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'We have been a bit optimistic'

IBA downgrades outlook as half of proton therapy projects stall

By John Brosky, Contributing Writer

PARIS – After two years steadily announcing new contracts for proton therapy systems worldwide and attracting investors who accelerated its stock valuation 360 percent, Ion Beam Applications SA (IBA) has hit a wall, reporting that half of its installation projects have been delayed, choking revenue generation. Investors ran for the exit, sending the Louvain-la-Neuve, Belgium-based company's stock on the

See IBA, page 3

Inside

Cell-based testing for better enrichment

Arcedi Biotech aims to advance prenatal testing to whole genome, noninvasively

By Katie Pfaff, Staff Writer

Arcedi Biotech ApS provides noninvasive cell-based prenatal testing options beyond traditional methods, like amniocentesis. The Vejle, Denmark-based company's technology isolates maternal and fetal cells for more comprehensive testing and rare cell detection in fetal samples.

"This is going to be the first cell-based noninvasive prenatal test that is going to be offered," said Ripudaman Singh, Arcedi Biotech's CTO, to *BioWorld MedTech*. In a recent article published

See Arcedi Biotech, page 4

Theraclion starts U.S. trial of combined echotherapy/ immunotherapy for breast cancer treatment

By Bernard Banga, Contributing Writer

PARIS – Theraclion SA has secured U.S. FDA approval for a clinical trial of its combined echotherapy/immunotherapy treatment for breast cancer.

"The aim of this clinical trial, which will be starting at the University of Virginia, Charlottesville in September is to assess the potential of combining our Echopulse device with Keytruda (pembrolizumab, Merck & Co. Inc.), an immunotherapy that targets PD-1 checkpoint

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Like riding a bicycle

B-Temia mobilizes interest in U.S. for dermo-skeleton

By David Godkin, Staff Writer

Clinical trials are underway to see if a wearable device designed to help patients overcome debilitating mobility issues can obtain FDA approval and make a splash in the U.S. mobility aids market. Developed by Quebec-based B-Temia Inc. and for sale in both Quebec and Ontario, the Keeogo (Keep-on-going) device features sensors placed at the knee and hip joints that evaluate a person's body position and help them move.

"We are really geared to people who have MS, arthritis of the knees or hips, Parkinson's disease, spinal cord injury and other muscle diseases,"

See B-Temia, page 6

Eligibility trips Cleveland Clinic in patent lawsuit

By Mark McCarty, Regulatory Editor

In a case reminiscent of the Supreme Court landmark of *Mayo v. Prometheus*, the Cleveland Clinic Foundation came up short in its lawsuit accusing True Health Diagnostics of patent infringement for a test that the Court of Appeals for the Federal Circuit said was too reliant on a law of nature and a clinician's judgment.

See Cleveland Clinic, page 7

BioWorld Medtech's Cardiology Extra

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

Read this week's edition

Financings

The European Investment Bank and Paris-based **Cellnovo Group**, a mobile, all-in-one diabetes management system, have closed a loan agreement for €20 million to help the company move to full industrial-scale operations. The loan is supported by the European Fund for Strategic Investments, part of the EC's Investment Plan for Europe. Called the Juncker Plan, it aims to fund research and innovation in the EU.

Daily M&A

San Carlos, Calif.-based **Sleepquest Inc.**, provider of obstructive sleep apnea care management, has acquired Alameda, Calif.-based **Grove Medical Equipment LLC** and began serving the company's customers earlier this month. The sale combines the companies' business and technology platform and extends Sleepquest's service base in Oakland and East Bay. Financial details were not disclosed.

Product briefs

Bioness Inc., of Valencia, Calif., started shipping the Bioness Integrated Therapy System (BITS) with its new bedside and mobile hardware configurations to U.S. and Canadian customers, with EU shipments beginning in August. Additionally, the entire BITS product portfolio is now available in German, French, English and Spanish to support the international market expansion. BITS is a touchscreen-based platform that operates a rehabilitative software application featuring 24 programs and four standardized assessments to challenge and assess a patient's physical, visual, auditory and cognitive abilities.

Masimo Corp., of Irvine, Calif., received CE marking on its Rainbow Super DCI-mini sensor, a reusable spot-check sensor that features Masimo SET (signal extraction technology) Measure-through Motion and Low Perfusion pulse oximetry and Rainbow SET technology with multiple physiologic measurements – including the ability to measure total hemoglobin, carboxyhemoglobin, methemoglobin and arterial oxygen saturation using the same noninvasive reusable sensor. The Rainbow Super DCI-mini sensor is not available for sale in the U.S.

Medtronic plc., of Dublin, reported FDA approval of the self-expanding Corevalve Evolut transcatheter aortic valve replacement (TAVR) platform to include patients with symptomatic severe aortic stenosis who are at an intermediate risk for open-heart surgery. With hemodynamic performance (a measure of blood flow efficiency) shown to be superior to surgical aortic valve replacement, according to the company, the Corevalve Evolut platform is designed to deliver valve performance for these patients who are often considered to be more active than high- or extreme-risk patients previously indicated for the procedure.

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IBA

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Euronext Brussel exchange plummeting 26 percent on July 5, 2017, as IBA adjusted downward its full year guidance from a range of 13 percent to 15 percent to 5 percent to 10 percent.

"It looks like we have been a bit optimistic," in the capacity of customers to build facilities and commission proton therapy systems, said CEO Olivier Legrain in a conference call with stock market analysts.

Highlighting the company's €1 billion (US$1.14 billion) backlog of contracts, he said, "We may face a bit of an issue with the speed of conversion of the backlog into revenues in the next 24 month. This will have an impact on 2017 for sure, it will create a vacuum for 2018 and 2019, but we believe it will wash out in the mid-term. And we believe in the long-term things will even out."

Responding to an analyst's question he acknowledged, "We cannot exclude that we may see other delays."

Revenue recognition for IBA depends on project milestones, which Legrain noted is dependent on a customer's progress.

"Nothing we report today changes our strong belief in the fundamentals of our business, our ability to convert our backlog, nor the future aspects of the proton therapy market. We will continue to grow, the pipeline is strong, and I believe we will remain the number one provider of proton therapy globally," he said.

Pushed to the background was the company's same-day announcement of a $60 million contract with Reston, Va.-based Inova Health Care Services for a two-room Proteusplus proton therapy with pencil beam scanning capability and an integrated cone beam CT that is expected to be patient-ready in 2020.

Neither the Virginia project nor the recently announced Proteusone treatment room for Children's Cancer Hospital Foundation Egypt in Cairo were counted among the 26 ongoing projects, for which 13 are now reported as delayed.

Two-thirds of the 13 delayed projects are in emerging markets and often the first such system to be installed in those countries, said Legrain.

"Both IBA and customers have been a bit optimistic about what it takes," he said, attributing 20 percent of the delayed projects to IBA management issues that might have been avoided while 60 percent of the delays are attributed to customer issues.

None of the delays have been caused by availability of IBA systems, he said. IBA currently services 21 proton therapy systems that are installed and operating.

"Some customers have told us they underestimated the licensing process and building construction has been pushed back," he said. Some projects are six months away from completion, others closer to completion have been pushed back to 2018.

Additionally, Legrain reported the company has also had to incur one-off costs related to project management issues in emerging markets that are estimated to be €6 million ($6.83 million).

The projects are split 50-50 between Proteusone and Proteusplus.

With the introduction of the compact Proteusone system the company said that construction and commissioning would be streamlined compared to the larger and more complex Proteusplus systems. In many cases Proteusone can be installed in an existing facility.

"A number of productivity initiatives aimed at reducing production costs have not been realized as quickly as anticipated," he said.

Thanks to a longer history of project management and installations with Proteusplus projects, Legrain said, "We were pretty good at modelling, though there have been some dramatic push backs."

With only two completed installations of the newer Proteusone, he said IBA did not have the same depth of reference and is passing through a learning curve with engineers revisiting the business planning model.

"We have some growth issues," he said.

With the Inova project in Virginia, IBA can claim to have won three of the four proton therapy tenders so far for 2017.

Asked if there was a slowdown in the market as 17 systems were contracted globally in 2015 and 15 systems were sold in 2016, Legrain said the first six months of the year are not a good measure of how the year will perform, as orders in the two previous years were back-loaded with contracts signed at the end of the year.

In mid-June the company broke ground on a €16 million (US$18.2 million) logistics and manufacturing facility in Louvain-la-Neuve, Belgium, to scale up its production capacity to meet what it cites as the growing demand for proton therapy treatment.

"With Proteusone we have, by far, the most competitive system in the market with a huge cost advantage against competitors," said Legrain. "If competitive bidding heats up, we believe our system is protected from that with the only compact, multiroom proton therapy system available."

Sector specialist Medraysintel, also based in Louvain-la-Neuve, estimated that by 2020 more than 330 proton therapy treatment rooms will be available to patients worldwide, and that by 2030 that number will expand to 1,200 to 1,800 treatment rooms open to patients worldwide.

The consulting agency estimated the value of the market in 2030 will reach $3.5 billion, up from $1 billion in 2018. ♦

Other news to note

Air Liquide SA, of Paris, has signed a partnership with **CERITD**, the French Center for Studies and Research for the Intensification of Diabetes Treatment. Air Liquide also acquired an equity stake in **Diabeloop SA**, a Paris-based start-up that is developing an electronic artificial pancreas. With this new collaboration, Air Liquide continues the approach initiated by CERITD based on cooperation between hospital teams and homecare nurses. At the request of physicians, nurses will be able to help provide even more personalized follow-up for patients with diabetes treated at home, such as adjusting the treatment in accordance with a strict protocol.

Arcedi Biotech

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in *Biomarkers in Medicine*, the firm explained its isolation of circulating fetal cells in maternal blood for detection and analysis. Their cell-based noninvasive prenatal diagnosis (cbNIPD) testing uses cells already present in the mother's blood and may offer an alternative method for finding genetic abnormalities compared to Chorionic Villi Sampling (CVS) and amniocentesis

The test uses a blood sample from a pregnant woman around the end of the first trimester. "Then we have developed a method where we process the blood sample. We slice all the RBCs [and] what we are left with are the white blood cells of the pregnant woman, then there are some rare fetal cells among them," explained Singh. The cells are enriched with a proprietary antibody on a magnetic cell sorting platform. Another set of antibodies which specifically target particular fetal cells are used to stain them, and they are identified via magnification and microarray.

Fetal cells in maternal blood

"Fetal cells do circulate in pregnant women's blood," according to the article, "Fetal cells in maternal blood for prenatal diagnosis: A love story rekindled."

"Even though rare in numbers, these cells can be enriched from maternal circulation and used for knowing the genetic status of the fetus. This opens up immense opportunities for prenatal screening," according to article's authors.

Arcedi's test is based on prior work that indicates fetal cells' overexpressed genes were specific in extravillous trophoblasts (EVTs), making that a target for cbNIPD. Using the EVT as a target, fetal cells can be enriched from the mother's blood in order to screen for chromosomal and related genome changes. A gene expression array analysis of 198 fetal cells was used to identify EVTs.

Prior to identifying EVT, researchers at Arcedi first worked to separate fetal cells with a nonenrichment tactic and by reducing maternal leucocytes with a magnetic-activate cell sorting platform. However, the methods led to overexpression of placental and endothelial genes instead of maternal cells.

Cell-free options

Current methods typically enlist cell-free noninvasive prenatal testing (cfNIPD), which uses cell-free DNA in the mother's blood. This method will show aneuploidies, or abnormalities in the number of chromosomes, but is not effective in pinpointing cop number variations (CNVs) since fetal and maternal DNA may be mixed. Authors suggest circulating fetal cells are better sources for testing to find aneuploidies and CNVs since the method uses "pure fetal genomes," according to the paper.

"The investigation of fetal cells in maternal blood dates back to the late 1950s when the first report on circulating fetal cells was published by Alvin Zipursky," said Singh. "Since then, a significant amount of research has been conducted to effectively isolate and assess these rare cells for use in prenatal testing, but with little success. Arcedi's research and technology has shown that cbNIPD is a clinically viable option to determine the genetic status of the fetus. This evolving approach has the potential to change the prenatal testing space and may ultimately result in making invasive testing obsolete."

> *"This is going to be the first cell based noninvasive prenatal test that is going to be offered.*
>
> Ripudaman Singh
> CTO, Arcedi Biotech

Traditional testing methods such as cfNIPT often require additional confirmation via chorionic villus sampling or amniocentesis, while Arcedi's method does not require additional confirmation testing, according to the company.

Other noninvasive prenatal testing methods exist on the market, typically offered by laboratories. For example, Sequenom Laboratories, of San Diego, offers carrier screening and NIPT genetic testing. The company's tests, Maternit Genome, Maternit 21 Plus and Visibilit provide a range of information from the baby's gender to genome-wide chromosomes, trisomy, monosomy to more specific tests like trisomy 21, trisomy 18, trisomy 13, abnormalities in sex chromosomes, sub-chromosomal and micro deletions. Gaithersburg, Md.-based Genedx also offers prenatal genetic testing based on familial conditions or for full testing requests. Tests include chromosome analysis for suspected conditions, rapid aneuploidy fluorescence in situ hybridization, prenatal chromosomal microarray, whole genome chromosomal microarray for products of conception, and additional tests for specific diseases.

While fetal cells, particularly nucleated red blood cells, were noted in maternal blood as far back as 1959, efforts to identify useful fetal cells for diagnosis and to enrich the cells for reliable testing had not advanced sufficiently until recent years. During the intervening decades, researchers had become skeptical of success in using circulating fetal cells for diagnosis, according to the article.

Testing standards

In order to maintain the quality of testing and thereby the momentum toward using such noninvasive testing of circulating fetal cells, study authors suggest that guidelines be used by those conducting tests. These include that testing with cbNIPD be targeted to a specific cell type and one that has reactive antibodies for it, the technology used to identify the antibodies should use independent parameters and platforms, and cells should be accessible for therapies. DNA also should be enriched enough to be used in next-generation sequencing and chromosomal microarray. The company is validating its research with a study among high risk pregnancies, which compares cell-based analysis and cell free NIPT and CVS. The company also plans to conduct a preclinical trial of pregnant women in Denmark in September to validate the test. ♦

Theraclion

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inhibitors," David Caumartin, Theraclion's CEO, told *BioWorld MedTech*.

Theraclion, of Malakoff, France, designed and manufactured the noninvasive technology protected by 25 patent families. This technology enables noninvasive tumor treatment via ultrasound-guided high-intensity focused ultrasound (HIFU). The Echopulse device combines ultrasound monitoring to locate targets with focused ultrasound therapy (10 MHz), causing tissue coagulation (at 85 degrees C) and hence necrosis. This technology has been CE marked since 2012 and has already proved effective for treating benign tumors. Since May 2017, more than 1,000 patients have received echotherapy during noninvasive treatment of thyroid nodules and breast fibroadenomas.

"This mature technology potentiates the body's immune response induced by immunotherapy drugs used to treat breast cancer," said Caumartin. Focused ultrasound ablation, as well as other ablative techniques, has been shown in animal studies to boost the immune response the malignant tumors. The combination of immunotherapy with HIFU has also been investigated in animal models. This will be the first time HIFU and immunotherapy are investigated for the treatment of breast cancer in a human study.

New indication – $500K invested

Every year, breast cancer accounts for 12 percent of all cancers diagnosed worldwide and is the second biggest cause of cancer-related deaths in women. In 2012, there were approximately 1.68 million new diagnoses worldwide and 520,000 deaths. About 6 percent of patients will have stage IV breast cancer at the time they are first diagnosed.

Stage IV metastatic breast cancer is especially difficult to treat. The prognosis for survival after endocrine therapy or chemotherapy treatment is less than 20 percent. Although immunotherapy drugs have been widely adopted and have demonstrated spectacular results on various indications, none have yet improved the outcome for women with stage IV metastatic breast cancer.

Over the past two years, Theraclion has invested $500K in R&D to develop a new medical protocol for certain types of breast cancer. The company has been supported by the breast surgery and hematology/oncology divisions at the University of Virginia (UVA), which has been its U.S. academic partner for the past four years. This medical center, which pioneered immunotherapy research with its Human Immune Therapy Center (HITC) at UVA in operation for more than 20 years, has just obtained the green light from the FDA for a clinical trial to treat breast cancer using the Echopulse system combined with pembrolizumab.

"Pembrolizumab was chosen because it has been shown to have efficacy in some patients with triple negative breast cancer. It is our hope that the addition of FUSA will increase the proportion of patients who respond," David Brenin, head of breast surgery at UVA and co-director of its breast care program, told *BioWorld MedTech*.

Theraclion has benefited from a fast-track procedure, which "enabled us to obtain FDA authorization in just 29 days. In contrast, we've been waiting 18 months for the French authorities to decide whether to include our medical invention in a forfeit innovation (French system for early reimbursement of innovative medical devices/procedures)," said Caumartin.

Echopulse system; Theraclion

This exploratory clinical trial will focus on a cohort of 15 patients with stage IV disease and a tumor in breast, chest wall, or axilla larger than 1 centimeter that can be treated with HIFU. There will be two Echopulse sessions for each patient. Each session should last only a few minutes.

"We will obtain CT-scans at several times during the study to asses for tumor response to treatment. We will also obtain repeat biopsies of the treated tumor and draw blood samples to asses for immune response, said Brenin.

$35B immuno-oncology market

"HIFU treatment could be used to pretreat tumors to reduce their overall volume and, perhaps more importantly, enable patients' immune system to reach and recognize malignant cells," Brenin said.

Patrick Dillon, assistant professor of hematology/oncology at UVA, said this new treatment method is expected to have fewer side effects than existing alternative cancer treatments.

According to Caumartin, "The Echopulse system offers great scope for improving immunotherapy. We believe we can make immunotherapy for cancer treatment three times more effective."

Theraclion is currently rolling out its medical technology everywhere. The results of around 15 clinical trials have already been published, while another dozen trials are in progress. A third of all these trials were conducted in the U.S.

Competitors include:

- Insightec Ltd., of Carmel, Israel, with its Exablate device;
- Sonacare Medical LLC, of Charlotte, N.C., with its Sonablate system;
- Royal Philips NV, of Amsterdam, with its Sonalleve system;
- EDAP-TMS SA, of Lyon, France, with its Ablatherm technology; and
- Haifu Technology Co. Ltd., Chongqing, China, with its Haifu system.

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B-Temia

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B-Temia Chief Operating Officer Paule De Blois told *BioWorld MedTech*. "We're hoping the trials give us FDA 510(K) clearance to start commercializing the product in the U.S. in 2018."

The Keeogo is dermo-skeleton technology, which like exo-skeleton technology is robotized to help people with impaired mobility walk, run, sit down or simply raise a leg. The difference, said De Blois, is an exoskeleton performs all these functions for patients who are completely immobilized by injury or neurological disease. Like an electric bicycle, the Keeogo relies on the residual capacity people in rehab have to move.

"If the person doesn't walk, it won't walk. The person initiates the movement, walking or climbing stairs," said De Blois. "Then, artificial intelligence interprets the data collected by the sensors at the hips and knees to assist the person in the exact movement they are trying to perform."

Worn around the waist like a belt and connected above and below the knee with Velcro straps, the Keeogo is far less bulky than exoskeleton devices. But it's the ability of software inside the belt to capture data and convert it into physical movement that is Keeogo's real value, De Blois said. If a person is seated, for example, the angle of both hips and knees is 90 degrees. As the person stands up the angles begin to open, a change the Keeogo detects and analyzes. "That will send a message to the motors located at the knees to help the person unbend the knee. If the person is standing up at 180 degrees, the system will help the person sit down without collapsing on the chair."

> *"Artificial intelligence interprets the data collected by the sensors at the hips and knees to assist the person in the exact movement they are trying to perform.*
>
> Paule De Blois
> Chief operating officer, B-Temia Inc.

A learning process

None of this would have been possible, De Blois stressed, without talking to orthopedists, physiotherapists and neurologists specializing in particular diseases affecting human muscle mobility. Among them is Sari Shatil, the owner of London, Ontario-based Neuphysio Rehabilitation PC who has used Keeogo to help several patients regain their mobility since acquiring the unit in early 2016.

"When our client is wearing the Keeogo and it's working well for them, we don't need to be moving their legs, the robot moves their legs," Shatil told *BioWorld MedTech*. "That gives them a better sense of independence while they learn how to manage their upper body."

This, in turn, gives physiotherapists more freedom to challenge the patient to work harder and obtain greater mobility, Shatil added. The physiotherapist can also adjust the amount of assistance the patient needs over time.

Keeogo dermo-skeleton device; B-Temia Inc.

"One of the things I think is spectacular about Keeogo is that, with guidance from the therapist, it can provide less and less assistance as the patient gets better and better."

The military calls

B-Temia got to this point in its Canadian development and commercialization of the Keeogo through undisclosed public and private sector financing, said De Blois. Those sectors are also financing clinical studies underway in Boston, Chicago, Toronto and Quebec City. Retailing at C$45,000, the market place will ultimately determine future enhancements to the Keeogo. In the meantime, the military calls.

"We signed a licence agreement with Lockheed Martin earlier his year for military and commercial applications of the product. Certainly at some point the company will have other major partners. That's how a small company grows, right? ♦

Other news to note

Alere Inc., Waltham, Mass.-based provider of rapid diagnostic tests, said its shareholders have voted to approve the previously announced amended merger with **Abbott Laboratories**, of Abbott Park, Ill. In a final count of the voting results, approximately 63 million votes cast at a special meeting were in favor of the amended merger, representing more than 72.5 percent of all outstanding Alere shares as of the May 31, 2017, record date. The final vote results will be filed on a form 8-K with the SEC. Upon closing of the merger, Alere shareholders will receive $51 per common share in cash, and Alere will become a subsidiary of Abbott.

Ascensia Diabetes Care Holdings AG, of Basel, Switzerland, entered an agreement with **Dexcom Inc.**, of San Diego, to provide the Ascensia Contournext One blood glucose monitoring system (BGMS) as part of the Dexcom G5 continuous glucose monitoring (CGM) System Medicare offering in the U.S. The complete bundle will be available to people with diabetes who are covered by Medicare and qualify for therapeutic CGM. The role of the Contournext One BGMS will be to provide highly accurate readings for CGM calibration.

Cleveland

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The Cleveland Clinic Foundation of Cleveland, Ohio, sued True Health Diagnostics, of Frisco, Texas, for purported infringement of four patents related to the former's test for myeloperoxidase, a test intended to indirectly measure blood vessel inflammation. CCF applied for the patents – one of which has survived two challenges – in 2003, but the foundation's case against True Health did not pass muster in a Ohio district court hearing in February 2016. In that hearing, Judge Patricia Gaughan dismissed the allegations of infringement for three of the purportedly infringed patents, and dismissed the fourth because CCF had failed to make a compelling case that True Health had infringed that patent.

CCF persuaded the Federal Circuit to hear the case, but the three-judge panel at the Federal Circuit had little more to offer. The court's decision noted that prior art had already disclosed that myeloperoxidase was suggestive, but not predictive, of cardiovascular disease. Another source of discomfort for CCF was perhaps that the patents had characterized the use of already commercially available kits appended with information regarding cut-off values for the marker, along with the sensitivities of those tests. The patent further relied on the compilation of population-level data to establish a control value for myeloperoxidase in healthy subjects.

CCF and True Health had a contractual history that entailed the latter's performance of myeloperoxidase testing for the CCF's clinical affiliate, the Cleveland Heartlab. True Health apparently broke off the contract so as to conduct the test itself, triggering the lawsuit and a failed attempt at injunction.

According to the Federal Circuit, the district court concluded that it was appropriate to consider whether the three ultimately rejected patents were eligible under §101 when True Health had moved to dismiss the charges. A review of the claims under *Alice v. CLS Bank* was no help to CCF because the test was directed to a law of nature, and because the execution of the test required that a clinician compare the subject's myeloperoxidase levels with a control value, which might constitute nothing more than "a bare mental process."

The claim pertaining to the sole remaining patent after the *Alice* test was thrown out in part because CCF did not demonstrate that True Health had induced anyone to infringe that patent. The Federal Circuit cited several elements of case law in examining the patentability of the CCF patents, including *Mayo v. Prometheus*, the case decided by the Supreme Court in 2012 in favor of the Mayo Clinic. (See *BioWorld MedTech*, March 21, 2012.)

The Federal Circuit then reaffirmed that patent claims dealing a correlation that exists independently of any human effort are essentially claims directed to a law of nature, and thus are not eligible. In addition to *Mayo*, the Federal Circuit cited *Ariosa v. Sequenom* as a case that offers little protection for patents for naturally occurring phenomena. (See *BioWorld MedTech*, Dec. 4, 2015.)

CCF had argued that its patents fall more into the category of claims addressed in *Rapid Litigation Management v. Cellzdirect*, but the Federal Circuit would have none of it, asserting that *Cellzdirect* involved a method of preservation of liver cells as opposed to what the court said was the use of "well-known techniques to execute the claimed method." (See *BioWorld MedTech*, July 11, 2016.)

As for the question of whether an inventive step could save the three patents in question, the Federal Circuit said the practice of the CCF method claims does nothing to transform the underlying natural phenomenon into a patentable invention. The court added that both *Mayo* and *Ariosa* require that a patent must call for more than a recitation of a natural phenomenon while urging that a clinician "apply it."

The law firm of Troutman Sanders did not respond to contact for comment. ♦

Regulatory front

The **European Commission** may impose a penalty of 10 percent of global revenues on **Canon Inc**., of Tokyo, for proceeding with the company's acquisition of **Toshiba Medical Systems,** of Otawara, Japan, prior to receiving the commission's full approval. The EC statement accused Canon of using a two-step transaction that allowed an unnamed "interim buyer" to acquire Toshiba prior to obtaining approval. This interim buyer is said to have picked up 95 percent of Toshiba's shares, after which Canon bought the remaining 5 percent and the interim purchaser's share options. The EC said that if it concluded that Canon had "indeed implemented the transaction prior to its notification or prior to adoption of the clearance decision, it could impose a fine of up to 10 percent of Canon's annual worldwide turnover."

Theraclion

Continued from page 5

But none of these med-tech competitors using HIFU technology are focused on immuno-oncology. According to analysts at the U.S. investment bank Citigroup, the immuno-oncology market will generate sales of up to $35 billion a year over the next 10 years.

"We're going to increase partnerships with other European clinical centers specializing in immunotherapy. This will enable us to run additional clinical trials in partnership with other pharmaceutical laboratories on the front line of immuno-oncology," said Caumartin.

Extending the runway

Theraclion has not ruled out tapping the equity markets next year to raise around $12 million. This will enable the company to continue funding clinical trials of its new combined therapy.

"As with angiography/mammography combined with medical imaging and contrast agents, we're convinced that a combined echotherapy/immunotherapy approach is going to push back the frontiers of cancer treatment," said Caumartin.

Meanwhile, Theraclion is extending the indications for which its Echopulse device is used. The company – whose market capitalization is $39.2 million on the Euronext stock exchange – is about to double its turnover this year. This has been achieved mainly by European sales (half in Germany) of the Echopulse device, whose unit sale price is $400,000.

Last year's equity investment by the biotechnology group Inner Mongolia Furui Medical Science Co. Ltd., of Beijing, (focused on fibrosis diagnosis) and setting up the Chinese joint venture Theraclion China Co. Ltd, in Shenzhen, are signs that the Echopulse device will be developed in Asia to treat liver and abdominal cancer. This will be another new clinical indication for the Echopulse system. ♦

Other news to note

The class action litigation against U.K.-based **Boston Scientific Ltd.** and Marlborough, Mass.-based **Boston Scientific Corp.** has been certified in Canada. The lawsuit involves Boston Scientific's transvaginal mesh device for treatment of stress urinary incontinence or pelvic organ prolapse. The class action seeks compensation for personal injuries allegedly relating to the use of the device as well as for damages allegedly suffered by family members. Boston Scientific denies any fault or liability and continues to defend the class action.

Immunarray Ltd., of Rehovo, Israel, and **Kindstar Global Co. Ltd.**, a specialty clinical testing company based in Wuhan, China, with locations throughout mainland China, have forged a partnership involving shared clinical studies and the launch of Immunarray's lupus rule-out test in China as the initial product offering. The companies will undertake joint clinical testing of up to 500 serum samples from Chinese patients who are healthy as well as those with symptoms consistent with systemic lupus erythematosus or lupus. The study will support the clinical implementation of Immunarray's SLE-Key Rule-Out test, which was introduced in U.S. markets in 2016.

Mdxhealth SA, of Herstal, Belgium, signed a commercial agreement with **IPS Genomix**, of Beirut, for the distribution of its Selectmdx for Prostate Cancer test in Lebanon, Egypt, United Arab Emirates, Saudi Arabia, Oman, Bahrain, Qatar and Jordan. Under terms of the agreement, IPS Genomix will handle distribution and reimbursement for Selectmdx within the Middle East, while Mdxhealth will perform the Selectmdx testing service in its ISO certified clinical diagnostic laboratory in Nijmegen, The Netherlands. IPS Genomix will reimburse Mdxhealth for all testing services performed.

Nemaura Medical Inc. (OTC: NMRD), Loughborough, U.K.-based developer of Sugarbeat, a wireless disposable adhesive skin-patch for adjunctive use by diabetics as a noninvasive and needle-free continuous glucose monitoring system, said it uplisted to the OTCQB Venture Market trading platform.

Nova Leah Ltd., of Dundalk, Ireland, reported that **Fresenius Medical Care AG & Co.**, of Bad Homburg, Germany, will implement its Selectevidence, a cybersecurity risk management system for connected medical devices. Fresenius operates dialysis clinics and produces dialysis machines and dialyzers.

A recently published study, funded by **Royal Philips NV**, of Amsterdam, showed that although positive airway pressure (PAP) therapy was associated with a reduction in hospitalization, more than 92 percent of patients studied were not receiving it in any form. The retrospective study revealed that only 7.5 percent of the more than 1.8 million COPD patients analyzed were receiving any form of PAP therapy.

Cardiology Extra

Keeping you up to date on recent developments in cardiology

By Katie Pfaff, Staff Writer

Diabetes spreading in sub-Saharan Africa

A study by the Lancet Diabetes & Endocrinology Commission and Harvard T.H. Chan School of Public Health reported diabetes has been diagnosed at high rates in sub-Saharan Africa. The report, "Diabetes in sub-Saharan Africa: from clinical care to health policy," published in *The Lancet Diabetes & Endocrinology*, reviewed data from 2004 to 2013 of 39,000 patients from 12 countries. Diabetes was found in nearly 22 percent of adults and 30 percent in men and women between 55 and 65 years old, though only half of those with the disease are diagnosed, and only 10 percent were receiving treatment, according to the study. About 90 percent of the diabetes cases were type 2, making the disease treatable with lifestyle changes alone. The spike was thought to be linked to aging populations as well as lifestyle changes, work practices and eating habits associated with higher incomes. "We were alarmed by both the magnitude of the problem, the speed at which diabetes has evolved, and how poorly health systems are responding," said Rifat Atun, professor of global health systems at Harvard Chan School and one of three lead authors of the report. "And because diabetes is a risk factor for other catastrophic illnesses such as heart disease, stroke and kidney failure, its increasing prevalence could propel a huge wave of chronic disease in many countries in sub-Saharan Africa." The health system has been formed to handle infectious disease but not to treat diabetes. However, the costs could quickly rise with diabetes if not mitigated to an estimated $59 billion by 2030, or 1.8 percent of the region's gross domestic product. Researchers called for more research and commitment from countries in the area to train health care personnel, to initiate community education efforts and to begin screening, diagnosis, and treatment efforts. The report was supported by the Rockefeller Foundation and the Harvard Medical School Center for Global Health Delivery.

BMI linked to hypertension, heart disease and type 2 diabetes

A *JAMA Cardiology* study suggests higher BMI is tied to increased risk of cardiometabolic diseases. The research used Mendelian randomization analysis using genetic information rather than prior studies that have been largely based on observation and could not account for confounding factors. This study was able to mainly overcome the issue in its research of 119,859 participants in the U.K. Biobank database, which included medical, demographic and genetic data. Patients reviewed were 47 percent men, average age was 57 years old, and BMI was linked to increased coronary heart disease, systolic and diastolic blood pressure, hypertension and type 2 diabetes. Age, sex, alcohol usage and smoking were not a factor in results; authors also suggested additional information like lipid and glucose testing would provide a more complete result. Study authors suggest results have a public health impact regarding managing obesity.

Monday and holidays high risk for heart attack

A Swedish registry study found a link between days of the week and holidays and myocardial infarction (MI) incidence, according to researchers from Uppsala University and Umeå University. Using those registered in the SWEDEHEART database of Swedes across the country, 156,000 patients were found to be more likely to experience MI on a Monday and during the winter holidays, with lowest incidence on weekends and summer vacations. The study was published in the *American Heart Journal* and used data from all hospitals in Sweden during 2006 and 2013, which examined symptom start and hospital admission with predefined hypotheses. "Our study seem to suggest that psychosocial demands on behavior influences basal biological systems, even to such an extent that they may be potential triggers for MI. When controlling for national data on temperature, air pollution and abroad traveling by air, the associations of calendar periods with MI rates are surprisingly robust. We have to remember that this is an observational study and be cautious with our conclusions. The systematic variation in MI rates is likely multifactorial. With that said, it is now more probable that stress explains a substantial portion of the fluctuation over time in population MI rates than it was before our study," reported John Wallert, study author. Heart attack was previously researched under the assumption it was triggered by specific stressful events, while this research suggests work life stress may be a trigger.

Blood clots can be found via imaging for receptors

A study published in the July issue of *The Journal of Nuclear Medicine* indicated that targeting a receptor involved in platelets sticking together could identify blood clots which can lead to stroke, heart attack and pulmonary embolism, conditions associated with mortality. In order to improve on current imaging options, researchers tagged GPIIb/IIIa receptors with a fluorine-18 (18F) labeled ligand. The newly developed novel small molecule tracer was paired with PET imaging to provide tracking for clotted platelets, compared to the current imaging practices of determining structural makeup. "Currently available diagnostic techniques of thrombus [blood clot] imaging rely on different modalities depending on the vascular territory," explained Andrew Stephens, of Piramal Imaging GmbH, of Berlin, Germany. "A single imaging modality that could visualize thrombi from various sources in different anatomic regions would be very valuable." The tracer bound with receptors at the site of thrombus formation, was not affected by anticoagulant medications, and cleared from blood quickly. Results from tracer and PET scan in a Cynomolgus monkey model were positive in pinpointing small venous and arterial clots as well as emboli in the brain and endothelial damage. A first-in-human study is currently underway. Research was funded by Bayer Pharma AG and Piramal Imaging GmBH.