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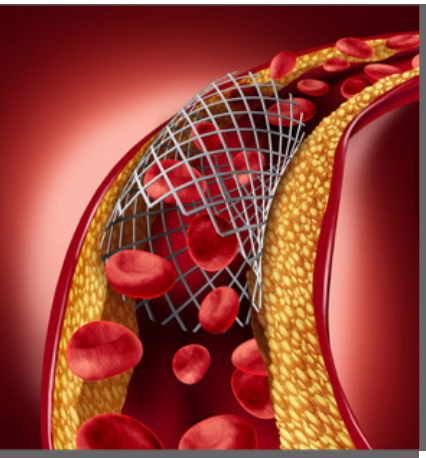

TCT 2017

HARMONEE study dings Orbus Combo thanks to impressive numbers for Abbott's Xience stent

By Mark McCarty, Regulatory Editor

DENVER – The coronary artery stent wars continue apace with the debut of one-year data for the CD34+-eluting Combo stent by Orbusneich of Hong Kong, one of the mainstays of the first day of the 2017 edition of Transcatheter Cardiovascular Therapeutics here in the Mile High City. Noted cardiologist Mitch Krucoff said that while the data from the 50-site study of the Combo stent might not have been

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Inside

Culprit-Shock study clears up multivessel issue for cardiogenic shock

By Mark McCarty, Regulatory Editor

DENVER – Medical society guidelines are rarely rewritten for a single study, but a presentation of the Culprit-Shock study for patients with cardiogenic shock and multivessel disease may have settled the matter in a lot of minds. Holger

See Culprit-Shock, page 4

Novartis tenders $3.9B offer for radiotherapy maker Advanced Accelerator Applications

By Michael Fitzhugh, Staff Writer

Novartis AG has proposed buying radiopharmaceuticals specialist Advanced Accelerator Applications SA (AAA) in a deal valuing the company at $3.9 billion. The transaction would add the EU-approved neuroendocrine

See Novartis, page 5

Firm brings in $20M since inception

Highlife brings in $14.3M to advance its TMVR offerings

By Omar Ford, Staff Writer

Highlife SAS has closed a $14.3 million investment round led by Sofinnova Partners, which becomes the main investor in the firm. The Paris-based company is focused on the development of a transcatheter mitral valve replacement (TMVR)

See Highlife, page 6

Device also used for RA study

Setpoint Medical shares early data on VNS device for MS

By Katie Pfaff, Staff Writer

Setpoint Medical reported positive data from its preclinical study of a bioelectronic treatment for multiple sclerosis (MS). Early data indicates that vagus nerve stimulation (VNS) can slow demyelination as well as speed remyelination related to MS in an animal model.

"This is very early data, but the results show promise for a possible bioelectronic treatment for MS and lay the groundwork for further studies," Yaakov Levine, director of applied research at Setpoint Medical and senior investigator of the study, told *BioWorld MedTech*. "This is a new

See Setpoint Medical, page 7

Kent Imaging says its device is the first line of defense in wound and tissue analysis

By David Godkin, Staff Writer

Calgary, Alberta-based Kent Imaging Inc. has unveiled its FDA-approved Kd203, a hand-held, multispectral imaging device for measuring wound and tissue oxygenation. Directly imaging oxygen perfusion provides more accurate

See Kent Imaging, page 8

BioWorld Medtech's Cardiology Extra

Staff Writer Katie Pfaff
on one of med-tech's key sectors

Read this week's edition

Appointments and advancements

Mologic Ltd., of Bedfordshire, U.K., reported the appointment of Mitch Brooker as general manager. The new role has been created to drive company growth, building on Mologic's current reputation as a successful R&D provider, and increasing its full-service offering. Booker will help lead these changes and take products from conception through to manufacture and commercialization.

Varian Medical Systems Inc., of Palo Alto, Calif., has named Terilyn Juarez Monroe as chief people officer, senior vice-president, Human Resources effective Oct. 30. Monroe, 50, is replacing Wendy Scott who is retiring after serving in this same role at Varian for 13 years.

Daily M&A

Lawrence, Mass.-based **Nxstage Medical Inc.**, a medical technology firm focused on renal care, said the company's stockholders voted to adopt the Aug. 7 reported merger with Fresenius Medical Care Holdings Inc., expected to close in 2018. Fresenius will acquire Nxstage through a subsidiary. Approximately 94 percent of the shareholders voted in favor of the merger. This represents approximately 72 percent of Nxstage's total outstanding shares of common stock as of the Sept. 20 record date and constitutes a majority of the outstanding shares of Nxstage common stock entitled to vote at the special meeting. Nxstage stockholders will be able to receive $30 in cash without interest for each share of Nxstage's common stock. (See *BioWorld MedTech*, Aug. 8, 2017.)

Quest Diagnostics Inc., of Madison, N.J., has acquired certain assets of **California Laboratory Associates** (CLA), of Burbank, Calif., a clinical lab network serving patients and providers in the Greater Los Angeles Area. CLA's operations and patients were previously supported by caregivers and the laboratory at Providence Saint Joseph Medical Center in Burbank.

Financings

Biolase Inc., Irvine, Calif.-based maker of dental lasers, will issue a proposed rights offering to holders of shares of its common stock beginning 5 p.m. EST Nov. 8. Terms of the offering and price will be determined prior to the date.

Quebec-based **Ortho Regenerative Technologies Inc.** reported a non-brokered private placement of about $1.5 million with up to 3 million units at a price of $0.50 per unit. Financing will be used to fund R&D, and general purposes. Each unit will consist of one class A common share and one half of one nontransferable share purchase warrant. Each whole warrant shall entitle the holder to acquire one share at an exercise price of $0.70 per share at any time on or before the close of business on a date that is 18 months from the closing date. If during that time,the weighted average share price for 30 consecutive trading days equals or exceeds $1, warrant holders may be asked to exercise their warrants within 30 days.

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Orbusneich

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overwhelming, the comparator Xience stent outperformed itself for target vessel failure at a year, dinging the study article's comparative numbers.

The Combo device has been in the crosshairs of payers for some time, as indicated by a noncoverage memo by Aetna of Hartford, Conn., which said no to the device in September 2016, but the device received a cool reception from Germany's Institute for Quality and Efficiency in Health Care completed in November 2015 as well. The Harmonized Assessment by Randomized, Multicenter study of OrbusNEich's Combo StEnt (HARMONEE) study was another in a series of the harmonization-by-doing between the FDA and Japan's Pharmaceutical and Medical Devices Agency (PMDA), and featured nearly 440 enrollees in Japan, who received the study article, and another 330 or so in the U.S. receiving the everolimus-eluting Xience by Abbott Vascular of Santa Clara, Calif.

Both arms of this study ended up with between 285 and 290 patients in their respective intent-to-treat arms, although only between 60 and 65 enrollees in each arm underwent optical coherence tomography at a year to check the condition of the target vessel. Krucoff noted that the device is the first to incorporate CD34+, a biological agent that captures endothelial progenitor cells in an effort to promote more rapid healing of the interior vessel wall, but he also noted that the study enrolled an additional 432 patients in a cohort C, data from which were not reported at the first day's session.

Krucoff said the Combo demonstrated superior healthy tissue strut coverage and greater homogeneous tissue in the affected vessel, but he noted that the target vessel failure rate was predicted to be 9 percent for both devices going in. However, the Xience held to a TVF rate of 4.2 percent, and even the Combo beat the predicted rate with a 7 percent showing for TVF. However, Krucoff cited "a highly statistically significant difference" in homogenous neointimal tissue in the affected area, with 81 percent of the Combo/OCT patients showing significant ingrowth of homogenous neointima, versus roughly 69 percent for the control device.

Krucoff said the numbers should not be terribly off-putting because the study was "a noninferiority design against the best in class." He made the case that while the study did not completely answer the question of whether this device is ready for prime time, "it's beginning to explore a space with the confidence . . . that we at least have a marker" to further develop the technology with some confidence.

Hybrid revascularization comes up short

A hybrid approach to treat multivessel disease has been proposed before, but a new study suggests that this approach has little to offer most patients. Roman Tarasov of the State Research Institute for Complex Issues of Cardiovascular Diseases (Kemerovo, Russia), presented on the HREVS (Hybrid coronary REvascularization Versus Standards) study, which he said is the first randomized study to assess safety and efficacy of PCI, coronary artery bypass, and the use of both (hybrid revascularization) in patients presenting with multivessel disease, including the left anterior descending artery.

Tarasov said the data "indicate no evidence for HCR [hybrid coronary revascularization] benefits," at 12 months, assuming there is no reason to think the patient would be a better candidate for one of these approaches than the others.

Roman Tarasov
State Research Institute for Complex Issues
of Cardiovascular Diseases

This was a single-center, open-label study that initially attempted to enroll slightly more than 200, although nearly one in four declined to be randomized. The remainder of 155 were randomized roughly equally and were checked at one year for residual ischemia as detected by single-photon emission CT (SPECT), the primary endpoint. Patients with prior PCI or bypass were excluded, as were those with stenosis of the left main artery.

Among the secondary endpoints were target vessel graft failure and a composite of death, stroke, infarct and clinically driven target vessel revascularization. Average age in all three groups was between 61 and 62 years.

Roughly 10 percent of the hybrid group was converted to straight bypass (five of 52), and as might be expected, members of the PCI-only group left the hospital much more quickly (3.2 days on average versus greater than 12 for the other two arms). At 30 days, the composite endpoint occurred in 8 percent of the bypass group, driven entirely by four infarcts. There were three infarcts in the hybrid group and two in the PCI group, but the hybrid group's numbers were also dinged by one case each of stroke and death, and by one instance of revascularization. There was no death, stroke or revascularization in either of the other two arms at this first interval.

The numbers evened out somewhat for 12-month residual infarct, however, with 6.4 percent in the hybrid group, 6.7 percent in bypass, and 7.9 percent in PCI. The composite endpoint, which did little to help the hybrid arm's numbers at 30 days, trended back toward this approach at one year. One bypass patient expired at that point, compared to three in the hybrid arm and two in the PCI group. Both bypass and PCI evinced four cases of infarct at a year versus three in the hybrid group.

In contrast to clinically driven revascularization, angiographically driven instances numbered six each in the hybrid group and the PCI arm, although the bypass group added only one additional case of revascularization to the one seen at 30 days.

Tarasov said the data "indicate no evidence for HCR [hybrid coronary revascularization] benefits," at 12 months, assuming there is no reason to think the patient would be a better candidate for one of these approaches than the others. He said follow-up of more than 12 months might disclose some benefit, particularly in the instance of bypass for the left anterior descending artery and PCI for the other affected vessels. ♦

Culprit-Shock

Continued from page 1

Thiele, director of cardiology at University Hospital in Leipzig, Germany, told an audience at TCT 2017 that most of these patients are better off if the physician goes after the culprit lesion and leaves everything else to be dealt with at a later date.

Culprit-Shock, a study of patients who present with cardiogenic shock at the time of infarct, was an investigator-initiated study that took place at 83 centers in 11 nations. Thiele said the centers screened more than 1,100 patients, more than 700 of whom were randomized in roughly even numbers to the study's two arms. More than half of patients in both arms underwent resuscitation, and there was some cross-over between the two arms. The primary study endpoint was the number of patients who expired for any reason or who undergo renal replacement therapy.

Thiele pointed out that the argument for multivessel treatment is backed by the notion that this would improve myocardial perfusion, but the offsetting hazards include renal impairment stemming from a concomitant use of a greater volume of contrast agent. He noted that there was already some evidence that 30-day mortality is higher for patients treated for multiple vessels, a proposition that Culprit-Shock did nothing to damage.

Treatment of multiple vessels in these patients shows up as a class 2a recommendation with a C grade in Europe, but U.S. guidelines are mum on this scenario, although there are appropriate use criteria from American societies. Thiele noted that the volume of contrast agent was 190 milliliters in patients undergoing treatment for single-vessel disease, a number that was overshadowed by the 250 milliliters in the patients who were treated for multiple vessels.

The composite of all-cause mortality and renal replacement occurred in 55.4 percent in control treatment, but only 46.9 percent for those treated only for the culprit lesion. This difference was "mainly driven by an absolute reduction of 8 percent in 30-day mortality," for all causes, Thiele remarked, which was 51.5 percent for the multivessel group and 43.3 for those treated only for one vessel.

As a stand-alone measure, renal replacement therapy came in at 16.4 percent for the multivessel group vs. 11.6 percent for the single-vessel group, although the p score of 0.07 did not seem to suggest this was a reliable set of data for drawing conclusions. Thiele said the data set "challenges current European recommendations and American appropriate use criteria." Nonetheless, overall mortality was roughly equal between the two groups.

QoL solid for bypass at 36 months

The coronary artery bypass is not quite the same procedure as it once was, and the results of a new study suggest that bypass matches percutaneous coronary intervention at 36 months for a number of quality-of-life measures in patients with diseased left main arteries. PCI showed better QoL numbers at one month, but Suzanne Baron of Saint Luke's Mid America Heart Institute in Kansas City, Mo., said that picture changes dramatically 35 months later, with reports of angina roughly equal between the two patient populations.

Baron's numbers are derived from enrollees in the Excel trial, which randomized patients with left main coronary artery disease and low to intermediate SYNTAX scores to revascularization via bypass graft or the Xience everolimus DES made by Abbott Park, Il.-based Abbott Laboratories. She said that while the rates of death, stroke or myocardial infarction were similar in both groups at three years, there were some notable differences in the timing of these clinical events, although rates of repeat revascularization differed between the cohorts, too.

At baseline, 10 percent of the nearly 900 enrollees in both arms had daily angina, and shortness of breath was seen in nearly identical ratios as well. This study showed higher numbers for all-cause mortality for the Xience, but stroke and infarcts were numerically higher for bypass.

At 36 months, angina was a problem for 81 and 82 percent (PCI and bypass, respectively), while shortness of breath was likewise a statistical dead heat (43 percent for Xience and 42 percent for bypass), and depression was also statistically indistinguishable. In an age of patient preference, the question for device makers is whether these QoL measures will filter back to patients who are on the horns of a bypass-vs.-PCI dilemma and begin to drive the occasional patient toward bypass and away from PCI. ♦

Product briefs

Entellus Medical Inc., of Plymouth, Minn., reported data from its first-in-human study of the Latera absorbable nasal implant from Spirox. The 18 and 24-month data demonstrate that patients who received Latera had significant improvement in nasal obstruction symptoms with no negative cosmetic changes. The results were selected for presentation at the 2017 Annual Conference of the European Academy of Facial Plastic Surgery and the 2017 Annual Meeting of the American Academy of Facial Plastic and Reconstructive Surgery. The study was conducted at three sites in Germany and included 30 adult patients with nasal valve collapse. A total of 56 Latera implants were placed in 30 subjects, and patients were assessed at one week and one, three, six, 12, 18 and 24 months postprocedure.

Indianapolis-based **Greenlight Guru** reported the addition of Grow to its existing quality management software platform, helping companies get medical devices to market faster and with less risk. Greenlight Guru's software can assist medical device companies after the launch of a device by connecting its entire quality ecosystem and advancing the success of high-quality devices already on the market.

Novartis

Continued from page 1

tumor therapy Lutathera (lutetium [177Lu] oxodotreotide) to the company's portfolio, as well as a new technology platform that Novartis said has potential applications across a number of early oncology development programs.

Neuroendocrine tumors, or NET, are a rare type of cancer that originate in neuroendocrine cells throughout the body. Novartis is already active in the indication, having gained FDA approval for both Afinitor (everolimus) for the treatment of certain NETs of gastrointestinal (GI) or lung origin and more limited approval for a long-acting version of Sandostatin (octreotide acetate) for GI NETs. An FDA approval for Lutathera could arrive early next year, ahead of a Jan. 26 PDUFA date. A regulatory OK for the deal is still pending, though it is not expected to receive opposition.

Under terms of the deal, approved by the boards of both companies, Novartis will make a cash offer of $41 per ordinary share of AAA (NASDAQ:AAAP) and pay $82 per American Depositary Share, each of which represents tow ordinary shares of the company. Novartis said that it will pay for the deal with funding derived from external short- and long-term debt.

Headquartered in Saint-Genis-Pouilly, France, AAA currently has 21 production and R&D facilities, and more than 550 employees in 13 countries. The company reported sales of €109.3 million (US$127.3 million) in 2016 and €69.2 million (US$80.6 million) in the first half of 2017. Primary drivers of its revenue growth have been its two positron emission tomography imaging agent kits for NET, both approved during 2016. One of the kits, Netspot, is approved in the U.S. for localization of somatostatin receptor positive NETs in adult and pediatric patients. The other kit, Somakit TOC, is approved in Europe for localization of primary tumors and metastases in patients with confirmed or suspected well-differentiated gastro-enteropancreatic neuroendocrine tumors (GEP-NET).

With Lutathera's approval by the European Commission for the treatment of adults with unresectable or metastatic, progressive GEP-NETs having arrived just at the end of September, AAA has yet to report sales of the therapy. But it was, at the time of the European approval, already highlighting the potential synergy between Lutathera and its PET test kits. NET patients who have had tumors successfully localized using either kit may also be candidates for therapy with Lutathera, it said, since the drugs bind to the same receptor.

Jefferies analyst Peter Welford forecast that the Lutathera could reach $650 million in peak sales treating mid-gut GEP-NETs, while adding that "adoption to treat other types of NETs could offer significant potential upside." Jefferies is acting as AAA's exclusive financial advisor in the deal.

J.P. Morgan analyst Jessica Fye was also positive on the deal, which in a note to clients, she said is "a strong fit within Novartis given the company's existing presence in neuroendocrine tumors." Calling Novartis "the most logical buyer" for AAA, she wrote that she would be "surprised to see another player step in."

Researchers at Houston's University of Texas MD Anderson Cancer Center reported in the October 2017 *JAMA Oncology* that "neuroendocrine tumors are increasing in incidence and prevalence owing to increased diagnosis of early-stage tumors." In light of that change, "there is a significant unmet medical need for a therapy which can demonstrate longer disease-free and overall survival in the treatment of metastatic or unresectable NETs," Novartis spokesman Eric Althoff told *BioWorld MedTech*.

Buying Lutathera gives Novartis the opportunity to meet that need by co-opting a medicine that has been shown to outperform a double dose of Sandostatin in patients with midgut NETs.

If completed, the deal would be at least the second multibillion dollar radiopharmaceuticals deal in recent times, after Bayer AG purchased Oslo-based Algeta ASA for $2.9 billion, a deal that led to the 2013 marketing of Xofigo (radium Ra 223 dichloride) for the treatment of prostate cancer and of a platform upon which it continues to develop targeted alpha-emitter therapies. ♦

Product briefs

Inscope Medical Solutions Inc., of Jeffersonville, Ind., announced its Inscope direct, a disposable laryngoscope that allows clinicians to maintain a clear view of the airway. Inscope direct's integrated suction removes secretions allowing a clear view of vocal cords for easy placement of the endotracheal tube. The device features a built-in LED light source and an anti-clog design with two controllable suction inlets eliminating the need for a yankauer suction catheter as it easily removes existing and re-accumulating secretions. Inscope direct connects to standard suction tubing and is compatible with wall suction and powered portable suction.

Physio-Control Inc., of Redmond, Wash., said it is launching a voluntary field action for specific production lots of Infant/Child Reduced Energy Defibrillation Electrodes produced by Cardinal Health. The company is notifying customers of an issue with the artwork on the defibrillation electrodes, as manufactured by Cardinal Health, which shows incorrect electrode placement for an infant. There is no issue with the performance or function of the defibrillation electrodes; however, if the user incorrectly places the defibrillation electrodes, it may result in ineffective energy delivery to the patient and serious injury or death. The defibrillation electrodes are used only with Lifepak Express AED, Lifepak Cr Plus AED, Lifepak 1000 defibrillator, or Lifepak 500 Biphasic AED with a pink connector. Adult defibrillation electrodes are not impacted. Approximately 14,200 electrodes have been affected. There have been no customer complaints reported for this issue. The company is contacting customers to notify them of the issue, and to provide customers with correct electrode placement instructions to be included with the AEDs until they receive their corrected defibrillation electrodes. Physio-Control will provide replacement products for all unused affected defibrillation electrodes.

Highlife

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system to treat patients suffering from mitral regurgitation. Livanova plc, which has provided funding to the company in the past, also participated in this financing round along with Highlife's founder and CEO Georg Börtlein.

Highlife was started in 2010 by Börtlein, who was previously a co-founder with Jacques Séguin at Corevalve Inc. The Irvine, Calif.-based company was focused on transcatheter aortic valve replacement (TAVR) and was acquired by Medtronic plc in 2009 for more than $700 million. (See *BioWorld MedTech*, Feb. 24, 2009.)

The $14.3 million in funding will be used for Highlife's clinical programs and its R&D pipeline, Börtlein said. Since inception, Highlife has raised about $20 million.

The company is in the early stages of development of the device and held a first-in-human study back in the Ukraine in 2016. Eight patients were treated in this study. Börtlein said the company will continue to generate more data for the device.

"We would likely apply for CE mark study sometime next year," Börtlein, told *BioWorld MedTech*. "Right now we have not yet enough data to support a submission. That's our target right now. In parallel, we intend to do a U.S. feasibility study, so that we can pave the way for an IDE study later on."

Highlife said its technology relies on the initial placement of a ring component around the native mitral leaflets in a reversible manner. Once this first component's position is confirmed, the bioprosthesis is delivered within minutes through the ring and finds its natural position inside the native annulus regardless of the access site.

This approach allows for transseptal access and delivery of the bioprosthesis after navigating up the femoral vein and reaching the native mitral valve via a puncture through the inter-atrial septum. Such route alleviates the need for a transapical puncture in the weakened heart muscle and is favored by physicians because further trauma to the patients is avoided.

Of acquisitions and investments

The TMVR market has been brimming with activity over the past few years.

In May, Highlife investor, Livanova acquired the remaining 51 percent of Caisson Intervention LLC for about $78 million in cash, to secure its position in the TMVR space. (See *BioWorld MedTech*, May 4, 2017.) Like Highlife, Caisson's TMVR implant is designed entirely for use via a transseptal approach.

In October, Medtronic plc treated its first patient in pivotal trial designed to evaluate the Intrepid TMVR system. The Dublin-based company's APOLLO Trial will evaluate the safety and efficacy of the Intrepid TMVR system in up to 1,200 patients with severe, symptomatic mitral valve regurgitation.

Edwards Lifesciences Corp., the undisputed pioneer in TAVR, has spent the last few years acquiring technologies for TMVR therapy. In November 2016, the valve specialist made an emphatic statement in the TMVR market when it said it would acquire Or Yehuda, Israel-based Valtech Cardio Ltd. for $340 million, with the potential for $350 million in additional milestone payments. (See *BioWorld MedTech*, Nov. 29, 2016.) Valtech Cardio had been courted for acquisition before by Medtronic plc's Heartware International Inc. (See *BioWorld MedTech*, Jan. 29, 2016.)

Highlife valve; Highlife Sas

> *"We would likely apply for CE mark study sometime next year. Right now we have not yet enough data to support a submission. That's our target right now. In parallel, we intend to do a U.S. feasibility study, so that we can pave the way for an IDE study later on.*
>
> Georg Börtlein
> Founder and CEO, Highlife

In July 2015, Abbott Laboratories reported plans to pay $225 million for the equity of Roseville, Minn.-based Tendyne Holdings Inc. that it did not already own at the time, making the total deal worth $250 million plus potential regulatory-based milestone payments. The company closed on that deal in September 2015. (See *BioWorld MedTech*, July 31, 2015.)

In a separate deal, the Abbott Park, Ill.-based company said it had invested in mitral valve repair company Cephea Valve Technologies Inc., of Santa Cruz, Calif., with an option to buy. Financial terms of the Cephea transaction were not disclosed. In August of 2015, Medtronic jumped into the TMVR pool paid about $458 million to acquire Redwood City, Calif.-based Twelve Inc. (See *BioWorld MedTech*, Aug. 26, 2015.) ♦

Setpoint Medical

Continued from page 1

potential treatment method for MS, a disease with a big need for innovative solutions due to low rates of prolonged response to most clinically approved drugs, which target disease flares but do not reverse disease progression."

Further animal studies on effects and dosing are planned before transitioning to in-human trials.

"The Setpoint device is currently under regulatory review to start prospective studies in the treatment of clinical rheumatoid arthritis," said Levine.

Vagus nerve to trigger inflammatory response

Setpoint's bioelectronics platform includes use of an implanted device which supplies electrical current to the vagus nerve. The electrical dose is set and administered digitally, and is intended to trigger the patient's inflammatory reflex, thereby producing a systemic anti-inflammatory response.

"Bioelectronic medicine uses a small implanted device to deliver targeted electrical pulses along existing physiologic pathways to activate mechanisms in the body, triggering the body's natural anti-inflammatory and disease resolving responses, creating a disease-fighting effect that can last hours or days," said Levine.

Study data was presented at the European Committee and Americas Committee for Research and Treatment in Multiple Sclerosis in Paris.

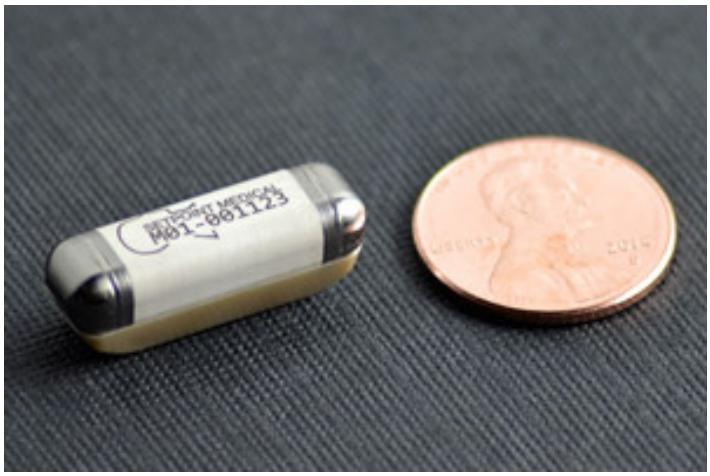
"Many patients with debilitating diseases such as MS do not respond well to pharmacologic or biologic treatments and are left with few options, driving our research into bioelectronic medicine as an alternative," said Anthony Arnold, CEO of Setpoint Medical. "Our focus is on immune-mediated diseases, targeting immune cells without drugs by delivering electric doses to the vagus nerve to drive a coordinated physiologic response against inflammation. MS is a logical expansion of our rheumatoid arthritis and Crohn's disease trials, and we look forward to exploring the potential of bioelectronic medicine to treat MS."

Company investors include Morgenthaler Ventures, NEA, Medtronic, Glaxosmithkline's Action Potential Venture Capital Limited, Topspin Partners and Boston Scientific.

Myelin sheath repair

Setpoint, of Valencia, Calif., aims to attack MS and other related immune-based diseases with the treatment, providing an alternative to medications. The VNS device also directly addresses the destruction of the myelin sheath in MS, according to the company, while medications typically address the immune system alone. Myelin sheaths are made up of a fat-like substance and protect nerves throughout the body. Myelin destruction results in nervous system dysfunction, including vertigo, vision loss, pain and difficulty walking.

"Based on our previous studies that have shown VNS activates protective neuro-immune reflexes that reduce inflammation, increase anti-inflammatory regulatory T-cell populations and are neuroprotective in the central nervous system – we theorized that a bioelectronic medicine approach could be effective in treating MS," said Levine. "Strikingly, a single dose of electrical stimulation not only reduced demyelination in this model, but also accelerated remyelination, which is a significant challenge in MS. Importantly, the study also demonstrated that VNS significantly reduced leakage of the blood-spinal cord barrier, which can prevent immune cell infiltration and further reduce disease progression."



Bioelectronic device; Setpoint Medical

> *"This is very early data, but the results show promise for a possible bioelectronic treatment for MS and lay the groundwork for further studies.*
>
> Yaakov Levine
> Director of applied research, Setpoint Medical

Additional treatments, VNS approaches

The firm has completed studies of VNS as an approach to treatment of rheumatoid arthritis (RA) and Crohn's disease, including a recent study on the former. Published online ahead of print in the *Proceedings of the National Academy of Sciences of the United States of America* in July 2016, the study "Vagus nerve stimulation inhibits cytokine production and attenuates disease severity in rheumatoid arthritis," suggests RA can be addressed by tamping down the immune response and resulting inflammation. According to the study abstract, activating the inflammatory reflex can "inhibit the production of tumor necrosis factor (TNF), an inflammatory molecule that is a major therapeutic target in RA. Although studied in animal models of arthritis and other inflammatory diseases, whether electrical stimulation of the vagus nerve can inhibit TNF production in humans has remained unknown. The positive mechanistic results reported here extend the preclinical data to the clinic and reveal that VNS inhibits TNF and attenuates disease severity in RA patients."

See Setpoint Medical, page 9

Kent Imaging

Continued from page 1

diagnosis than existing technologies, Kent Imaging's CEO Pierre Lemire told *BioWorld MedTech*, which will also lead to more effective treatment planning and patient monitoring.

"This is a huge milestone for the company," Lemire said. "The wound market has been underserved in terms of imaging technology and what this device will do is give surgeons insights about what's happening in the wound they haven't had before."

Launched earlier this month at the Symposium on Advanced Wound Care in Las Vegas, the Kd203 measures the percentage of hemoglobin carrying oxygen along the smaller blood vessels and veins to the wound site. This is distinct from pulse oximetry, for example, which measures oxygenation of the larger carrier vessels and will tell you if your heart and lungs are okay, Kent Chief Science Officer Michael Sowa told *BioWorld MedTech*. "But it won't tell you how well surrounding tissues are oxygenated."

Kd203's closest competitor, however, is transcutaneous oxygen pressure monitoring or $TcP0_2$, the current gold standard for perfusion quantification in surrounding wound tissue. $TcP0_2$ involves measuring oxygenation through the skin via placement of electrodes around the periphery of the wound. Problem: that physical contact won't allow you to measure oxygenation within the wound bed itself.

"You also have to infer the oxygenation of the wound from the measurement of oxygen you receive around the periphery of the wound," said Sowa. "We measure that wound bed directly and in an imaging format."

The Kd203 camera uses lasers to locate areas of the wound to be imaged and determines the ratio of oxygenated to deoxygenated hemoglobin. "Once the ratio of oxygenation dips below 40 percent we suggest clinicians really pay attention to that area," said Lemire. Being aware of low oxygenation ratios also helps surgeons prepare the patient's treatment plan, he said.

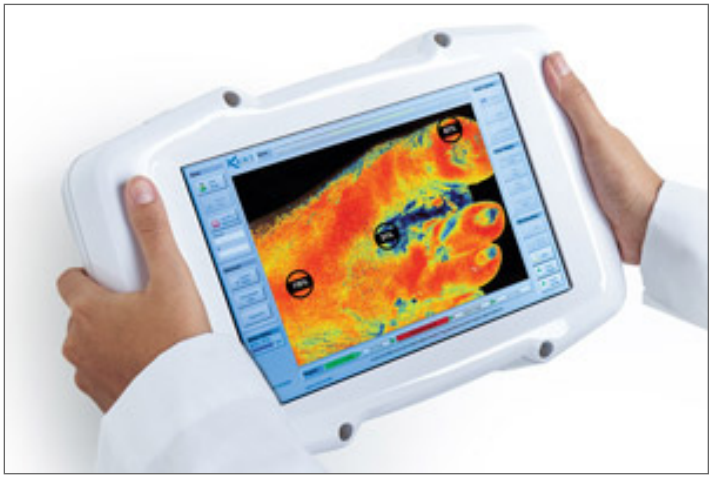
"That's why when we say 'wounds' we also mean acute wounds that would be surgical, so that you could even use this inter-operatively during post-op reconstruction.

No more wasting time

Equally important to the patient's treatment plan, added Lemire, is the speed of the technology: no more waiting for placement and heating up of electrodes on the skin to measure perfusion. Instead, Kd203 imaging takes less than a second. "Our device is about the same level of complexity and time invested as taking a digital picture with a camera or your phone. So we don't disrupt workflow, you take your image and move on."

"Because the imaging is quite simple to do and takes very little time, you can also follow up on the ward as the patient recovers, especially if you saw something immediately suspicious in the immediate post-op image, he said"

Surgeons and wound care specialists will also be pleased with the Kd203's near instant calibration prior to its use, said Lemire. Hospitals, meantime, will be happy eliminating second surgeries that occur because surgeons are unable to adequately measure poor tissue oxygenation. At US$26,000, the Kd203 is also less expensive than traditional technologies, Lemire said, "because there are no disposables and dyes. It doesn't cost anything to operate the device."



Kd203 hand-held imaging device; Kent Imaging

> *"The wound market has been underserved in terms of imaging technology and what this device will do is give surgeons insights about what's happening in the wound they haven't had before.*
>
> Michael Sowa
> Chief science officer, Kent Imaging

Perfusion in the marketplace

Developed over 10 years through private and public sector investments, the object now is to expand its adoption in other markets for which it is cleared, for example, imaging of burn wounds, while eventually penetrating markets in Europe and Australia as well. Sowa calls the Kd203 "the next step in perfusion imaging."

"Whether it's a chronic wound, acute injury or following surgical intervention, we give physicians the first line of defense to determine if the tissue has a chance to survive and remain viable." ♦

Setpoint Medical

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Nerve stimulation devices have seen numerous uses in recent years for a range of conditions. Earlier this month, Neuropace Inc. won $74 million in funding for its Neuropace RNS, a closed-loop neurostimulation system for patients experiencing partial onset seizures. The device is intended for patients 18 years and older with refractory partial onset epilepsy in one or two brain areas who have been unable to control seizures with medication. (See *BioWorld MedTech*, Oct. 25, 2017.) Electrocore Medical LLC launched its gammacore VNS system this summer for patients dealing with episodic cluster headaches. Its hand-held device is administered through a patient registry. (See *BioWorld MedTech*, July 19, 2017.) In May, Enteromedics published three-year data on its Vbloc DM2 among patients with obesity, type 2 diabetes mellitus. Study data indicated the device increased weight loss and reduced A1C. (See *BioWorld MedTech*, May 24, 2017.) ♦

Product briefs

Viveve Medical Inc., an Englewood, Colo.-based med-tech company focused on women's health and wellness, reported the launch of direct sales of the Geneveve treatment to physicians and health care providers in Canada. Delivered by the internationally patented Viveve system, the Geneveve treatment improves sexual function by treating the vaginal introitus, after vaginal childbirth.

Other news to note

Cerus Corp., of Concord Calif., entered into a supply agreement with Centro de Transfusión de la Comunidad de Madrid (CTCM) for the Intercept Blood System for platelets. CTCM provides blood and blood components to all hospitals in Madrid. Each year, CTCM manages about 250,000 blood donations allowing for the distribution of 45,000 units of platelets. Earlier this year, CTCM issued a public tender for the inactivation for part of its platelet components.

Golden Meditech Holdings Ltd., of Hong Kong, said the board of directors of the company resolved to initiate an application for the voluntary delisting of the Taiwan depository receipts from the Taiwan Stock Exchange Corp., the repurchase of TDR resulting from the Voluntary Delisting and the TDR conversion offer. In view of the group's future business directions, the company said it intends to submit the application of the Voluntary Delisting to TWSE in or about November 2017. If the application is approved by TWSE, the TDR shall cease to be listed on TWSE with effect from a date to be determined by TWSE.

Neurocog Trials Inc., of Durham, N.C., received a 2017 Fast Track grant from the National Institute of Health to study the validation of a performance-based measure of functioning in mild cognitive impairment and early Alzheimer's disease using NCT's technology, the Virtual Reality Functional Capacity Assessment Tool. The VRFCAT is a solution developed to improve clinical trials by detecting functionally meaningful improvements in patient's everyday lives.

Performance Solutions, Kalamazoo, Mich.-based **Stryker Corp**.'s health care transformation business, reported the launch of its Practice Excellence Program, a new implementation service to help physician practices nationwide specializing in orthopedics drive profitability, efficiency and quality outcomes. The Practice Excellence Program starts with a comprehensive financial and operational analysis and report of the health of the physician practice to determine areas for improvement.

Cardiology Extra

Keeping you up to date on recent developments in cardiology

By Katie Pfaff, Staff Writer

Study finds prescription PCSK9 inhibitors often not approved or filled by patients due to cost

A recent retrospective analysis study reported less than half of patients received insurance approval for prescribed PCSK9 inhibitors, in a study published Oct. 30, 2017, in the American Heart Association's journal, *Circulation*. The study, "Proprotein convertase subtilisin/kexin type 9 inhibitor therapy: payer approvals and rejections, and patient characteristics for successful prescribing," was based on a nationwide review of electronic medical records, lab tests and pharmacy claims from 9.357 patients who received a prescription between July 2015 and August 2016. Among the patients, 4,397 or 47 percent were approved for a PCSK9 inhibitor medication, and 4,960 or 53 percent were denied. Of those rejected, 60 percent had previously been diagnosed with atherosclerotic cardiovascular disease. PCSK9 inhibitors are shown to remove low-density lipoprotein (LDL) from blood by up to 60 percent and are tied to reduced costs for cardiac care through fewer cardiac events. "With the controversy surrounding whether or not these drugs were cost effective, we were anticipating that there might be some reluctance by insurance companies to cover these medications," said senior author Robert Yeh, director of the Smith Center for Outcomes Research in Cardiology at Beth Israel Deaconess Medical Center in Boston. "However, we were surprised by the very high rate of rejection, even when prescribed to patients with known atherosclerotic cardiovascular disease, very high LDL levels and those who were intolerant of statins, for example." Insurance type was indicative of approval, with Medicare granting the highest rates and private insurance the lowest rates of approval. Additionally not all approved patients filled their prescriptions. As many as one in three who were approved did not purchase the medication, most often due to the cost of the prescription.

Stroke mobile unit to assist in time-essential patient treatment

UCLA Health, of Los Angeles, has taken stroke care to the streets with its mobile unit. The mobile stroke unit brings necessary medications to patients who rely on quick administration to save their lives of function. Under a pilot program and in coordination with the Santa Monica fire department, the unit – made up a specially outfitted ambulance and treatment team – responded to stroke-related calls to 911 in September in Santa Monica. "Rapid response is critical, because the sooner a stroke is treated, the better the patient's outcome," said May Nour, medical director of the UCLA Arline and Henry Gluck stroke rescue program. "We know from research at UCLA that in a typical stroke, every minute that goes by without treatment, 2 million brain cells die. To be able to take care of stroke patients in the very first minutes after onset, when there is the most brain to save, is our ultimate goal," she said. "Recovery and quality of life for stroke survivors is of utmost importance. By providing treatment in the most efficient timing, we offer patients the greatest possibility of improved clinical recovery." The ambulance includes a CT scanner, mobile laboratory for blood testing and personnel, including a neurologist, critical care nurse, paramedic and CT technologist. The ambulance will begin serving Los Angeles County, and possibly Compton, Carson, Long Beach and Westwood. Los Angeles county board of supervisors supports the effort, which may grow further and increase to a four to nine unit service. Results from the project and data on patient outcome, speed and cost effectiveness will be evaluated for possible CMS reimbursement. While a neurologist is currently on board, the program will eventually use the specialists' services via a video connection from the Ronald Reagan UCLA Medical Center. Design and rollout of the stroke unit was supported by philanthropic funding to UCLA from the Arline and Henry Gluck Foundation. LA's board of supervisors also approved funding of nearly $1.5 million for operation of the mobile unit, allowing the vehicle to operate each week rather than the earlier planned every other week, extending its coverage areas, and its study pilot program from 18 to 30 months.

Diabetes and blood flow to the brain

Type 2 diabetes, more common in overweight or obese patients, is detrimental to circulation since it commonly leads to atherosclerosis and decreases oxygen flow, and ultimately effects cognitive ability. A study published Oct. 30 in the *Journal of the American Geriatrics Society* looked at the impact of lowered calorie diet and increased physical activity on type 2 diabetes effects, and long term impact on cognition. The study, "Long term impact of intensive lifestyle intervention on cerebral blood flow," reviewed data from a 10-year study, Action for Health in Diabetes (Look AHEAD), which coached patients on making healthy lifestyle changes. The study included two groups of patients, the first called the intensive lifestyle intervention with 1200-1800 calories per day and 175 minutes of physical activity weekly. Patients were expected to lose weight in this group. The second, control group attended education and support classes for diabetes. All patients were seen weekly in the initial six months, three times monthly for the following six months, and once a month during years two through four. Mental function was tested in the study; at 10 years after enrollment, 321 had received an MRI brain scan. Results indicated those overweight or obese who completed the behavioral changes had improved blood flow in the brain, though the improvement seemed to be strongest in those overweight rather than obese.