BioWorld MedTech

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Backbeat CNT; Orchestra Biomed Inc.

Orchestra Biomed raises $34M to advance circulatory solutions

By Meg Bryant, Staff Writer

New Hope, Pa.-based Orchestra Biomed Inc. scooped up $34 million in a series B-1 preferred stock financing led by Perceive Advisors, RTW Investments and Soleus Capital. The funds will be used to advance development of the company's Backbeat cardiac neuromodulation therapy (CNT) system, to support commitments to Orchestra's strategic global partnership with Tokyo-based Terumo Corp. for the development and marketing of the Virtue sirolimus-eluting balloon (SEB) and to grow the

See Orchestra Biomed, page 3

Inside

FDA gives nod to Centerline's surgical navigation product in aortic interventions

By Liz Hollis, Staff Writer

Centerline Biomedical Inc., of Cleveland, has received a nod from the FDA to market its Intra-Operative Positioning System (IOPS). Specifically, the surgical navigation product won clearance for descending aortic interventions.

"To our knowledge, there are no direct competitors on the market. Other technologies are available that address some of the same pain points we seek to address – to reduce operator radiation exposure, or to improve intraoperative visualization, for example – but our IOPS

See Centerline, page 4

FDA drops discussion of promotion in final guidance for live cases

By Mark McCarty, Regulatory Editor

The live case has become a staple for medical society meetings that deal with cutting-edge medical technology, and the FDA had proposed in a 2014 draft guidance that the sponsor of the investigational device explain in a regulatory filing why that live case broadcast is not in violation of the general ban on promotion of unapproved devices. That language does not appear in the live case final guidance, however, removing a potentially show-stopping hurdle from one of the most popular means of disseminating information

See FDA, page 5

Israel's Dia Imaging partners with Konica for AI analysis solution

By David Ho, Staff Writer

HONG KONG – Dia Imaging Analysis Ltd., of Be'er Sheva, Israel, has teamed up with Konica Minolta Healthcare Americas Inc. to explore the analytic potential of Dia's Lvivo Toolbox for cardiac analysis combined with Konica Minolta's Exa cardio PACS platform.

"Konica offers powerful reporting systems to cardiac function analysis that enables users access patient's information anywhere. Arming Konica Minolta's PACS systems with Dia's AI cardiac toolbox would add another layer of

See Dia Imaging, page 6

Open-source artificial intelligence predicts outcomes of RCTs

By Annette Boyle, Staff Writer

Researchers at the Massachusetts Institute of Technology (MIT) have developed machine-learning and statistical techniques that predict the outcomes of randomized clinical trials (RCTs) for medical devices and potential new drugs.

See RCTs, page 7

BioWorld MedTech's Orthopedics Extra

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

Read this week's edition

Regulatory front

The **FDA** said in a June 20 warning letter to **Clinicon Corp.**, of Oceanside, Calif., that the manufacturer of single-use, surgical laser probes had failed to revalidate a sterilization procedure since 2015 despite that the initial validation protocol called for a subsequent revalidation. The company was also cited for failure to revalidate a packaging procedure for the Sureprobe laser probes, and for failure to calibrate a pneumatic sealer per company standard operating procedures. Clinicon is also said to have failed to document its evaluation of suppliers, and had no procedures for device history records. Clinicon provided the agency with a response to the April 4, 2019, inspection with an April 12 letter promising a further update within 90 days, but the FDA said the absence of "objective evidence to verify corrections," left the April 4 response inadequate.

The **FDA** said it approved 63 original PMAs and another three PMA supplements in fiscal year 2017, and that 16 of those PMAs were for pediatric uses or included indications for use for pediatric populations. The agency's annual FDA report to Congress for medical devices with pediatric indications noted that two humanitarian device exemptions had been approved for pediatric use in FY 2017, and that two of the PMAs were exempt from user fees due to a primary indication for use in pediatric patients. The median review time for the 16 PMAs was 179 FDA days and 327.5 total days.

The U.K. **National Institute for Health and Care Excellence** said the evidence in support of diagnostics for monitoring of therapy for inhibitors of tumor necrosis factor alpha (TNFa) is "promising," but insufficient to recommend routine use for patients under treatment for rheumatoid arthritis. The scope of the health technology assessment is limited to tests using enzyme-linked immunoabsorbent assay (ELISA) technologies, and addresses TNFa tests made by several manufacturers, including those made by Sanquin Diagnostics Services of Amsterdam. NICE recommended further research into the clinical effectiveness of these tests.

Financings

Dublin-based **Medtronic plc** reported early results of its cash tender offers for up to $5.525 billion. Investors tendered $642 million of the $1.175 billion notes and $7.95 billion of the $4.35 billion maximum tender offer notes.

One Biomed Pte Ltd., a Singapore-based medical diagnostics company, closed a $5 million series A financing round, led by Singapore-based Biopath Ventures and U.S.-based Arch Venture Partners, with Enterprise Singapore's investment arm, Seeds Capital, also participating. The company is developing platform technologies for diagnostics testing. It will use these funds to commercialize its first product, an automated sample preparation device for purification and isolation of nucleic acids from a variety of samples.

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Orchestra Biomed

Continued from page 1

company's product pipeline and pursue future collaborations. Terumo and existing investors from Sternaegis Ventures also participated in the round.

In addition to the $34 million, Orchestra stands to reap up to $57 million in follow-on investments from existing shareholders based on the series B-1 round and a 2018 series B financing that raised $41 million. Combined with other capital inflows, such as the Terumo partnership, the company has raised more than $64 million this year alone.

"We plan to expand on our pipeline and possibly to consider acquisitions and in-licensing products in the future that we think fit with our core business strategy and, as that strategy unfolds, this financing structure, which provides additional capital from our existing investors, is something that enhances our ability to execute on future opportunities," David Hochman, founder, chairman and CEO of Orchestra Biomed, told *BioWorld MedTech*.

High impact solutions

Focused on providing high-impact solutions for large unmet needs in procedure-based medicines, Orchestra won FDA breakthrough device designation for the Virtue SEB for coronary in-stent restenosis in April. A first-in-class combination product, Virtue SEB delivers sustained-release bioabsorbable nanoparticle-encapsulated sirolimus directly to the artery during balloon angioplasty with requiring a coating.

> *"We plan to expand on our pipeline and possibly to consider acquisitions and in-licensing products in the future that we think fit with our core business strategy.*
>
> David Hochman
> Chairman and CEO, Orchestra Biomed Inc.

In the EU-based multicenter, prospective SABRE clinical trial, the product performed well on safety and efficacy in patients with coronary intracoronary stent restenosis.

With Terumo, the company plans to launch U.S. and Japan registrational trials for that indication within the next year. The companies are also looking at clinical trials of Virtue SEB in other indications, such as small coronary vessels and below-the-knee peripheral artery disease in the U.S., Japan, China and other markets.

Under terms of the partnership, reported last month, Orchestra received an upfront payment of $30 million, plus an equity commitment of $5 million and future payments related to clinical and regulatory milestones. (See *BioWorld MedTech*, June 14, 2019.) The agreement also maintains Orchestra's rights to its sustained-release sirolimus formulation and to develop it in future applications outside of coronary and peripheral indications.

"We believe we have a platform that we can really drive further," Darren Sherman, Orchestra's founder, president and chief operating office, told *BioWorld MedTech*. "The safety and efficacy of this sustained-release formulation is well documented in these initial indications, but we believe the value of this drug and its application in other indications is going to be equally successful. Our focus in the short term is bringing forth preclinical development work and early clinical work in some of these other indications."

Expanded indications

While not revealing possible future indications, Hochman noted that sirolimus and analogue -limus drugs are well established in interventional cardiology for managing post-procedure inflammation and the development of scar tissue. "We think the formulation that we developed for Virtue SEB . . . can be harnessed in a lot of other areas where you have that acute effect of the procedure or you have chronic conditions where inflammation and fibrosis play a targeted role," he said.

Orchestra's other major candidate is the Backbeat cardiac neuromodulation therapy (CNT) for hypertension. Data from the Moderato I study showed a 14.2 mmHg drop in 24-hour ambulatory systolic blood pressure at three months and a 23.4 mmHg reduction in office cuff systolic blood pressure at two years. (See *BioWorld MedTech*, May 28, 2019.) A European nonregistrational, randomized, double-blind trial to further establish Backbeat's safety and performance recently completed enrollment and is expected to report six-month results later this year.

The trial is noteworthy, according to Hochman, because control arms in studies of device-based hypertension therapies typically involve sham procedures, meaning the patient is blinded but not the physician. "We're excited about this because it's really one of the first double blind trials in the device hypertension area, and it's facilitated by the effect that our therapy is an activated algorithm on an implanted device, so you really can do a double-blind trial," he said. "It's a first-of-a-kind in an exciting field that I feel has been difficult in terms of clinical execution."

All of this has Orchestra Biomed feeling optimistic about its future and its business strategy. "We're in a good capital position, we're in a good position to execute on additional capital raises with strong support from our existing shareholders, and we think that we have a business model that, whether its as a private company or eventually a public company, really can be attractive and create value for shareholders by being cash flow-focused," Hochman said. ♦

Centerline

Continued from page 1

technology combines electromagnetic tracking with patented anatomical mapping techniques in a novel way," Vikash Goel, Centerline Biomedical's founder and CTO, told *BioWorld MedTech*.

The solution is non-radiation-based to help in minimally invasive surgery. It leverages anatomical mapping algorithms and electromagnetic tracking technology to provide 3D color visualization and guidance in real time during endovascular procedures. The system was developed at the Cleveland Clinic's Heart and Vascular Institute and looks to offer an alternative to X-ray fluoroscopy, which serves as the current standard of care despite visualization challenges. For example, X-ray fluoroscopy suffers from a lack of soft-tissue visualization and involves 2D grayscale imaging, harmful radiation and contrast dyes, the company noted.

Centerline Biomedical said the offering has sensor-equipped catheters and guidewires similar to those used in existing operating rooms to assist with clinical decision support, including more accurate placement of stents and endografts. It also highlighted the potential for lower health care costs, as the product can help reduce treatment times, resulting in fewer errors and less need for follow-up procedures.

Cleveland Clinic

Centerline is a Cleveland Clinic spinoff company that was founded in 2014. It is a joint venture of G2 Group Ventures and the Cleveland Clinic, which praised the company following the FDA's action. "To date, Cleveland Clinic has partnered with some 87 companies; among these, Centerline has been particularly rewarding[,] and we are very excited about them having received 510(k) clearance. Most certainly as partners, shareholders, and prospective customers, we at Cleveland Clinic look forward to continuing support of the exciting research and commercialization efforts of this rapidly growing company," explained Jim Zalar, general manager of business solutions at Cleveland Clinic Innovations and Cleveland Clinic's appointee to the company's board.

Looking ahead

When asked about rollout plans, Goel noted that the focus will be on a few high-volume research hospitals. Taking that route will allow for significant clinical experience and show the product's value as a way to ease a broader launch.

"In parallel with our domestic market launch, we are currently working on obtaining the CE mark for marketing within the European Union," he added.

Goel noted that the company will continue to view Cleveland Clinic as a crucial partner. "In addition to significant financial investment provided by the institution, we benefit from being housed in the Cleveland Clinic-operated Global Cardiovascular Innovation Center incubator facility, from access to research labs, preclinical testing facilities, and global experts on clinical matters as well as hospital administration and business matters. Now that we have received clearance to legally market our system, it is our hope that the Cleveland Clinic will be one of the first hospitals, if not the very first hospital, to deploy the technology."

> *"Other technologies are available that address some of the same pain points we seek to address – to reduce operator radiation exposure, or to improve intraoperative visualization, for example – but our IOPS technology combines electromagnetic tracking with patented anatomical mapping techniques in a novel way.*
>
> Vikash Goel
> Founder and CTO, Centerline Biomedical Inc.

When asked about the near term, Goel said the company plans to expand its team to support the market launch, back regulatory progress in Europe and continue R&D efforts, "including execution of an NIH-funded study applying our IOPS technology to structural heart interventions," Goel concluded.

The FDA nod comes months after the company reported the submission to the FDA. That announcement also introduced new CEO Mark Modica. "We're like Google Maps for the human body," Modica said at the time. "With our data, IOPS will apply AI and machine learning to extract information that has never been encoded before, making it a real game changer."

The company noted at the time that it was raising series B funding in anticipation of market entry. ♦

Daily M&A

Franklin Park, Ill.-based surplus medical equipment company **Centurion Service Group** has acquired equipment refurbisher and retailer **Ganim Medical Inc.**, of Delaware, Ohio. No financial details were disclosed.

Medical equipment manufacturer **Hillrom** (formerly Hill-Rom Holdings Inc.), of Batesville, Ind., entered a definitive agreement to sell selected surgical consumable products and related assets to an affiliate of Boston-based **Audax Private Equity** for $170 million in cash. The divestiture includes Bard-Parker scalpels and blades, as well as other operating room accessories, which are expected to generate annual revenue of about $100 million in fiscal 2019, according to the company. The deal is expected to close in Hillrom's fiscal fourth quarter, ending Sept. 30.

Transenterix Inc., of Morrisville, N.C., reported the sale of certain Autolap image-based laparoscope positioning system assets to British Virgin Islands-based **Great Belief International Ltd.**, for total proceeds of $47 million.

FDA

Continued from page 1

to physicians regarding these novel technologies.

The draft guidance emerged with the notation that live case presentations may constitute protocol deviations for investigational device exemptions (IDEs), in part because the subject of the live case is by definition unblinded to adjudicators. The draft also highlighted the hazards associated with additional personnel and video equipment in the operating room or cath lab, but the agency also made the argument that the guidance would cut down on the need for supplements to investigational device exemptions that are filed strictly for the purpose of obtaining FDA approval for the live case. (See *BioWorld MedTech*, April 21, 2014.)

The Advanced Medical Technology Association (Advamed) indicated opposition to the requirement that the sponsor explain why a live case does not qualify as a promotional activity, stating that such a requirement is "overly burdensome and unnecessary." Tara Federici, then the association's VP for technology and regulatory affairs, said the agency might reasonably expect the sponsor to explain the need for a live case, but that the FDA should be able to determine whether a request for a live case constitutes a violative promotion based on the sponsor's request.

Cook's Ferguson: Prescience in short supply

The docket for the draft also drew comment from Stephen Ferguson, board chairman of the Cook Group Inc., of Bloomington, Ind., who said the net effect of the draft might be to discourage live case presentations. Ferguson said the draft's claim that the intent was to reduce the need for IDE supplements solely for live case presentations would seem to suggest that sponsors can accurately predict the number of live cases that would ultimately be requested. He requested that the FDA drop the live case presentation requirement from the draft prior to finalizing the guidance.

The final guidance omits the discussion of reduced requests for live cases, seemingly in response to Ferguson's comments. However, Advamed's Federici likewise took aim at the notion that a sponsor will be plausibly able to anticipate any and all need for live cases. Federici urged the agency to revise the passage by making clear that information about a specific live case presentation – or even whether such a presentation will be conducted – will not be known as of the date of the IDE filing. However, the final guidance requires that sponsors report on all live cases in the related regulatory filing, including live cases that were attempted and abandoned as well as those that were approved but not performed.

The FDA said in the draft that any live cases being webcast into the U.S. from other nations should comport with the provisions of the draft, although the draft also said, "foreign manufacturers and study sponsors should follow the laws and regulations" of the controlling national jurisdiction as well. Ferguson suggested that the FDA make clear in the final that the laws of the nation where the live case takes place will supersede the FDA's guidance and regulation, whereas Federici suggested that the agency tighten the scope of this provision to live case presentations performed "by investigational sites" outside the U.S. (OUS). Her reasoning in this instance was that the device in question might be approved in that OUS jurisdiction and thus the manufacturer has "limited ability to control the broadcast" of that live case. The FDA apparently concluded that this consideration could not be tenably addressed as it is omitted entirely from the final.

Despite urging sponsors to spell out their expectations regarding live case presentations, the draft repeatedly cites those instances as protocol deviations, which Federici said called for some clarification. She said not all live cases constitute protocol deviations, and suggested that each proposed live case ought to be individually evaluated for its potential impact on the study. Ferguson said the draft had implied that all live cases constituted protocol deviations even though the broadcast of the procedure might constitute the only difference in that patient's treatment. The term "protocol deviation" appears only once in the final guidance, however, in a section that lists the general conditions for requests for live cases, whereas the draft stated that an investigational plan must account for live cases, even in single-arm studies in which bias due to lack of randomization is not a concern.

The final guidance offers a few more suggestions regarding the impact of live cases on the study protocol, however, including a suggestion that the sponsor describe how bias in selection of patients for live cases would be minimized. The sponsor will also have to determine prospectively how the live case or cases will affect the endpoint analyses, including whether the live case subjects would be reported as a separate cohort. The effect on sample size should also be calculated and reported in the IDE application, the final guidance said. ♦

Appointments and advancements

Cantel Medical Corp., of Little Falls, N.J., said that Eric Nodiff, executive vice president, general counsel and secretary, will be retiring on July 31, 2019, after 32 years of service to the company. Jeff Mann has been appointed as senior vice president, general counsel and secretary, effective Aug. 1, 2019. Nodiff informed the board earlier this year that he will retire at the end of the company's fiscal year, and the board selected Mann as his successor. Mann joined Cantel in 2018 and has provided oversight of legal matters pertaining to the company's domestic commercial operations.

Dia Imaging

Continued from page 1

automation and objectivity to cardiac analysis, so clinicians could save time and manage patients even better," Hila Goldman Aslan, the CEO of Dia, told *BioWorld MedTech*.

"AI could assist in making ultrasound analysis smarter and help the medical staff to make decisions based on more objective data," Aslan said

Reducing subjectivity

The companies involved believe the use of pattern recognition, deep learning and machine learning algorithms through Dia's vendor-neutral toolbox can reduce the subjectivity that can result from manual or visual analysis of cardiac ultrasound images. Its algorithms automatically imitate how the human eye detects borders and motion.

"Millions of cardiac ultrasound scans are performed annually. Yet, the acquisition and analysis of ultrasound images are done mostly visually. Such a process is subjective, time-consuming, error-prone, cumbersome and highly dependent on users' experience," said Aslan.

The collaboration aims to make ultrasound analysis more accessible to more users with various levels of experience. As it can help optimize patient management, it can therefore reduce costs.

"With Dia's Lvivo Toolbox, Konica Minolta offers clinicians decision support with objective data," said Andrew Horning, cardiology product manager for Konica Minolta.

"Through this partnership, we will integrate innovative, AI-based cardiac analysis into Exa's already powerful and user-customizable structured reporting system; all available anywhere – from a multimonitor workstation on a hospital network, to a laptop PC on Wi-Fi. This helps cardiologists make better decisions sooner," he added.

But Aslan also sees the partnership with Konica Minolta as a long-term relationship that will extend beyond implementing Lvivo Toolbox.

Can AI solve ultrasound challenges?

The Israeli provider of artificial intelligence-powered ultrasound analysis tools foresees AI playing a major role in solving the two big challenges in ultrasound: acquisition of the right images and analyzing the images accurately.

"By using AI tools, clinicians could shorten analysis time and focus on tasks yielding higher reimbursement. New users are projected to adapt ultrasound to their workflow and AI will make their adaptation more accessible and feasible," said Aslan.

In short, assisting ultrasound users with AI will improve both productivity and patient management.

And in the future, AI will probably be adapted to more medical systems, making them smarter.

Though Aslan believes AI is actually driving medical imaging, she is quick to note that implementing AI in medical systems will not replace physicians or sonographers.

> *"AI could assist in making ultrasound analysis smarter and help the medical staff to make decisions based on more objective data.*
>
> Hila Goldman Aslan
> CEO, Dia Imaging Analysis Ltd.

Rather, she thinks it will actually empower them and will contribute to a medical staff's efficiency.

"It could help clinicians receive quantitative indications, instead of qualitative estimations, to support their decisions. Machine learning and deep learning algorithms will be more accurate, faster and easy to use than ever," said Aslan.

Lvivo clinical results

Dia also recently shared the findings of two studies that supported the use of the company's Lvivo EF AI-based solution that generates fully automated Left Ventricular (LV) Ejection Fraction (EF).

The first study tested the accuracy of the Lvivo EF tool on 76 patients by retrospectively running it on cardiac 4 chamber clips. The results were compared to those obtained by MRI EF as a gold standard.

"Based on the study's findings, Lvivo EF has the potential to provide accurate and objective quantification of LV EF to support clinicians in the decision-making process, right at the patient's bedside, saving time and resources. This is specifically important in patients with low EF, where accuracy has clinical and therapeutic implications," said Martin Goldman, associate director of the CV Institute, who led the study.

"Moreover, by providing the endocardial border overlay on the moving images, it also facilitates immediate confirmation of its accuracy by the reader."

This led to a second study that compared Lvivo EF results to physicians' evaluations of EF using transthoracic echocardiography, with and without contrast agents.

The results indicated that in non-contrast studies compared to cardiac MRI, Lvivo EF was significantly better than physicians' assessments ($R^2=0.823$ vs. $R^2=0.622$).

For contrast studies that are often used to improve LV EF analysis, Lvivo EF on non-contrast images and physicians' quantification of contrast enhanced images were similar ($R^2=0.913$ and $R^2=0.873$). ♦

RCTs

Continued from page 1

The collaboration between MIT's Laboratory for Financial Engineering (LFE) and Informa Pharma Intelligence, called Project ALPHA (Analytics for Life-sciences Professionals and Healthcare Advocates), leverages the largest dataset to date in its predictive models.

The goal of the software, which will be available with an open-source license, is to develop sophisticated analytics that reduce the risk of drug and device development. A study in the *Harvard Data Science Review* found the model accurately predicted the transition of therapeutic compounds from phase II to approval and from phase III to approval.

"Everyone is affected by the risk of a drug failing in its clinical trial process," says Andrew Lo, the study's senior author and director of MIT's LFE and a principal investigator at the university's computer science and artificial intelligence laboratory (CSAIL). "With more accurate measures of the risk of drug and device development, we hope to encourage greater investment at this unique inflection point in biomedicine."

The ability to forecast clinical trial outcomes at the earliest possible date could reduce costs, speed drug approval times, and attract more money to research from more risk-averse investors.

Reducing risk has increased in importance as costs associated with new drug development have risen. The transformation of medical care with the emergence of immune therapies, gene therapies and gene editing have made the drug development and approval process ever more complex and costly. As a result, drug development productivity has dropped steadily over the past 50 years, the researchers noted.

"These breakthroughs generate novel therapies for investigation, each of which requires many years of translational research and clinical testing, costing hundreds of millions to billions of dollars and yet often face a high likelihood of failure," researchers said.

"Anyone involved in the clinical trials process – from researchers all the way down to the patient – can benefit from greater understanding of the landscape and use of new technologies evaluating what's working and what's not," said Mark Gordon, EVP Corporate Development and Innovation in Informa's business intelligence division.

Key predictive factors

The researchers applied machine learning techniques to drug development data and clinical trial results from 2003 to 2015. The analysis involved several thousand drug-indication pairs examined for more than 140 features. The trials covered 15 disease groups.

The team found that six factors had the greatest impact on success: trial outcomes, trial status, trial accrual rates, study duration, prior approval for another indication and the sponsor's previous record of approvals. Predictive accuracy rose with time, as both data quality and quantity improved over the rolling five-year windows studied.

The results proved more accurate than complete case analysis and resolved the problem of missing data. The model used statistical methods to impute missing data to permit use of the full dataset in the algorithm.

With the estimates for missing data, the model had a predictive value of 0.78 at phase II and 0.81 at phase III that a drug would make the transition to approval, using the area under the receiver operating characteristic curve metric.

"It's the difference between looking back at historical wins and losses to predict the outcome of a horse race versus handicapping the likely winner based on multiple factors like the horse's pedigree, track record, temperament, the training regimen, the condition of the track, the jockey's skill, and so on," said Lo.

Kien Wei Siah and Chi Heem Wong, two LFE/CSAIL PhD students who co-authored the publication, observed that, "You can't manage what you don't measure, so this is a new tool for measuring the risk of clinical trials more accurately, allowing all stakeholders to plan more effectively for these risks."

Looking forward

The collaboration moves drug development forward on two key paths – increased transparency and greater use of advanced technology in the clinical trial process, both of great interest to investors and regulators.

In conjunction with programs that promote sharing of patient-level clinical trial data, the researchers concluded, "such predictive analytics can be used to make more informed data-driven decisions in the risk assessment and portfolio management of investigational drugs at all clinical stages." ♦

Other news to note

ABB Robotics, part of Zurich, Switzerland-based ABB Group, said it will introduce collaborative robots to medical laboratories as it opens a new health care hub at the Texas Medical Center (TMC) innovation campus in Houston. The facility will be ABB's first dedicated health care research center when it opens in October. The team will work on the TMC campus with medical staff, scientists and engineers to develop non-surgical medical robotics systems, including logistics and next-generation automated laboratory technologies.

Battelle Memorial Institute, of Columbus, Ohio, is combining brain-computer interface projects, such as Neurolife, with its expertise in machine learning and artificial intelligence under a new award from Defense Advanced Research Projects Agency (DARPA). The award is part of DARPA's Artificial Intelligence Exploration program called Intelligent Neural Interfaces.

Circassia Pharmaceuticals Inc., of Oxford, U.K., won a group purchasing agreement for pulmonary function and metabolic analyzers with **Premier**. The new agreement allows Premier members to take advantage of special pricing and terms pre-negotiated by Premier for Niox asthma diagnosis and management devices.

Other news to note

A cyber vulnerability has been discovered in hospital anesthesia machines, according to the U.S. Department of Homeland Security's Industrial Control Systems – Cyber Emergency Response Team. The vulnerability, which was discovered by New York-based health care cybersecurity provider **Cybermdx**, could allow an attacker to impair respirator functionality, changing the composition of aspirated gases – silencing alarms, and altering time/date records. The team found this vulnerability in the protocol of GE Aestiva and GE Aespire devices (models 7100 and 7900). Through the vulnerability, remote commands can be sent to interfere with the normal working order of the device.

Day Zero Diagnostics Inc., a Boston-based infectious disease diagnostics company using genome sequencing and machine learning to combat the rise of antibiotic-resistant infections, received a phase I Small Business Innovation Research award from the National Institute of Allergies and Infectious Disease of the NIH. The award will fund the development of Ksim, an algorithm to automate the determination of infection relatedness in suspected hospital-acquired infection outbreaks.

Imaging and informatics company **Fujifilm Medical Systems U.S.A. Inc.** and surgery solutions company Fujifilm New Development U.S.A. Inc, both of Waltham, Mass., reported the opening of new company headquarters in Lexington, Mass. The 28,000-square-foot facility will bring Fujifilm's computed tomography, digital radiography, women's health, endoscopy, minimally invasive surgery and Medical IT units under a single roof for the first time. The company will continue to operate satellite offices in North Carolina, Wisconsin, New York and New Jersey. An office in Stamford, Conn., closed in April.

Myovant Sciences Ltd., a London, U.K.-based company developing therapies for women's health and endocrine diseases, and San Mateo, Calif.-based health analytics company **Evidation Health Inc.** are teaming up on a digital study of the prevalence and impact of menstrual symptoms experienced by American women. The study, which aims to better understand attitudes of men and women around menstruation, will target 20,000 people with questions delivered via Evidation's health app, Achievement. The companies hope to present their findings in the second half of 2019.

Amsterdam-based health technology company **Royal Philips NV** and **Centre Hospitalier Régional Universitaire de Nancy**, of Nancy, France, reported that they have entered a 10-year agreement to deploy Philips' Intellispace enterprise imaging system. The comprehensive imaging system includes the Intellispace Universal Data Manager, Intellispace Radiology and Intellispace Radiology Workspace and Illumeo with adaptive intelligence. Separately, Philips reported that it has joined Pittsburgh-based **Teletracking Technologies Inc.**, as a founding sponsor of BRI Network's inaugural Command Center Summit: Connected Care Delivery, slated for July 15-16 in Chicago.

Soliton Inc., a Houston-based company providing rapid acoustic pulse (RAP) technologies for health care applications, reported that it has added a second site to its upcoming expanded pivotal cellulite trial. The trial, which will evaluate the effectiveness of the noninvasive Soliton RAP in removing unwanted cellulite, plans to have a total of four sites.

San Clemente, Calif.-based **Spinal Singularity Inc.**, a company focused on spinal cord injuries and diseases, reported that it was awarded more than $3.6 million from the U.S. Army Medical Research and Material Command's Congressionally Directed Medical Research Programs during fiscal year 2018 for the Spinal Cord Injury Research Program. The program challenges researchers to explore and address ongoing issues around understanding and treatment of spinal cord injuries.

Austin-based diagnostics company **Volitionrx Ltd.** reported that it has received further nondilutive funding in the form of a $1.4 million nonrepayable cash grant from the Walloon Region in Belgium. The grant brings to roughly $6 million the amount of nondilutive funding Volition has been awarded by the region. The company said it will support a specific project being conducted in collaboration with GIGA at the University of Leige, Belgium.

Veeva Systems, a Pleasanton, Calif., company offering cloud-based software for life sciences companies, reported that eye care products company **Alcon**, of Elkridge, Md., has selected the Veeva Vault clinical data management system (CDMS) as its enterprise CDMS for electronic data capture. In addition, Alcon is a suite of Veeva products, including Vault Promomats, Vault Etmf, Vault CTMS, Vault Submissions, Vault Submissions Archive, Vault Qualitydocs and Vault Training.

Product clinical data for June 10, 2019

Company	Product	Description	Indication	Status
Respicardia Inc., of Minnetonka, Minn.	Remedē system	Implantable neurostimulation system	Treatment of central sleep apnea (CSA) by restoring a more normal breathing pattern during sleep	Published 24- and 36-month data in *SLEEP*; demonstrated long-term safety and sustained improvement in sleep metrics from phrenic nerve stimulation in adult patients with moderate to severe CSA; results from 109 patients at 24-months showed a 99% reduction in the median of the central apnea index from baseline, a 59% reduction in the median arousal index from baseline and 93% of patients had a reduction in the apnea-hypopnea index from baseline

Notes

For more information about individual companies and/or products, see Cortellis.

Product regulatory actions for June 10, 2019

Company	Product	Description	Indication	Status
Centerline Biomedical Inc., of Cleveland	Intra-Operative Positioning System	Non-radiation-based surgical navigation system; uses anatomical mapping algorithms and electromagnetic tracking technology	Provides color visualization and guidance in real time during endovascular procedures	Received 510(k) clearance from the U.S. FDA
Insightec, of Haifa, Israel	Exablate Neuro	Focused ultrasound platform	Treatment of medication-refractory essential tremor, tremor-dominant Parkinson's disease and neuropathic pain	FDA approval and CE mark for compatiblity with the Signa Premier MRI system from GE Healthcare
Nemaura Medical Inc., of Loughborough, U.K.	Sugarbeat	Noninvasive continuous glucose monitor	Helps people with diabetes and pre-diabetics better manage glucose levels by spending more time in range	Submitted its de novo 510(k) application to the U.S. FDA

Notes

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Orthopedics Extra

Keeping you up to date on recent developments in orthopedics

By Holland Johnson, Executive Editor

Mini 'magic' MRI scanner could diagnose knee injuries more accurately

Researchers at Imperial College London have developed a prototype mini MRI scanner that fits around a patient's leg. The team say the device – which uses so-called 'magic angle' effect – could potentially help diagnose knee injuries more quickly, and more accurately. In a proof-of-concept study using animal knees, the results suggest the technology could be used to show all the structures of the knee. The scientists say the device could help diagnose conditions such as anterior cruciate ligament injuries. Furthermore, the small size of the device could enable it to be used in local clinics and even GP surgeries, potentially reducing National Health Service waiting times for MRI scans. Following knee injury a doctor may refer a patient for a MRI scan to help establish which part of the joint is injured. MRI scans use a combination of radio waves and strong magnets to 'flip' water molecules in the body. The water molecules send out a signal, which creates an image. However, tendons, ligaments and meniscus are not usually visible with MRI, due to the way water molecules are arranged in these structures, the scientists said. To overcome this problem, they harnessed the power of a phenomenon called the 'magic angle': "The brightness of these tissues such as tendons and ligaments in MRI images strongly depends on the angle between the collagen fibers and the magnetic field of the scanner. If this angle is 55 degrees the image can be very bright, but for other angles it is usually very dark." The team explain the magic angle is achieved in their scanner because they are able to easily change the orientation of the magnetic field. This is not possible in current hospital MRI scanners, which are also much more expensive than the prototype scanner. In a new study, published June 28, 2019, in the journal *Magnetic Resonance in Medicine*, the multidisciplinary team scanned the knee joints of six goats and 10 dogs in a conventional MRI scanner. The results showed that using the magic angle can accurately detect ligament and tendon damage. The team say now they know magic angle scanning can be used to visualize the knee, combining this with the new prototype mini scanner could enable knees to be accurately scanned with this technology – and hope to progress to human trials of the 'mini' scanner within a year.

BioSA – Bridging the gap with biodegradable metals

Millions of patients all over the world undergo surgical procedures related to bone defect repair every year. With an ever-increasing life expectancy and the issues that come with a decaying skeleton, the number of interventions can only increase in the coming years. This is why orthopedic surgeons are constantly looking for improved medical implants for the treatment of bone repair. The University of Malta has teamed up with Mater Dei Hospital to address the shortcomings of current bone scaffolds on the market in a project titled Biodegradable Iron for Orthopaedic Scaffold Applications (BioSA). The team members are pooling their expertise to develop an improved bone regeneration scaffold design with optimized characteristics. Despite the fact that ceramic scaffolds are widely used, their tendency to break due to their brittle nature, has made them inadequate for use in bones that are subjected to sudden loading, while polymeric scaffolds lack the mechanical strength to be used in load-bearing applications. Metals, on the other hand, have the potential to exhibit the perfect balance between strength and toughness. The BioSA scaffold is being designed such that it corrodes at a controlled rate within the body, to match the rate at which the bone is healing. This aspect could result in reducing the necessity of a second surgical intervention to remove the implant after bone has healed. The BioSA team is focused on understanding the corrosion behavior of such an implant while also studying the effect that such an implant has on cells found in the bone. Through an innovative processing technique, based on the use of metal powders, the team also aims to gain control over the shape of the final scaffold. Accidents can happen to everyone and defects can be bigger than the body can heal naturally. So ideally scaffolds are not designed as one-size-fits-all but can also be custom-made for a specific patient.

Nuvasive launches Pulse spine surgery platform

Nuvasive Inc., of San Diego, reported the launch of the Pulse integrated technology platform. The company said that Pulse is the first, single platform to include multiple technologies designed to help surgeons adopt more efficient, less disruptive surgical approaches in all spine procedures. The Pulse platform combines neuromonitoring, surgical planning, rod bending, radiation reduction, imaging and navigation functions, with extensible capabilities to enable increased surgical efficiencies in the operating room (OR). These integrated technologies are designed to improve a surgeon's ability to utilize minimally invasive surgery (MIS) techniques, which have been shown to reduce blood loss, hospital stays and result in less operative morbidity compared to open spine surgery. Nuvasive completed limited clinical release testing of the Pulse platform, providing initial validation that its structural design supports broad clinical utility throughout the entire surgery, and is usable in 100% of spine surgeries, from fusions to complex corrections. Its independent device access allows OR staff to simultaneously view the technologies' imaging and insights in real time and in parallel, creating a seamless, optimized OR workflow. In addition, the open and modular architecture of the Pulse system allows for flexible technology packages, allowing surgeons to select the exact tools they need to address specific pathologies in spine surgery procedures.