent in local currency terms, which will raise the market to ZAR20 billion (US$1.59 billion) by 2020.

"We are anticipating high single-digit growth in every year between 2017 and 2020. Growth in local currency terms will be underpinned by a rise in government health spending, which is programmed to increase at an average annual rate of 7.6 percent through to FY2017-18. This is higher than the previous medium term growth target for health spending of 6.4 percent," Ethel Kuntambila, analyst at BMI Research, told *Medical Device Daily*.

The market is estimated to grow about 9.1 percent this year, performing better than in 2016, as the economy begins to pick up from a real GDP growth rate of only 0.5 percent in 2016.

"We note that the government's decision to protect health care spending within a tightening fiscal framework will limit the impact of budget cuts on the health care sector, meaning health care expenditure will continue to increase in real terms," he added.

However, market growth in U.S. dollars will be much weaker due to the weaker rand. BMI forecasts a 2015-2020 CAGR of about 1.8 percent, which will raise the market to $1.1 billion by 2020.

"All product areas including consumables, diagnostic imaging, dental products, orthopedics and prosthetics, patient aids and other medical devices will register low single-digit growth," said Kuntambila.

SOUTH AFRICA MOST EVOLVED

South Africa has the largest medical device market in the SSA region, driven by an increasing elderly population. Although many of the urban poor are underserved, the country has better urbanization – and therefore better access to health care – than its neighbors. However, only the wealthier population has access to advanced medical services.

The country's medical device market is still highly reliant on imports, mostly from the U.S. and Germany. Some multinationals (MNCs) have expanded to the country, and domestic players such as Litha Medical Group Ltd., Lodox Pty Ltd., Medi-Safe Surgicals Pty Ltd. and Southern Group are reflective of the sector's positive outlook.

"Domestic production in South Africa is growing in sophistication, facilitated by an increase in private-public partnerships," said Kuntambila.

Some of the MNCs manufacturing in South Africa are BSN Medical GmbH and Fresenius Kabi. BSN Medical's South African subsidiary has a manufacturing plant in Pinetown that manufactures consumables, including adhesive dressings, elastic bandages and gauze swabs. Fresenius Kabi has a manufacturing plant in Port Elizabeth that manufactures infusion solutions in bags and bottles and IV-administered drugs in glass ampoules for the South African market and also for export.

South Africa outperforms the SSA region in terms of economic diligence and business transparency, but there are still many challenges to overcome when operating in the country.

"Currency volatility over the years has hampered industry planning, and extensive labor regulations result in a rigid labor market. In addition, there is a very high crime rate," said Kuntambila.

Health care barriers include a chronic shortage of medical personnel and poor infrastructure, particularly in the extensive rural areas, which limits efficiency of healthcare delivery, says Kuntambila. There are also complex and fragmented purchasing procedures hindering the medical device market.

The South African government is trying to provide universal health care, but the progress is likely to be slow. Successful implementation of the national health insurance (NHI) scheme relies on persuading more private practitioners to contract with the public sector and uptake has been slow, said BMI.

The government has also introduced new medical device regulations, which will establish an internationally aligned regulatory framework.

"We anticipate that the new requirements will drive up standards in South Africa's medical device market and help develop a domestic industry capable of competing in international markets," said Kuntambila. **//**

Medlumics

Continued from page 4

series A round in 2011 from Caixa Capital and Ysios Capital. Then in 2015, Medlumics spun out dermatology focused Dermalumics to apply the OCT technology to noninvasive skin diagnostics; it is already on the market in Europe. Those early investors backed the spinout as well.

With its series B, Medlumics attracted high-profile European investor Edmond de Rothschild Investment Partners (EdRIP) to lead the round with participation from new investors Seroba Life Sciences, Innogest Capital, an undisclosed strategic investor as well as existing investors Caixa Capital and Ysios Capital. EdRIP's Olivier Litzka, Seroba's James Greene and Innogest's Claudio Rumazza all are joining the Medlumics board with this financing.

Summed up Margallo, "We have refocused on what we believe is our biggest opportunity for Medlumics: tools with this optical technology that can be made really small and placed at the tip of complex devices. We match an unmet medical need and give eyes to the doctor, so they can see what they are doing." //

OTHER NEWS TO NOTE

Tryton Medical Inc., of Durham, N.C., said the first U.S. commercial case using the Tryton Side Branch Stent to treat a coronary bifurcation lesion involving a large side branch (appropriate for a ≥2.5 millimeter stent) was completed at New York-Presbyterian Hospital/Columbia University Medical Center in New York City. The Tryton Side Branch Stent has now been used to treat more than 12,000 patients worldwide. It is commercially available in multiple countries within Europe, the Middle East and Africa, and is approved for use in the U.S.

Varex Imaging Corp., of Salt Lake City, entered a renewed three-year pricing agreement with **Toshiba Medical Systems Corp.**, of Otawara, Japan, under which Varex Imaging will continue to supply its computed tomography (CT) tubes for integration into Toshiba Medical's CT imaging systems for the global market. This renewed agreement will be effective April 1. Potential sales of CT tubes associated with this renewed agreement are estimated to be in the range of $345 million to $385 million. In addition, Varex has in place separate one-year pricing agreements to supply to Toshiba Medical other imaging components, including digital detectors and high voltage connectors.

PRODUCT BRIEFS

Akashi Therapeutics Inc., of Cambridge, Mass., said the U.S. **FDA** has completed its review and concluded that Akashi may resume clinical development of HT-100 (delayed-release halofuginone) in patients with any of the genetic mutations that cause Duchenne muscular dystrophy, a rare disease that results in muscle degeneration and premature death in boys. Akashi plans to initiate a new study, HALO-DMD-04. HT-100 is an orally available, small molecule drug candidate designed to reduce fibrosis and inflammation and promote healthy muscle fiber regeneration in DMD patients. HT-100 has been granted orphan designation for DMD in both the U.S. and EU, and fast track designation in the U.S.

Biosensors International Group Ltd., of Singapore, reported the enrollment of the first American patient in LEADERS FREE II, its new Biofreedom pivotal study, conducted under an Investigational Device Exemption, which will include sites in the U.S., Canada, Denmark, France Germany, Italy and the U.K. The Biofreedom drug-coated stent has been implanted in more than 150,000 patients outside the U.S. Data from the LEADERS FREE II trial will be used in obtaining FDA approval for the Biofreedom DCS. The therapeutic focus of this new U.S. pivotal IDE trial is on patients at high bleeding risk who receive an ultra-short dual antiplatelet drug regimen of only one month.

Edap Tms SA, of Lyon, France, reported the publication of a peer-reviewed article in the *British Journal of Urology International* that retrospectively analyzed its Ablatherm Robotic HIFU for prostate tissue ablation in patients who had previously undergone radiotherapy treatment. The article concludes that HIFU should be considered as a valuable therapeutic option for carefully selected patients who failed a previous radiotherapy treatment. The results were compiled from the Ablatherm treatment registry, a multicenter secure online database for patients who have undergone prostate HIFU with Ablatherm. Inclusion criteria for the analysis were applied to the database, resulting in 418 patients with available data. Statistical models were applied to the data, using the longest available follow-up timepoint for each outcome and patient. Based on the Kaplan Meier survivorship analysis of this data, the rates of overall survival, cancer specific survival and metastasis free survival at seven years were 72 percent, 82 percent, and 81 percent, respectively.

HTG Molecular Diagnostics Inc., of Tucson, Ariz., said it has obtained CE marking in the E.U. for its HTG Edgeseq ALKplus Assay EU, an in vitro diagnostic assay intended to measure and analyze mRNA ALK gene rearrangements in formalin-fixed, paraffin-embedded lung tumor specimens from patients previously diagnosed with non-small-cell lung cancer. The assay may be used to aid in the identification of patients eligible for treatment with ALK-targeted therapeutics, such as crizotinib, and is automated on the HTG Edgeseq system.

Invitae Corp., of San Francisco, reported the availability of a new genetic test for the diagnosis of Spinal Muscular Atrophy (SMA), a neuromuscular disease. The new test, announced during the American College of Medical Genetics Annual Clinical Genetics Meeting, features a custom methodology. Invitae leverages advanced next generation sequencing and a customized bioinformatics solution to accurately identify sequence changes and copy number changes in both the SMN1 and SMN2 genes from a single test, is which critical for the diagnosis and treatment of SMA.

PRODUCT BRIEFS

Medtronic plc, of Dublin, reported **FDA** approval and launch of the Corevalve Evolut Pro valve for the treatment of severe aortic stenosis for symptomatic patients who are at high or extreme risk for open heart surgery. The approval comes on the heels of new 30-day clinical data that was unveiled at the American College of Cardiology 66th Annual Scientific Session, which showed high survival, low rates of stroke, minimal paravalvular leak (PVL) and excellent hemodynamics for the self-expanding valve. (See *Medical Device Daily*, March 22, 2017.) Larry Biegelsen, an analyst with Wells Fargo, said "Based on the available data, we believe Evolut Pro may represent a step forward for Medtronic's transcatheter aortic valve replacement platform." He said, "We think Pro will help better position Medtronic against Boston Scientific Corp's Lotus valve, which is a self-expanding valve and features best-in-class PVL rates as well as Edward Lifescience Corps.' Sapien 3, which also has a skirt to reduce PVL."

National Medical Products Inc., of Irvine, Calif., said its J-Tip Needle Free Injection System has received an Innovative Technology contract from **Vizient Inc.**, of Irving, Texas. The contract was based on a recommendation of the J-Tip by hospital representatives with expertise in this category who serve on one of Vizient's member-led councils. The J-Tip Needle Free Injector is a FDA cleared, single use jet injector that administers lidocaine without the use of a needle.

Nucleix Ltd., of Rehovot, Israel, received CE mark approval for marketing its Bladder Epicheck test in the EU. The Bladder Epicheck is aimed to help urologists to better monitor their bladder cancer patients. This regulatory approval follows the completion of a multicenter, prospective and blinded clinical study with more than 400 patients recruited in their first year of follow up. The test compared the results of the Bladder Epicheck to the current gold standard follow up sequence (cystoscopy, cytology and pathology for the positives). The Bladder Epicheck results showed 99 percent negative predictive value (excluding Ta-LG patients), 92 percent sensitivity (excluding Ta-LG patients) and 88 percent specificity.

Personal Genome Diagnostics Inc. (PGDx), of Baltimore, reported an expansion of its cancer testing contract with the U.S. Department of Veterans Affairs that replaces an earlier tumor profiling assay with the company's new Cancerselect 125 test. Cancerselect 125 is a comprehensive, clinically actionable pan-cancer profiling test that includes microsatellite instability status, a biomarker used to assess potential patient response to checkpoint inhibitor immunotherapies. Cancerselect 125 will be available to cancer patients treated at VA centers nationwide.

ORTHOPEDICS EXTRA

Keeping you up to date on recent developments in orthopedics

By Holland Johnson, Executive Editor

Bariatric surgery positively impacts joint replacement outcomes in morbidly obese patients

A study from Hospital for Special Surgery (HSS) finds that in morbidly obese patients, bariatric surgery performed prior to a total hip or knee replacement can reduce in-hospital and 90-day postoperative complications and improve patient health, but it does not reduce the risk of needing a revision surgery. The study was presented at the American Academy of Orthopedic Surgeons Annual Meeting in San Diego. "With our data, I think we can say with confidence that bariatric surgery prior to total joint replacement is not a harmful recommendation," said lead study author Alexander McLawhorn, an assistant attending orthopedic surgeon at Hospital for Special Surgery in New York City. Morbid obesity (a body mass index greater than or equal to 40 kg/m2) is associated with poor postoperative outcomes after total knee arthroplasty (TKA) and total hip arthroplasty (THA), including increased risk for revision surgery, postoperative infection, and medical complications. Previous studies have shown that bariatric surgery in patients who are morbidly obese can reduce weight and comorbidities, but clinicians have not known whether the surgery is helpful or harmful to morbidly obese patients undergoing a joint replacement. Researchers at the Hospital for Special Surgery turned to the New York Statewide Planning and Research Cooperative System (SPARCS) database, a comprehensive all payer data reporting system. They identified all morbidly obese patients who had a THA or TKA in New York State between 1997 and 2011. There were 2,636 patients who underwent a total knee replacement and 792 who underwent a total hip replacement after bariatric surgery. The researchers then used propensity score matching to build control groups of morbidly obese patients receiving total hips and knees without prior or subsequent bariatric surgery. Propensity score matching is a statistical technique that attempts to estimate the effect of a treatment by accounting for the covariates that predict receiving treatment. The propensity score was defined as the conditional probability of a patient undergoing bariatric surgery, given his or her baseline characteristics, including: age, year in which a total hip or total knee replacement was performed, laterality (unilateral versus bilateral surgery), sex, health care payer, region (rural versus urban), and Elixhauser comorbidities. Statistical analyses showed that bariatric surgery lowered the comorbidity burden of patients prior to total joint replacement ($P<0.0001$ for TKA and $P<0.005$ for THA). Morbidly obese patients who had bariatric surgery had lower rates of in-hospital complications for total hip replacement (1.5 percent vs. 5.3 percent; $P<0.0001$) and for total knee replacement (2.7 percent vs. 3.9 percent; $P=0.021$). Put another way, morbidly obese patients who had bariatric surgery were 75 percent less likely to have in-hospital complications from a total hip replacement and 31 percent less likely to have in-hospital complications for a total knee replacement. The risk for 90-day postoperative complications was also lower in patients who received bariatric surgery, 14 percent lower in the THA group (odds ratio [OR], 0.86; $P=0.041$) and 61 percent lower in the TKA group (OR, 39 percent; $P=0.0019$). Bariatric surgery did not lower the risk of having a revision surgery or the risk for a hip dislocation. Other health care claims database studies have been conducted looking at joint replacement in morbidly obese patients, but results have been inconsistent, most likely due to selection bias. "When you look at the design of the other studies, the single biggest flaw is they don't try to account for the very real selection bias that exists for morbidly obese patients who received bariatric surgery versus those that do not," said McLawhorn. "The patient population that is indicated for bariatric surgery is different than the universe of patients who are just morbidly obese. They tend to have a much higher comorbidity burden, and they tend to be sicker and heavier. We accounted for this selection bias in our study."

New material regrows bone in mouse model

A team of researchers repaired a hole in a mouse's skull by regrowing "quality bone," a breakthrough that could drastically improve the care of people who suffer severe trauma to the skull or face. The work by a joint team of Northwestern University and University of Chicago researchers was a resounding success, showing that a potent combination of technologies was able to regenerate the skull bone with supporting blood vessels in just the discrete area needed without developing scar tissue – and more rapidly than with previous methods. "The results are very exciting," said Guillermo Ameer, professor of biomedical engineering at Northwestern's McCormick School of Engineering, and professor of surgery at Feinberg School of Medicine. The research was published in the journal *PLOS One*. Injuries or defects in the skull or facial bones are very challenging to treat, often requiring the surgeon to graft bone from the patient's pelvis, ribs or elsewhere, a painful procedure in itself. Difficulties increase if the injury area is large or if the graft needs to be contoured to the angle of the jaw or the cranial curve. But if all goes well with this new approach, it may make painful bone grafting obsolete. In the experiment, the researchers harvested skull cells from the mouse and

Continues on next page

Continued from previous page

engineered them to produce a potent protein to promote bone growth. They then used a special hydrogel, which acted like a temporary scaffolding, to deliver and contain these cells to the affected area. It was the combination of all three technologies that proved so successful. The protein, BMP9, has been shown to promote bone cell growth more rapidly than other types of BMPs. Importantly, BMP9 also appeared to improve the creation of blood vessels in the area. Being able to safely deliver skull cells that are capable of rapidly regrowing bone in the affected site, in vivo as opposed to using them to grow bone in the laboratory, which would take a very long time, promises a therapy that might be more surgeon friendly, and not too complicated to scale up for the patients. The article is titled "Repair of critical sized cranial defects with BMP9-transduced calvarial cells delivered in a thermoresponsive scaffold."

Bone-derived hormone suppresses appetite

A hormone secreted by bone cells can suppress appetite, according to mouse studies conducted by New York-based Columbia University Medical Center (CUMC) researchers. The hormone – called lipocalin 2 – turns on neurons in the brain that have been previously linked to appetite suppression. The findings reveal a previously unknown mechanism for regulating the body's energy balance and could lead to new targeted therapies for the treatment of obesity, type 2 diabetes and other metabolic disorders. The study was published online in the journal *Nature*. In 2007, a CUMC team was the first to discover that bone is an endocrine organ that regulates energy metabolism through the release of a hormone called osteocalcin. The first clues to a second hormone came in 2010, when researchers at CUMC discovered that disabling a gene called FOXO1 in mouse osteoblasts caused the mice to eat less and improved their glucose balance. In the current study, the CUMC researchers demonstrated that FOXO1-deficient osteoblasts express unusually high amounts of a protein called lipocalin 2. Lipocalin 2 was previously thought to be primarily secreted by adipocytes (fat cells) and to contribute to obesity. But the researchers showed, using mice that could not produce lipocalin in either their fat cells or osteoblasts, that lipocalin 2 is primarily secreted by osteoblasts and reduces appetite and weight. Lipocalin 2 also affected appetite and weight in normal-weight mice and in mice that were obese due to a lack of the leptin receptor and leptin signalling. In both types of mice, lipocalin 2 suppressed appetite, improved overall metabolism, and reduced body weight. The researchers also found that lipocalin 2 crosses the blood-brain barrier. In the brain, the protein binds to and activates melanocortin 4 receptor (MC4R) neurons in the hypothalamus, the primary brain region that regulates appetite. MC4R neurons are known to be involved in triggering appetite suppression. Initial findings in humans are encouraging. In an analysis of patients with type 2 diabetes, the researchers found that blood levels of lipocalin 2 were inversely correlated with body weight and blood A1c levels, a long-term measure of blood sugar.

Stryker launches Mako robotic-arm assisted TK application

Mahwah, N.J.-based Stryker Orthopaedics reported the commercial launch of its robotic-arm assisted total knee arthroplasty application for use with its Mako system at the American Academy of Orthopaedic Surgeons (AAOS) annual meeting in San Diego. This latest advancement allows the technology to be used across the joint replacement service line to perform total knee, total hip and partial knee replacements. Mako Total Knee combines Stryker's advanced robotic technology with its Triathlon Total Knee System, enabling surgeons to have a more predictable surgical experience with increased accuracy, the company said. Through CT-based 3-D modeling of bone anatomy, surgeons can use the Mako system to create a personalized surgical plan and identify the implant size, orientation and alignment based on each patient's unique anatomy. The Mako system also enables surgeons to virtually modify the surgical plan intra-operatively and assists the surgeon in executing bone resections.