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FIRST TO MARKET FOR THIS NEW INDICATION

Medtronic Evolut approved for lower-risk TAVR patients in Europe, sales on the incline

By John Brosky, Contributing Writer

PARIS – Medtronic plc., based in Dublin, won the first regulatory approval for extending transcatheter aortic valve repair (TAVR) to patients with an intermediate risk for traditional surgery, a controversial indication that has been eagerly sought by some clinicians but resisted by others.

Medtronic announced its next-generation Corevalve Evolut R System to treat aortic stenosis has received a CE mark to treat intermediate risk patients where a decision for the procedure is made by an interdisciplinary heart team.

The approval was based on positive clinical data from the 280-patient Nordic Aortic Valve Intervention (NOTION) Trial and from a subset analysis from the Corevalve High

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TAKING OUT THE NOISE

Oticon uses pupil size to develop new hearing devices and measure brain strain

By Amanda Pedersen, Senior Staff Writer

Oticon Inc. is using pupillometry science – a measurement of pupil dilation – to develop hearing aid technology designed to reduce listening effort and conserve energy so that people with hearing loss remember more of what they've heard.

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EXPECTING COMPLETION IN 2017

Foundation Medicine's cancer diagnostic to receive accelerated reviews from FDA, CMS

By Varun Saxena, Staff Writer

Foundation Medicine Inc.'s Foundationone pan-cancer comprehensive genomic profiling assay will be reviewed via FDA's Expedited Access Pathway. In addition, it will be evaluated for reimbursement via the FDA/Centers

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REGULATORY

CMS affirms no new technology add-on payment for Edwards' Intuity in FY 2017

By Mark McCarty, Regulatory Editor

The inpatient prospective payment system final for fiscal 2017 finally emerged, and Edwards Lifesciences Corp., of Irvine, Calif., received a not-unexpected bit of bad news. The company's application for a new technology add-on payment (NTAP) for its Intuity Elite aortic valve came up short for the upcoming fiscal year, but the device will still be eligible in FY 2018.

The U.S. Centers for Medicaid and Medicare Services (CMS) seemed skeptical of Edwards' cost analysis for the Intuity valve, but the agency noted that the FDA had yet to approve the device by the July 1 deadline for NTAP applications, hence the decision to pass. The draft IPPS included some discussion of the clinical data provided in support of the NTAP application, including a remark by CMS that transcatheter aortic

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DAILY M&A

Myriad Genetics Inc. said it will pay $225 million up front and possibly $185 million in additional performance-based payments to acquire Assurex Health Inc. Myriad, of Salt Lake City, said it expects the deal to close at the end of its first quarter in fiscal year 2017. Assurex, of Mason, Ohio, makes genetic testing products, such as the Genesight test, for psychotropic medicine selection. The acquisition provides Myriad an entry into the neuroscience market with a product designed to improve patient outcomes and lower health care costs. Myriad said it intends to fund the transaction through cash on hand and debt and has already obtained committed debt financing from JPMorgan Chase & Co. A the end of the fiscal third quarter Myriad had cash and cash equivalents of $286 million. J.P. Morgan Securities LLC is Myriad's financial advisor and Mintz Levin Cohn Ferris Glovsky and Popeo PC are providing legal counsel.

FINANCINGS

Ornim Inc. reported an initial raise of $20 million in a series C financing led by Longtec Hongtao China Ventures LP. Existing investors, including Orbimed and GE Ventures, also participated. Ornim, of Kfar Saba, Israel, said the financing will support expanded global commercialization of its lead product, the C-flow patient monitoring system. The company said it anticipates raising up to $10 million more in the round.

San Diego-based **Statrad LLC** said it received a $13 million equity investment from an undisclosed institutional partner. The company said the funding will be used to accelerate development of its medical image management technology. The investment also will support growth in teleradiology services and the company's Radconnect cloud-based image sharing solution, Satrad said.

APPOINTMENTS AND ADVANCEMENTS

Novanta Inc., of Bedford, Mass., said it has named Matthijs Glastra as CEO and a director of the company, effective Sept. 1. Glastra currently serves as Novanta's COO, and will succeed John Roush as CEO. Roush will continue to serve in an advisory role after Sept. 1, 2016 for a limited transition period.

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Medtronic

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Risk Pivotal Trial in the U.S.

Eberhard Grube, director of the structural heart program at the University Hospital in Bonn, Germany, said that "the highly-anticipated intermediate risk indication marks an important milestone for the industry as we look to safely expand TAVR access to younger and less sick patient populations."

Medtronic spokesperson Joey Lomicky told *Medical Device Daily*, "A majority of the patients treated with TAVR in Europe will continue to be of the extreme and high-risk patient populations, but expanding indication for the Corevalve Evolut R system will help heart teams provide excellent clinical outcomes for broader indicated patient populations."

EUROPEAN TAVR SALES EXPECTED TO REACH $1B IN 2016

TAVR procedures currently hold a 37 percent share of the market in Europe, against traditional surgical aortic valve repair (SAVR) according to estimates provided by Senior Medical Device Equity Research Analyst Larry Biegelsen with New York-based Wells Fargo Securities LLC.

Medtronic devices are used in 31.5 percent of those procedures against a 52 percent share for Irivine Calif.-based Edwards Lifesciences Corporation, according to Biegelsen.

He estimated total sales of TAVR devices in Europe will crest the $1 billion milestone in 2016.

In both Europe and the U.S., TAVR to this point has only been approved for use in a patient population at high-risk for undergoing SAVR.

CoreValve Evolut R first won CE mark approval in September 2014. The device was approved by the U.S. FDA in June 2015 for severe aortic stenosis patients who are at high or extreme risk for surgery.

The opportunity for expanding TAVR penetration with the indication for a vastly larger population of patients at intermediate risk for SAVR is not known, though widely expected to be significant.

Edwards reported to investors that it filed for a CE mark for expansion into intermediate risk patients for its Sapien 3 TAVR valve in 2Q16 and that it expects approval in late 2016 or early 2017.

Edwards CEO Michael Mussallem said he expects the company to invest up to 16 percent of sales into research and development to expand patient access to TAVR. (See *Medical Device Daily*, Dec 10, 2015.)

Earlier this year Medtronic completed enrollment in the Surtavi clinical trial and according to Lomicky, the company is working collaboratively with the FDA on an accelerated path for submitting an approval for intermediate-risk patients.

The company is also enrolling the Evolut Low Risk Trial that will include up to 80 heart centers in the U.S. that will randomize 1,200 patients between SAVR and TAVR using the Evolut R system.

In Europe, the extension of TAVR to lower risk patients was the focus for The Great Debate in May 2016 at EuroPCR 2016 that pitted three leading clinicians on either side of the question. (See *Medical Device Daily*, May 18, 2016.)

Evidence from head-to-head clinical trials have indicated that SAVR and TAVR are fairly evenly matched for efficacy, though with different complication profiles.

Traditional surgery poses a greater risk for bleeding, kidney damage and the onset of atrial fibrillation requiring a pacemaker implantation. TAVR has struggled against persistent paravalvular aortic regurgitation and a significant pacemaker implantation rate.

Yet for patients at lower risk for traditional surgery, who tend to be younger, the key concern among clinicians is the durability of the valve leaflets on TAVR devices.

SAVR vales have a long history regarding durability that can stretch to 25 or 30 years.

Yet little is known about the durability of TAVR valves that were first introduced in 2002 and did not reach a significant patient population until 2007.

Placing a prosthesis that is expected to last eight years in an 80-year-old patient at high risk for surgery may be seen as a benefit in extending the patient's life from an expected one year out to eight years.

The question of placing a shorter-term TAVR device in a 70-year-old patient who could undergo surgery instead of a SAVR valve with a history of extending life out 30 years is at the heart of the current controversy.

The debate at EuroPCR quickly centered on valve durability as earlier the same day results from the first effort to study valves beyond the three to five years in manufacturers' studies was released.

Danny Dvir, from St. Paul's Hospital in Vancouver, British Columbia, effectively punctured the balloon of TAVR enthusiasm with a report titled, "A First Look at Long-Term Durability of Transcatheter Heart Valves: Assessment of function up to 10 years after implantation."

Among the 378 patients enrolled, Dvir reported that the median time to degeneration of the implanted valve was five years, and at eight years, half of all patients with early TAVR devices were affected.

"Everyone should know there is a phenomenon of THV degeneration so that when we target younger patients, lower risk patients who may survive longer, their valve may fail," he concluded. //

Oticon

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In a recently completed study, researchers at the Denmark-based Eriksholm Research Center and the VU University Medical Center investigated how hard the brain has to work to understand speech in different environments and how that knowledge could be leveraged for use in new hearing devices.

Thomas Behrens, head of audiology for the center of applied research at Oticon, told *Medical Device Daily* that when people pay attention to sound, the muscles in their eyes contract and release based on listening effort. The more challenging the task, the larger the pupil.

"Hearing loss imposes a load on the brain," he said. "It's more difficult for the brain to get some of the little details in speech and to separate foreground noises from background noises."

In most social situations, such as a family dinner or eating at a restaurant, it's harder for the brain to function because there are multiple people speaking and other noise going on in the background.

In the study, researchers showed how pupillometry could be used to measure strain on the brain's processing power when trying to understand speech. The results allowed Somerset, N.J.-based Oticon to measure how technology in the company's new Oticon Opn hearing aid not only reduces listening effort, he said, but also allows people to save energy so they can remember more of the conversation.

Oticon's technology is designed to open up different environments for people with hearing loss by removing background noise to make it easier for their brain to process what they're hearing, Behrens said.

The researchers reported that in the study, which included 24 people, in looking into the eyes of Opn wearers compared to people with the company's older Alta2 Pro hearing aids, they saw 20 percent less listening effort when trying to understand speech while others are speaking. Additionally, they saw an average reduction in peak pupil dilation of 26 percent during the speech-noise reduction task using Opn compared to Alta2 Pro.

"We placed speech and noise all around the person to mimic the family dinner," Behrens said. He said the Opn reduced cognitive load for study participants by about 25 percent. This provided an objective measure of the cognitive load imposed by hearing loss, which is something audiologists have long searched for, he said, as most research in this area is based on more subjective measures.

Without the help of a hearing aid like this, he said, people with hearing loss get tired easily in these environments and tend to avoid social situations. But that's not the best solution, he said, because social situations stimulate the brain in many good ways and works against Alzheimer's and reduces cognitive decline.

"Social situations activate those parts of the brain that you need to keep fresh," he said.

The company is now tasked with continuing to develop and improve the technology based on user feedback. One of the key challenges Oticon has faced in developing Opn, Behrens said, is actually limiting the technology's power because early testers of the device reported that it was too effective and reduced too much of the background noise.

"We know we have a lot of power in this technology," he said.

In the near future the company also wants to explore more ways to make the device more integrated with the wearers brain and more automated than they are today, Behrens said.

The company has started to receive feedback on the technology from people who have used Opn after suffering from hearing loss for many years. For example, Behrens said one person who uses the device is a lawyer who told the company that before having Opn he wasn't really able to sense what mood people were in – something that made it difficult for him to be fully effective in court.

Others have reported a notable reduction in their anxiety levels because the device gives them the extra cognitive capacity they need to be more certain about what they are doing.

"People feel more free and empowered to live their life the way they want," Behrens said. //

Foundation

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for Medicare and Medicaid Services (CMS) parallel review program.

As a result, the diagnostic will have a shorter review time, and should be eligible for nationwide Medicare reimbursement upon FDA approval. The Cambridge, Mass.-based company said it anticipates the parallel review will conclude in the second half of 2017.

The company performed 8,864 Foundationone tests during its recently completed quarter under the CLIA rules that govern laboratory-developed tests (LTDs).

"We have separately made a voluntary decision to seek FDA-approval of our laboratory-developed test," Lakshman Ramamurthy, Foundation Medicine's global regulatory lead, told *Medical Device Daily*.

The decision coincides with signals that the FDA intends to increase its regulatory scrutiny of LDTs in the years ahead. Most notably, the agency in October 2014 released a draft guidance that described its plans to review LDTs. Finalization of the controversial guidance has stalled, but once a final version is released, the diagnostic tests performed in specialized laboratories will need to meet the FDA's stringent standards by demonstrating analytical and clinical validity.

Currently, tests carried out at the CLIA-certified laboratories do not require FDA approval, but some companies like Foundation Medicine are seeking it anyway, both in anticipation of the future and out of a desire to earn a regulatory gold star.

"We want to be an honest and diligent participant in patient health care," Ramamurthy said.

EXPEDITED REVIEW PROGRAM LENGTHENS ITS PIPELINE

Foundationone uses next-generation sequencing tools to detect genomic alterations, such as insertions, deletions, copy number alterations and gene rearrangements in hundreds of genes using DNA isolated from formalin-fixed paraffin-embedded tumor tissue specimens. In turn, the genomic data is used to guide the selection of targeted medications that are intended for patients with tumors that have specific genomic alterations.

"Upon successful completion of parallel review, Foundationone could become the first comprehensive genomic profiling assay, or CGP, to be FDA approved and with a national coverage determination for Medicare beneficiaries. We believe this universal companion diagnostic will be transformational by setting a new standard in assessing the molecular blueprint of cancer to better inform therapeutic options," Foundation Medicine CEO Michael Pellini said during the company's Aug. 2 second quarter earnings call.

"Our strategy is to remove the guesswork for physicians by providing a comprehensive view of CDx claims through Foundationone. Today, given the increasing number of single marker companion diagnostics, oncologists are quickly becoming overwhelmed with the complexity in selecting the appropriate test for each patient. Our test will be a single validated CGP assay of 324 genes, including a range of companion diagnostics, providing physicians with much of the necessary genomic information to point them to the relevant approved cancer therapeutics and do so with documented regulatory level quality," he continued.

Breakthrough devices that receive a review under the FDA's expedited access pathway are supposed to be approved (or rejected) quicker, and receive benefits such as priority review, more interactive review, senior management involvement and assignment of a case manager. In addition, and perhaps most importantly, the agency is more likely to be accepting of an abbreviated clinical trial. Ways in which clinical trials can be made smaller have been spelled out in a variety of FDA guidance documents, such as a July 2016 one on adaptive designs for medical device clinical studies.

Foundationone's acceptance into the program signifies that the FDA believes that the device is "intended to treat or diagnose a life-threatening or irreversibly debilitating disease or condition" and "offers significant, clinically meaningful advantages over existing legally marketed alternatives." Any plans for shorter clinical trials must be described in Foundation Medicine's data development plan, which the FDA must accept prior to submission into the program. Ramamurthy declined to disclose any details of the development plan.

In May, the FDA said it had accepted 17 devices for review under the expedited access program out of a total of 29 submissions at the program's one-year mark.

ACTION AROUND PARALLEL REVIEW PROGRAM

The FDA's relationship with the device industry has steadily improved due to initiatives like the expedited access program, but the same can't be said about the CMS, which has become increasingly restrictive about reimbursement of new devices and diagnostics.

FDA and CMS officials often talk about the need for interagency cooperation in a bid to speed up reimbursement decisions, and tout the parallel review program as the centerpiece of the initiative.

But since its inception in 2010, the program has resulted in one joint decision in 2014, that of Marlborough, Mass.-based Exact Sciences Corp.'s DNA-based Cologuard diagnostic for colorectal cancer, which simultaneously received FDA approval and a National Coverage Decision from CMS.

So, the addition of another diagnostic to the pipeline provides

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valves would have been a more appropriate comparator than the other minimally invasive valve placement procedures and systems used to support the Intuity application. (See *Medical Device Daily*, April 20.)

Abbott Vascular, of Temecula, Calif., came in with a win for its Mitraclip device in the IPPS final thanks to CMS's decision to collapse three Medicare severity-adjusted diagnostic related groups (MS-DRGs) into two, a move undertaken to deal with the transition from ICD-9 to ICD-10. The changes to the DRG allotment gave Abbott a new payment set point for its Mitraclip device without the need for an NTAP, and an investor note by Wells Fargo of San Francisco pegged the new reimbursement rate for the Mitraclip at a bit less than $34,600, a considerable boost from the $31,000 or so the device is said to have drawn in the NTAP program.

Advocates of a new set of DRGs for total ankle replacement fared no better in the IPPS final than in the draft. The placement of these devices/services in DRGs 469 and 470 was said to have the potential for complicating the agency's Comprehensive Care for Joint Replacement (CJR) program due to co-occupancy by other joint replacement devices and procedures, but CMS said the volume of ankle replacements was too small to exert much effect on the CJR program's results.

CMS held to its position that no new DRG is needed for automatic implantable cardioverter defibrillator (AICDs) generators to adjust for severity, which will continue to work from within DRG 245 as proposed in the draft IPPS. CMS examined a three-way split and a two-way split of 245 to adjust for severity, but the three-way split faltered on the point of a cost differential of at least 20 percent between each category. The two-way split lost out because the category of major complications/comorbidities failed to account for at least 500 cases.

Among the companies that managed to retain NTAP payments were C.R. Bard and Medtronic, which both saw another year of payments for their Lutonix and In.Pact Admiral drug-coated balloons for peripheral artery disease. Bard projected a higher set of costs associated with the Lutonix, projecting a unit price of $1,900 and an average per-procedure use of just shy of 1.4 balloons, while Medtronic estimated a unit cost of $1,350 and an average of 1.4 units per procedure. CMS declined to use a different NTAP payment level for the two offerings, opting instead for a weighted average cost calculation that resulted in a maximum per-case payment of $1,306.

Cardiomems, the Atlanta-based company acquired by St. Jude Medical Inc. of St. Paul, Minn., will retain eligibility for an NTAP payment, which will come to $8,875 in FY 2017, although the news does not seem to insulate the device from a coverage with evidence development mandate by one Medicare administrative contractor (MAC) and a non-coverage determination by another. A representative of St. Jude told *Medical Device Daily* earlier this year that the company had request a national coverage determination for the system. (See *Medical Device Daily*, Feb. 23.)

Nuvasive of San Diego has a year of NTAP payment coming for its Magec spinal rod system for use in children with scoliosis. The device, which Nuvasive added to its portfolio via an acquisition of Ellipse Technologies Inc., will take in a Medicare payment of $15,570 per case.

FDA POSTS IEC/X-RAY IMAGING DRAFT

The FDA has published a draft guidance for X-ray imaging system compliance with an eye towards harmonization with IEC standards, although the document also makes reference to a need to deal with overlap between device regulations and the Electronic Product Radiation Control provisions of the statute.

The draft guidance's scope is limited to X-ray systems and their components, and the agency pointed out that most such systems are regulated as class I or II devices. The draft takes up a number of standards in the IEC 60601 series, and the agency said that conformance with these standards may suffice to demonstrate substantial equivalence to a predicate, thus in some cases eliminating any need to file a 510(k) application so long as the manufacturer files an abbreviated report.

The draft also offered an IEC method for demonstrating compliance with the regulations for reports for listed electronic products, specifically for product, supplemental, annual and abbreviated reports. On the other hand, the FDA listed several EPRC requirements that cannot be fulfilled with IEC compliance, a list that includes assembler responsibility and lateral plane patient entrance point.

The agency is taking comment through Nov. 1, 2016, under docket number FDA-2016-D-2049.

AETNA OKAY WITH TMS FOR DEPRESSION

Aetna of Hartford, Conn., will henceforth cover transcranial magnetic stimulation (TMS) as treatment of depression assuming some conditions are met. However, the payer is not inclined to cover the treatment as a maintenance regime for depression, and listed several conditions for which coverage is not available. Among the non-covered indications are epilepsy, central post-stroke pain and dysphagia. Aetna said it will revisit TMS coverage again in May 2017. **//**

PRODUCT BRIEFS

Carpinteria, Calif.-based **Agilent Pathology Solutions'** Dako, reported CE mark certification for use of a new companion diagnostic assay that can reveal whether a patient with advanced non-small cell lung cancer is likely to respond to Keytruda (pembrolizumab), an anti-PD-1 therapy.

Fujifilm Medical Systems Inc., of Stamford, Conn, reported 510(k) clearance from the FDA for the marketing of the FDR Visionary Suite and the simultaneous release of its FDR Clinica X-Ray Components. While the Visionary Suite is a premiere digital x-ray suite designed for mid-to-large sized hospitals and health systems, the FDR Clinica X-ray Components were specifically created with outpatient facilities in mind.

Burlington, N.C.-based **Laboratory Corporation of America Holdings** (Labcorp) reported the nationwide availability of testing for Zika virus using the Zika Immunoglobulin M (Igm) Antibody Capture Enzyme-Linked Immunosorbent Assay developed by the Centers for Disease Control and Prevention (CDC). The test received Emergency Use Authorization from the FDA, initially on February 26, and reissued on June 29 for the qualitative detection of Zika virus Igm antibodies in serum or cerebrospinal fluid (collected alongside a patient-matched serum specimen), and is being made available for the first time to commercial laboratories. It is intended to be used in the diagnosis of Zika virus infection in individuals meeting clinical and/or epidemiological criteria established by CDC for Zika virus infection risk.

Seegene Inc., of Seoul, Korea, a developer of multiplex real-time PCR technologies said it has introduced the automated development of in silico-based multiplex real-time PCR assays. Real-time PCR is the best method for molecular diagnostics but its development process is complicated due to extensive development period and high cost. With an in silico-based development solution, Sgsilico, Seegene has greatly simplified the process of real-time PCR assay development and is looking to expand its use in molecular diagnostics.

OTHER NEWS TO NOTE

Cure Forward Corp., of Cambridge, Mass., and **Personal Genome Diagnostics Inc.** (Pgdx), of Baltimore, reported an agreement that will enable cancer patients using the Cure Forward Patient Activation platform to select Pgdx as their genomic testing service provider. Pgdx will make its genomic testing results directly available to cancer patients through the Cure Forward platform. The data will be provided in interoperable formats, so that it can be directly applied by patients to further their own care. Further details of the non-exclusive agreement were not disclosed.

Eurofins Qta Inc., of Westchester Township, Ohio and **Q-Interline A/S**, of Denmark, signed a collaboration for the North American market. This process will take effect immediately and seeks to strengthen the market offering of both Eurofins Qta and Q-Interline. Eurofins Qta will provide installation, application support, calibration development and maintenance services for this new technology.

Nanthealth Inc., of Culver City, Calif., entered into a commercial license agreement with Sanford Health for the use of its eviti, the evidence-based treatment intelligence and web-based oncology decision support platform. Sanford Health's network of oncologists will have access to Nanthealth's eviti Connect decision support solution, providing them with evidence-based regimens, condition-specific clinical trial options and the potential for more efficient preauthorization and expedited reimbursement.

Foundation

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a boost to the program, whose funding has in the past been described as iffy.

Currently Foundationone receives nationwide coverage for analysis of non-small cell lung cancer through a third party payer, and is broadly reimbursed for the analysis of a variety of tumors though a handful of regional players.

A National Coverage Decision from the CMS would make the diagnostic available to all beneficiaries nationwide, Ramamurthy said. Typically there is a long lag time between FDA approval and nationwide CMS reimbursement, but due to the parallel program, both decisions should be announced simultaneously if all goes as planned.

"Upon completion [of the review process], we would expect approval across the entire Foundationone assay as well as a number of CDx claims. The initial claims may include FDA approved drugs for a range of solid tumor indications such as lung, breast, colon, gastric, ovarian and melanoma. These tumor types alone make up approximately 43 percent of the advanced metastatic patient population in the U.S. or more than 450,000 patients annually, which represents almost one-half of our total available markets," Pellini said. **//**

ORTHOPEDICS EXTRA

Keeping you up to date on recent developments in orthopedics

By Holland Johnson, Executive Editor

Scientists trace origin cell of bone and soft tissue tumors, test drug target

Scientists at Duke Health are part of a team that has discovered a type of cell surrounding blood vessels can also serve as a starting point for sarcoma, a form of cancer that occurs in bones and connective tissues. The findings, made through studies of mice, offer insights that could aid in the development of potential new treatments for this rare, but deadly form of cancer. In an article to be published online in the journal *Cell Reports*, the international team of researchers describe tracing the lineage of the cancer back to the pericyte, a cell that supports the body's blood vessels. According to the findings, genetic mutations in these cells led to osteosarcoma and soft-tissue sarcoma, as well as non-cancerous tumors. Alman and fellow authors - who represent Duke as well as the Hospital for Sick Children and Mount Sinai Hospital in Toronto, Tokyo Medical and Dental University Graduate School and Faculty of Medicine, and Seoul National University Hospital - found that cancer cells contained less of a protein called beta catenin compared to the pericytes from which they originated. Alman said this suggests that at some point, the beta catenin was "turned off" in the cell. When the researchers activated beta catenin in cells using lithium, a drug already used in patients, this appeared to limit the size and growth of the cancers that formed. The researchers hope to further investigate the use of lithium to regulate beta catenin.

Fracture risk assessment and management should be part of weight loss care.

Severely obese patients undergoing weight loss surgery are more likely to have increased fracture risks both before and after the surgical procedure compared to obese and non-obese people people who don't need surgery, finds a large study published by *The BMJ*. Obesity may not be as protective for fracture as originally thought, say the authors, and they suggest that fracture risk assessment and management should be part of weight loss care. The study, carried out by researchers in Canada, examined the incidence and sites of fracture in severely obese patients who had undergone weight loss surgery, and compared them to obese and non-obese controls matched for sex and age. Data was analysed from the Quebec Integrated Chronic Diseases Surveillance System (QICDSS) on 12,676 patients, and 38,028 obese and 126,760 non-obese people in the control groups between 2001-2014.Before surgery, 10.5 percent of patients in the weight loss surgery group had at least one fracture compared with 8.1 percent obese and 6.6 percent non-obese people in the control groups. After a mean follow-up of 4.4 years, 4.1 percent of the weight loss surgery patients had at least one fracture compared with 2.7 percent of obese and 2.4 percent of non-obese groups. The median time to first fracture was 3.9 years. The authors speculated that the increased fracture risks are due to falls and obesity related conditions, such as type 2 diabetes, as well as anatomical changes, and nutritional deficiencies induced by weight loss surgery. The article is titled "Change in fracture risk and fracture pattern after bariatric surgery: nested case-control study."

Researchers coax human stem cells to rapidly generate bone, heart muscle

Researchers at the Stanford, Calif.-based Stanford University School of Medicine have mapped out the sets of biological and chemical signals necessary to quickly and efficiently direct human embryonic stem cells to become pure populations of any of 12 cell types, including bone, heart muscle and cartilage. The ability to make pure populations of these cells within days rather than the weeks or months previously required is a potential game changer in the field of regenerative medicine - potentially allowing researchers to generate new beating heart cells to repair damage after a heart attack or to create cartilage or bone to reinvigorate creaky joints or heal from trauma. The study also highlighted key, but short-lived, patterns of gene expression that occur during human embryo segmentation and confirm that human development appears to rely on processes that are evolutionarily conserved among many animals. These insights may also lead to a better understanding of how congenital defects occur. Irving Weissman, the director of Stanford's Institute for Stem Cell Biology and Regenerative Medicine, and also of its Ludwig Cancer Center said that within five to nine days his team "can generate virtually all the pure cell populations that we need." The study will be published in *Cell*. Stanford research graduate student Kyle Loh "The ability to generate pure populations of these [pluripotent]cell types is very important for any kind of clinically important regenerative medicine," said Loh, "as well as to develop a basic road map of human embryonic development. Previously, making these cell types took weeks to months, primarily because it wasn't possible to accurately control cell fate. As a result, researchers would end up with a hodgepodge of cell types."

Ortho Regenerative Tech enters private placement and closes first tranche

Ortho Regenerative Technologies Inc., of Kirkland, Quebec, is proceeding with a non-brokered private placement of equity units of the companyof which it has completed a first tranche raising gross proceeds of $460,000. The company intends to complete further tranches of the offering in the coming weeks. Canaccord Genuity Corp. has acted as finder for the first tranche on a non-exclusive basis. The net proceeds from the offering will be used for working capital as well as for progressing the development of its lead candidate for rotator cuff injuries and extending patent coverage to international territories. Following the closing of the first tranche, the company has 14,926,500 class A shares issued and outstanding.