MEDICAL DEVICE DAILY™

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CLEVELAND CLINIC INNOVATION SUMMIT

Cleveland Clinic gets 'personal' with cancer therapy during innovation summit

Omar Ford, Staff Writer

CLEVELAND — Personalized medicine – particularly as it pertains to cancer treatments – is the focus of this year's **Cleveland Clinic** Medical Innovation Summit. The 12th annual summit titled, "This time It's Personal," will bring in more than 1,500 attendees to the Cleveland Convention Center.

The summit, which has almost doubled in size over the last four years and ends on Wednesday, is a chance for different pieces of the healthcare innovation puzzle to come together, the Cleveland Clinic said.

"We always have a basic theme and I think it's important

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NEWCO ON THE GO

LifeBond aims to reduce leakage from GI procedures with new sealant device

By Amanda Pedersen, Senior Staff Writer

LifeBond (Caesarea, Israel), a startup company developing bio-surgical medical devices for tissue repair, is seeing promising results for its flagship product, LifeSeal. The product is a surgical sealant designed to help surgeons performing GI and bariatric surgeries minimize post-operative complications such as staple-line leakage and potentially save lives by providing staple-line reinforcement.

The company presented results from its preliminary clinical study of LifeSeal late last month at the European Society of Coloproctology's meeting in Barcelona.

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ASIA IN THE SPOTLIGHT

Opportunities for med-tech companies improve with Sino-Euro cooperation

By Kristine Yang, Staff Writer

Early in October, Chinese Prime Minister Li Keqiang visited Germany, Russia and Italy as part of his second European visit this year. While the discussions focused on widespread issues of trade, Chinese medical device companies are likely to benefit from the outcome of the visit and changes in European attitudes that could facilitate the expansion of Chinese companies in that market.

On the Chinese side, a key outcome of the trip is likely to be the opening of the service sector, including hospitals. This should provide a significant opportunity for both domestic and

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INSIDE THE BELTWAY

CHI report cites leaner reviews, but 'work remains to be done'

By Mark McCarty, Washington Editor

The third iteration of the device user fee agreement includes a doubling of device user fees over the second version, presumably giving FDA more resources to review pre-market applications in a more timely fashion. A recent report by the **California Healthcare Institute** (CHI; La Jolla, California) indicates that the trends are suggestive of speedier reviews, but CHI's interim CEO, Todd Gillenwater, told *Medical Device Daily* that some of the numbers show no improvement over the pre-user fee era and that hence, "work remains to be done."

The Medical Device User Fee Agreement III (MDUFA III) will

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INSIDE

NEUROLOGY EXTRA

Staff Writer Robert Kimball on one of med-tech's key sectors

Read this week's Monday Special

LATIN AMERICA

Home healthcare market in Latin America may surpass $17B in 2020

By Sergio Held, Staff Writer

The Latin American home healthcare market could almost double by 2020 to $17.5 billion as the incidence of chronic diseases rises and social changes drive demand for more such services.

In a study focused on Argentina, Brazil, Mexico and Colombia, market intelligence firm **Transparency Market Research** (Albany, New York) said the market across the region was worth $9.8 billion in 2013 and is poised for rapid growth.

"There are various factors which are impacting this market," Preeti Bagade, who led the research, told *Medical Device Daily* in a phone interview from India.

"Brazil, as far as our analysis are concerned, has the largest market share [for home healthcare products in the region]," said Bagade. "Then comes Mexico."

Those two markets along with Argentina and Colombia are the strongest in the region for the sale and distribution of home healthcare devices, which include diagnostics and monitoring devices, therapeutic devices, mobility assist devices and medical supplies. The report also took into account markets for healthcare-related services, including rehabilitation, telehealth, telemedicine and respiratory and infusion therapies.

The report forecasts a compound annual growth rate (CAGR) of 8.7% from 2014 to 2020 for this particular sector.

"All the key players that have a presence in this market, are coming up with technologically advanced devices, data efficient and user friendly [products] which attracts [new] customers," said Bagade.

"High acceptance of medical devices coupled with technological advancements fuel the growth of the home healthcare market in Latin America," said Transparency Market Research in a press release in which this new report was announced. The market intelligence company forecasts that the introduction of automated and portable devices to the market is playing a significant role in the market's behavior.

The range of devices used for home healthcare includes blood glucose monitors, blood pressure monitors, heart rate monitors, temperature monitors, sleep apnea monitors, coagulation monitors, pregnancy test kits, pulse oximeters and pedometers. At the same time, the study included a series of therapeutic devices such as insulin delivery devices, nebulizers, medical ventilator and CPAP devices, intravenous equipment and dialysis equipment.

Home healthcare is a much bigger business than it once was. The sector that was once driven by mobility products like wheelchairs, cranes and crutches has evolved substantially. An aging population with greater healthcare needs is also driving the growth of home healthcare.

"According to the United Nations, by 2050, the ratio of

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FINANCINGS

Kareo gets $15M in mezzanine debt from Excalate Partners

Staff Report

Kareo (Irving, Texas), a provider of cloud-based medical office software for small medical practices, has received $15 million in mezzanine debt from Escalate Capital Partners, an institutionally backed mezzanine fund that invests in high growth companies in the technology, healthcare and Software-as-a-Service (SaaS) industries. In 2014, Kareo has secured a total of $47 million in funding, reinforcing the company's unprecedented growth and further enhancing Kareo's role as the independent physician's trusted partner. The latest financing brings Kareo's total capital raised to $90 million.

Kareo enables independent physicians and their staff to streamline patient engagement, clinical documentation, billing, and other critical administrative processes in order to focus on what matters most – providing quality patient care. The $15 million in new growth capital will be used to further expand Kareo's reach and deepen its solution set to meet inevitable demand due to patient-driven shifts in the industry, while accelerating the development and innovation of the company's cloud-based technology.

"The shift toward consumer-driven care is continuing to gain momentum," said Dan Rodrigues, founder and CEO of Kareo, "and we believe that independent practices are uniquely positioned to benefit from this trend and provide the most appropriate and highest quality care to patients. We are delighted to have the backing and confidence of Escalate as we further enhance our products to better support small practices."

Kareo says its mission has been affirmed by its significant growth. The company has been consistently recognized as one of the fastest growing private companies in the U.S., realizing a 552% increase in revenue over the past three years. The company now serves more than 25,000 healthcare providers with its award-winning EHR, practice management and billing services platform, and is adding more than 500 provider customers per month.

The latest financing brings Kareo's total capital raised to $90 million. New investor Escalate Capital Partners joins Kareo's group of top-tier institutional investors which also include OpenView Venture Partners, Greenspring Associates, Stripes Group, Silicon Valley Bank and Western Technology Investments.

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In other financings news: **MTS Health Investors** (New York), a private healthcare private equity firm, said that funds managed by MTS have completed a majority investment in **myNEXUS** (Brentwood, Tenneessee). myNEXUS is a technology-driven, care management service. The company delivers its program on behalf of healthcare payors and in collaboration with a broad array of provider groups and technology affiliates. This investment was made from MTS Health Investors, Harpeth Capital advised the company on the financing. Terms of the transaction were not disclosed.

myNEXUS's proprietary data and analytics enable an accurate and informed care management process to determine optimal care use. Furthermore, overall healthcare costs are reduced by incorporating daily biometric monitoring technology to facilitate more informed and timely intervention for the chronically ill. myNEXUS is positio ned to provide these services to many of the leading healthcare industry stakeholders including insurers, employer groups, accountable care organizations, hospital systems and integrated delivery networks. //

MDD Stock Watch

10 BIGGEST WINNERS FOR THE WEEK

By Percent		By Dollars	
Edwards Lifesciences	17.94	Edwards Lifesciences	17.76
The Spectranetics	16.15	Idexx Laboratories	15.85
Boston Scientific	14.25	C.R. Bard	11.70
Align Technology	13.49	3M	11.19
IDEXX Laboratories	13.28	Zimmer Holdings	7.77
BSD Medical	11.90	Intuitive Surgical	7.77
Imris	11.76	The Cooper Companies	7.46
RTI Surgical	10.48	Covidien	7.44
Fluidigm	9.18	Athenahealth	6.21
Covidien	9.05	Align Technology	6.12

10 BIGGEST LOSERS FOR THE WEEK

By Percent		By Dollars	
TearLab	-9.62	Quidel	-1.65
Kips Bay Medical	-8.33	Volcano	-0.64
Iridex	-7.28	Iridex	-0.53
Volcano	-5.94	TearLab	-0.30
Quidel	-5.80	iCAD	-0.27
iCAD	-2.91	Biolase	-0.03
Hansen Medical	-2.04	Hansen Medical	-0.02
Biolase	-1.27	Kips Bay Medical	-0.02
Mazor Robotics.	0.00	Mazor Robotics.	$0.00
Echo Therapeutics	0.00	Echo Therapeutics.	0.00

WORLD IN REVIEW

BSD Medical presents study results using MicroThermX

Staff Report

BSD Medical (Salt Lake City), a provider of medical systems that treat cancer and benign diseases using heat therapy, said that French researchers JY Gaubert, P Chevallier, and V Vidal, presented the results of their animal study using the MicroThermX Microwave Ablation System, made by BSD, at CIRSE 2014. The study was sponsored by Terumo Europe N.V. The objective of the study was to determine reproducibility of the ablation volumes in liver and lung animal studies using the MicroThermX. The researchers examined the results of 18 liver ablations and 24 lung ablations and concluded that ablation volumes generated with the MicroThermX were reproducible in *in-vivo* liver and lung tissues.

"The positive results of this study reflect BSD's and Terumo Europe N.V.'s ongoing, long-term commitment to drive innovation and expand treatment options for patients," said Sam Maravich, VP of international sales and marketing at BSD Medical. "This study, and others to follow, could help pave the way for our MicroThermX system to be adopted by hospitals and treatment centers all over the world. Microwave ablation therapy has the potential to improve treatment outcomes and quality of life for patients."

The MicroThermX is a compact, mobile, proprietary system that includes a microwave generator, single-patient-use disposable antennas, and a thermistor-based temperature monitoring system. The innovative design of the MicroThermX is the first of its kind that allows delivery of higher power levels using a single generator.

The MicroThermX uses synchronous phased array technology that was developed and patented by MicroThermX BSD to provide a wide range of uniform zones of ablation. The MicroThermX includes innovative, high-end disposables (SynchroWave antennas) that are used in each ablation treatment and will provide a significant ongoing revenue stream.

The FDA has granted the company clearance to market the MicroThermX for ablation of soft tissue. BSD has also received CE Marking for the MicroThermX System, which allows BSD to market the MicroThermX in Europe. CE Marking is also recognized in many countries outside of the EU, providing BSD the ability to market the MicroThermX to a number of international markets.

Myriad establishes tumor lab in Europe

Myriad Genetics GmbH (Zurich) has established a Tumor BRACAnalysis CDx laboratory in Europe. Myriad's next-generation Tumor BRACAnalysis CDx test is a companion diagnostic that will identify up to 50% more patients with BRAC mutations who may benefit from treatment with PARP inhibitors, such as olaparib, compared to conventional germline testing alone.

Olaparib is a novel PARP inhibitor being developed by **AstraZeneca** (London). Last week, the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) recommended marketing authorization for olaparib as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed BRCA-mutated (germline and/or somatic) high grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy. It is estimated that more than 22 percent of all ovarian cancer patients carry a deleterious germline or somatic mutation in the BRCA1 or BRCA2 genes and may benefit from olaparib therapy.

"BRCA mutation screening is critical in ovarian cancer patients to identify the subset of women who might benefit from PARP inhibitors," said Colin Hayward, European Medical Director at Myriad. "Tumor BRACAnalysis CDx testing is the best method for screening ovarian cancer patients because it detects both germline and somatic mutations, significantly increasing the total number of patients who may benefit from this life-saving drug."

More than eight years ago, Myriad pioneered the development of germline BRCA testing as a companion diagnostic for use with PARP inhibitors and other agents. The new Tumor BRACAnalysis CDx test will expand the reach of this important new therapeutic class to many more ovarian cancer patients. Tumor BRACAnalysis CDx will be widely available throughout all of Europe and testing will be conducted in the company's laboratories in Munich.

Myriad's Tumor BRACAnalysis CDx is the most robust and accurate companion diagnostic test for identifying both germline (hereditary) and somatic (tumor) cancer-causing mutations in the BRCA1 and BRCA2 genes. Tumor BRACAnalysis CDx has undergone significant analytic validation and has been shown to identify up to 50% more patients with cancer-causing BRCA1/BRCA2 mutations compared to germline testing alone. Myriad is actively collaborating with leading pharmaceutical companies to develop Tumor BRACAnalysis CDx as a companion diagnostic for use with certain PARP inhibitors, platinum-based drugs and other chemotherapeutic agents.

Myriad Genetics makes molecular diagnostics dedicated to making a difference in patients' lives through the discovery and commercialization of transformative tests to assess a person's risk of developing disease, guide treatment decisions and assess risk of disease progression and recurrence. //

Cleveland

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to realize that the discussions are not exclusive to cancer and personalized medicine," Tom Graham, chief innovation officer for the Cleveland Clinic, told *Medical Device Daily*. "We are really the foremost forum to convene all the stakeholders – the innovators; the inventors; other representing institutions; the investment community; along with industry and government officials around the concept of innovation."

Yesterday, the summit kicked off with a new session called the Innovation Base Camp. The half-day session focused specifically on giving those involved the tools they need to cultivate innovation.

"Adding this new session [Innovation Base Camp] has really expanded our aperture," Graham said. "We decided that as the leaders of innovation in academic healthcare, that we not only had an opportunity, but the responsibility to educate others and expose them to what we believe is the modern practice of innovation. And that's one that is extremely disciplined and metrics driven."

Graham added, "We were being asked by our colleagues and constituents how have we been successful at establishing this as not only a cultural directive, but also a really great opportunity to develop a margin of difference to recruit, retain and reward top talent and frankly to generate non-clinical revenue."

The summit will also feature the "New Ventures in Healthcare Challenge," a competition being held today that will connect angel investors and venture capitalists with entrepreneurs. Four start-up health information technology companies will present their business plans as they vie for the chance to be named MIS2014 Challenge Champion.

On Tuesday, the summit will feature the return of IBM's Watson – a supercomputer that has become a staple of the conference in the past few years. Conference organizers were mum on the detail's of Watson's involvement, but promised it would be interesting.

Perhaps one of the biggest draws of the summit will come Wednesday, when the Top Ten Innovations of 2015 will be named.

"The fact that we have defined the exercise in what has become nationally and internationally recognized as our top 10, it really needs to be understood that those are advances that we believe will be hitting the market in the upcoming year," Graham said. "These are the projections and this is as close to what we have as a crystal ball."

He added, "We also go back and look at our track record and that's something that many who opine, never have to do. But we hold ourself to that level. We go back and see if we were right. We ask ourselves was it important? Was it a game changer? Did it come in on the type of chronology that we predicted? We feel as if it is a unique responsibility of ours as a leader in healthcare innovation to start to identify where the [hockey] puck is going ."

The summit comes at a time of transition on the healthcare landscape.

"What's interesting about this is that at a time when we are striving to get our arms around population management in healthcare, we also have this burgeoning opportunity to get as specific as the care of an individual around their own genome," he said. "That's really what I think is fascinating about this year's topic –something as broad as cancer yet as absolutely laser focused as personalized medicine, yet they go so well together."

Graham said that despite having a focus on cancer and personalized therapy, a variety of topics relevant to healthcare would be discussed at the summit.

"It's creating an environment that is catalytic to advance healthcare innovation and making sure that there is something there for everybody, and the ultimate winner is the patient," he said. //

DAILY M&A

Globus acquires Texas-based allograft tissue processor, TTOT

Staff Report

Globus Medical (Audobon, Pennsylvania), an implant manufacturer, said it has acquired allograft tissue processor **Transplant Technologies of Texas** (TTOT; San Antonio). TTOT provides human tissue products including bone allografts, biomaterials, and soft tissue products for spine, orthopedics, sports medicine, dental and wound care markets.

The company said it would provide additional details about the transaction during its Oct. 30 quarterly earnings call.

"This acquisition of TTOT will complement the Globus biologics product portfolio and represents a key step in fulfilling our strategy of building a broad business in regenerative biologics. TTOT's products and capabilities will better position Globus in existing allograft markets while also providing a dedicated source of supply for our extensive pipeline of products utilizing human allograft tissue. We expect to continue our mission of bringing health to patients with musculoskeletal disorders through the gift of life from donors," said David Paul, chairman/CEO of Globus.

TTOT processes sterile human tissue and distributes a wide range of allograft implants including machined spine implants, demineralized bone matrix, sponge allografts, and traditional bone allografts. Globus said it anticipates TTOT to contribute roughly $2 million in additional sales and to be neutral to fully diluted earnings per share for the fourth quarter 2014. For 2015, Globus said it anticipates a contribution from TTOT of about $12 million in annual sales and a neutral impact to fully diluted earnings per share for the year.

"Since our inception our mission has been to lead the transplant community through excellence and innovation for the benefit of fellow man, and view every donation as an opportunity to serve. I am glad that we have partnered with a company such as Globus that shares our mission regarding patient care and values the gift of life from donors," said Joe Mims, CEO of TTOT. //

LifeSeal

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Lars Påhlman, a professor of surgery at the University of Uppsala, Sweden and principal investigator of the LifeSeal study, said that 10 patients with rectal cancer were enrolled in the study between January and May 2013. The patients were randomized to either the LifeSeal group or the standard of care group. In the LifeSeal group, one unit of the sealant was applied on the staple line re-connecting the rectum. No safety concerns were raised relating to the product, he said, and no leaks were identified along the surgical connection where LifeSeal had been applied.

The company said it has also completed enrollment of 70 patients in a larger, multi-national pilot study of LifeSeal at seven colorectal surgery centers in Europe. This study seeks to further confirm safety and usability of the sealant as well as to assess the performance of LifeSeal in reinforcing the anastomotic staple-line during open or laparoscopic lower anterior resection procedures. Results are expected by the end of the year.

"Should the results of the pilot study be as positive as the first study, LifeSeal is likely to change how we do things in the operating room and become an essential part of the next generation surgical tool box," Påhlman said. "LifeSeal has the potential to make a significant and welcome impact."

Anastomotic (point of surgical connection) leakage after a colorectal resection occurs in as many as 15% to 19% of patients and is a life-threatening complication. Gideon Sturlesi, president/CEO of LifeBond, told *Medical Device Daily* that LifeSeal is the only bio-surgical sealant of its kind designed to reduce leakage associated with complications from colorectal surgery and the need for repeat operations.

"So, in a matter of speaking, we're creating a new market," Sturlesi said.

LifeSeal is comprised of natural origin bio-surgical materials with established safety profiles, according to LifeBond. Designed for application in both open and laparoscopic procedures, One of the differentiating features of the technology, Sturlesi said, is its ability to be applied easily to places surgeons normally are unable to reach. LifeSeal uses a special ergonomic applicator designed to easily and efficiently apply the sealant to tissues, including in very low, hard-to-reach locations. The sealant itself is comprised of two components which combine real-time inside the applicator. The resulting sealant is then applied in a gel form to the staple lines. Once applied, LifeSeal transforms into a durable, elastic and transparent protective layer designed to conform well to tissue and imitate its natural properties. LifeSeal's adhesive properties are intended to enable it to remain in place long enough to create an environment that supports the body's natural healing and tissue repair process, before degrading into the body, the company noted.

Sturlesi said the company expects to see similar results from the larger pivotal study as it did in the smaller preliminary study.

"Our products combine the unique properties of bio-surgical implants with the regulatory benefits of a medical device. This is beneficial as, comparative to the overall market, manufacturing processes are shorter, delivery is simpler and the products are generally less expensive," Sturlesi said. "We have made great progress in the last year and the industry has noticed, both in the clinic and in the board room. We are engaged in several high level discussions with leading companies regarding market introduction."

So far the company has received positive feedback from surgeons that have received hands-on experience with LifeSeal, Sturlesi said. "Basically all of them have said, first of all, that it is very simple to use," he said. "The need is so strong that I have no doubt in critical cases it will be used, people are dieing, basically, people are dieing from leakage."

In addition to the LifeSeal, the company is developing a self-fixating hernia mesh called LifeMesh, which is in pre-clinical development. Other pipeline products include tissue adhesives and absorbable hemostats, LifeBond noted. //

HIT BITS

ResMed launches application for patients with breathing disorders

Staff Report

ResMed (San Diego) said that it introduced myAir, a new personalized therapy management application for patients with sleep-disordered breathing. myAir equips patients with the information they need to resolve basic therapy issues so they can increase their comfort and stay compliant. By providing well-timed support, education and troubleshooting tools, myAir helps patients feel confident and motivated to start and stay on therapy. Empowering patients to take an active role in their health, myAir helps drive operational efficiencies for home medical equipment providers (HMEs) and gives them more time to focus on patients who need it most.

"myAir is personalized to each individual patient's therapy journey – they can see important information about their sleep therapy, make adjustments to improve the treatment experience, and share their progress with family members and loved ones, all on a daily basis," said Raj Sodhi, vice president, ResMed Healthcare Informatics. "If and when issues arise patients receive the information they need through myAir, allowing HMEs to focus on other patients more in need of support."

myAir is a key component of ResMed Air Solutions, the forward-thinking connected care solution for treating sleep-disordered breathing launched earlier this year. With its mobile responsive design, patients can access myAir from their mobile phones and tablets, anytime, anywhere. The platform has been designed exclusively for ResMed's AirSense 10 and AirCurve 10 devices, both of which are wirelessly enabled to automatically

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LifeBond

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international device companies.

"For the time being, cooperation between China and Europe is mainly in trading. Now the message is clear – it will further open up service industry to each other. And 'green hospitals' will be one of the points of focus," Xu Chao, managing director, Germany, from **Osmunda Medical Device Services**, a clinical trial contract research organization, told *Medical Device Daily*. "My understanding is China has opened up the hospital market to foreign capital. Medical companies can embrace [large] opportunities."

With a surprisingly large delegation of 15 ministers, Li's trip included his first visit to the Asia-Europe Meeting (ASEM) Summit in Milan since taking office. The meeting, the 10th annual such event, was held on October 16 and 17. Medical device companies in both China and Europe are expected to benefit from the outcome.

The opening of the services sector in China is ongoing. The first wholly internationally owned hospital in the country, **Artemed Hospital**, opened in the Shanghai Free Trade Zone in July. German healthcare operator and healthcare products provider Artemed Group and Beijing-based Silver Mountain Capital invested in the hospital. A month after the opening of Artemed Hospital, China's Ministry of Commerce (Mofcom) and the National Health and Family Planning Commission jointly reported that wholly foreign-owned hospitals would be allowed in seven cities and provinces.

China is now also considering including foreign-owned hospitals in the national medical insurance scheme, said Qiu Lixin, vice-director of Mofcom's Foreign Investment Management Department during a media conference on September 23.

The shift in focus to the service industry also means companies should rethink their business model to provide more integrated services that would bring together different sectors.

"Many big companies like Siemens, are talking about integrating their businesses like its lighting and medical product and introducing a comprehensive solutions," said Xu.

This integration could also lead to more investment both in and out of China. Medtech companies like **Mindray** (Shenzhen, China) and genomics services provider **Beijing Genomics Institute** (BGI) could lead the way with more mergers and acquisition activities.

"Mindray has set a good example of overseas acquisition in medical device field. BGI also established networks across Europe," Xu said. "On the other hand, China is in the process of re-constructing its regulation system. Many European companies have an eye on the huge China market."

From January to July this year, the 28 European Union members invested in 840 projects in China, an increase of 3.3% year-on-year to $3.62 billion. Meanwhile, China's non-financial direct investment in the EU hit $7.04 billion, tripling the figure from the same period last year, according to Li Yizhong, Chairman of China Federation of Industrial Economics.

While European companies continue to look to China for growth, Chinese companies are looking the other way. Three key focus areas could help Chinese companies expand in Europe.

The first is growing co-operation in high-tech industries.

"China and the EU should expand cooperation in multiple domains like high tech industries, strategic new industries, modern manufacturing sectors, joining efforts in R&D, investments and market development in order to provide greater dynamic for each other's growth," said Li.

As part of this growing co-operation more funding is available for R&D. Germany, for example, provides funding for research teams that have already secured private investment. This could benefit Chinese investors, said Xu.

A second area of focus is outsourcing, which could benefit Chinese companies with good but less expensive processes.

Osmunda is one company that is looking to expand in Europe to better serve clients. As Xu explained: "Service outsourcing has been raised up as a important sector to support. Many European companies would consider clinical trials outsourcing as China companies still have the advantage of price."

In-vitro diagnostics (IVD) is a good example of an industry that could benefit from this outsourcing because "due to genetic differences, companies will need different specimens both from China and European," said Xu.

A third area of focus is growing support in Europe for small and medium enterprises (SMEs).

"SMEs in the EU boast great strengths, advanced technologies, excellent skills and great competitiveness in capital & technology intensive industries and service sector while SMEs in China are still in the stage of structural optimization, transformation and upgrading," said Li. "This is a very good news for medical devices as many medical device companies are SMEs," said Xu. //

Beltway

Continued from page 1

provide FDA with nearly $600 million in user fees over the five-year term, although the sequester has shaved tens of millions off that sum already. The agreement called for more than 120 new hires in the first two fiscal years, most of which would go to the Office of Device Evaluation in an effort to clear out application backlogs and bring review times up to par. The user fees are subject to an inflation index as well, however (*Medical Device Daily*, Feb. 2, 2012).

The CHI report shows some positive trends in PMA review times, although the duration of reviews began to trend down before MDUFA III went into force. Gillenwater said the analysis did not include PMA supplements, however. The analysis, he explained, is "exclusive to original PMA submissions," but he added that they looked briefly at the numbers for PMA supplements, "which pointed to no real sign of a dramatic decrease in supplements."

"Our belief is that looking at original PMA is a critical, singular" measure of performance, but he pointed out that there is a trend toward fewer PMA applications. This drop, he said, "is cause for some concern, and is cause for at least asking why."

"We don't have any hard determinant reason," for that fall-off, Gillenwater said, although he acknowledged that the much-discussed first-in-human studies problem "is a roadblock." This is only one factor "in recent trends . . . which has led industry to look increasingly at launching first overseas."

Nonetheless, the CHI report notes that PMA average decision times are down to 262 days for fiscal 2013, roughly 200 days less than the high-water mark of 464 in 2009. Gillenwater cautioned that not all the applications filed in 2013 have gone through the process yet – the report indicates that the backlogged number of PMA filings for fiscal 2013 stood at 52 in September 2013, down from nearly 100 in August 2011 – but he said the available numbers are "beginning to show a turning of the corner." Gillenwater said that it is difficult to assign causation to the lower volume of backlogged PMAs given the lower volume of new filings, however.

The picture for 510(k) filings is more complex, but as device makers know, the complexity of 510(k) filings varies quite a bit, too. Gillenwater said the data did not include enough detail to analyze the role of longer and/or more complex filings in 510(k) review times, remarking only that these review times "remain far above historical averages," including pre-user fee averages.

The CHI report said that FDA turned around the more than 4,000 reviews in 2000 within 106 days on average, a metric that dropped to 99 days four years later. The average days ballooned to nearly 170 days by 2010 despite that manufacturers filed 324 fewer applications than in 2000. With roughly 88% of 510(k) filings completed for fiscal 2013, the average review time is down to 123 days, although the volume of filings is off by roughly 14% compared to 2010.

"Things are beginning to get back on track in the MDUFA III era," Gillenwater said of 510(k) reviews, but he cautioned, "in contrast to PMAs, there's a significant amount of work that needs to be done."

The report offers some data on the performance of the branches at the Office of Device Evaluation without naming the branches, and Gillenwater said CHI opted to examine the situation "because anecdotally we would hear from industry that in one division," applicants experienced constructive communications and a predictable, transparent process "where for another technology, the process would be quite the opposite, almost the proverbial black hole."

"The data illustrate there is something to that" discussion of under-performing ODE offices, Gillenwater said. "In addition to some of the mechanisms in the user fee authorization – the overall legislative and administrative improvements – there are some lessons to be learned about branches and divisions that are performing, "and those that aren't."

The quality of the regulatory filings for all application types has prompted FDA to issue guidances dealing with refuse-to-accept policies, but Gillenwater said, "the flip side of that same coin is ensuring FDA reviewers are trained" on how to handle applications, including how to review a filing without requesting additional information needlessly.

"We believe strongly that the improvements put into writing from the user fee agreement ... are going to address those types of problems much earlier," Gillenwater said, adding that the agency's efforts will allow sponsors to assemble better applications and hear from the agency about problems instead of hearing from FDA about problems with an application at the 11th hour.

Gillenwater said that there were indications that reviews were "pretty rigid, pretty legalistic, sometimes a check-the-box process" rather than a reflection of an effort to establish whether the needed data were in the filing. "The general tone and framework of the conversations between the agency and industry are vastly improved from a few years ago," he remarked, adding, "we're beginning to get on the same page earlier in the process."

Among the other metrics displayed in the report is a drop in the backlogs of 510(k) applications, from an high of more than 1,900 in 2010 to an estimated 1,400 for the as-yet incomplete fiscal 2013 cohort. FDA indicated it has received 19 de novo applications for fiscal 2013, a number that is up by only eight from 2011, the year FDA published the draft guidance for de novo submissions. //

Latin American

Continued from page 2

geriatric population with respect to the total population will increase to an average of 21 percent in Brazil, Mexico and Chile," the company noted in a release.

And it is not just on the demand side that the growth is visible.

The supply side of this particular equation is also on the rise as more manufacturers step up their presence in the region and leverage the interest of local governments in more home healthcare solutions that could help take some of the strain out of stretched healthcare systems.

"Developed countries [from regions] like North America and Europe are increasingly investing in this region," said the report.

"Companies are also expanding their presence in these geographies, and the governments are expanding their healthcare infrastructure," said Bagade. "Health awareness in these regions [is also increasing]," she added.

"Changing demographics and lifestyle of this people and opting for home-based services and health services is also supporting the growth of this market."

Another home healthcare study recently developed by **Grand View Research** (San Francisco) supports the idea that this market is growing fast thanks, in large part, to increasing awareness of health.

"The presence of untapped potential in emerging markets such as India, Brazil and China and increasing health awareness are expected to serve this market as future growth opportunities," noted Grand View Research.

According to Grand View, the global market for home healthcare is expected to reach $355.3 billion by 2020, growing at an estimated CAGR of 7.8% from 2014 to 2020.

By this measure, Latin America would account for only a five percent of the global home healthcare market of products and services.

The key players in the home healthcare market in the region highlighted by the two independent reports include **Johnson & Johnson** (New Brunswick, New Jersey), **Medtronic** (Minneapolis), **GE Healthcare** (Chalfont, UK), **The Linde Group** (Munich, Germany), **Philips Healthcare** (Amsterdam, the Netherlands) and **B. Braun Melsungen** (Melsungen, Germany), among others. //

Hit

Continued from page 6

deliver therapy data into myAir on a daily basis.

With myAir, patients receive a myAir score each morning calculated from their therapy data, providing them with a quick, snapshot view of their treatment. They can also click through to see how their myAir Score was calculated from metrics such as usage time and mask seal. Together with trend charts of the previous two weeks, myAir makes it easier for patients to track their sleep progress which can help them feel more confident and encouraged night after night.

In other HIT news:

• **AirStrip** (San Antonio) will work with **IBM** (Armonk, New York) to develop a mobile monitoring solution to help clinicians predict declining health in acute and critically ill patients. IBM will provide the streaming analytics technology which allows AirStrip's solution to use data from numerous data sources in real time.

The new solution, being co-developed by AirStrip with the **University of Michigan** (U-M; Ann Arbor) Center for Integrative Research in Critical Care, will bring together data from electronic medical records, body sensors and other sources with predictive analytics to create an AirStrip mobile Acute Care Early Warning System (mACEWS), that ultimately could be used to provide critical health insights to doctors' mobile devices. The system will be designed by AirStrip and the U-M Center for Integrative Research in Critical Care (MCIRCC) to help hospitals better manage acutely ill patients.

• **Medsphere Systems** (Carlsbad, California) and **Valley General Hospital** (VGH; Monroe, Washington) said that VGH is up and running on Medsphere's OpenVista electronic health record. The Snohomish County community hospital, located northeast of Seattle, now looks forward to Meaningful Use 2014 certification later this year and federal reimbursement early next year. Both Medsphere and VGH estimate that federal Meaningful Use funds will cover most if not all of the initial five-year subscription costs for OpenVista.

OpenVista is a comprehensive clinical, financial and patient accounting system and is fully certified by InfoGard for Meaningful Use 2014. Combined with Medsphere's proven and rapid implementation process, OpenVista will enable VGH to quickly qualify for federal stimulus dollars available through the American Recovery and Reinvestment Act (ARRA). Medsphere's subscription service pricing model—a pay-as-you-go structure with no huge upfront fees—will also mitigate financial pressure on the hospital. //

PRODUCT BRIEFS

• **Castle Biosciences** (Arlington, Virginia) said results from a second validation study of its multi-analyte test, DecisionDx-EC, confirmed the test's ability to identify which esophageal cancer patients are unlikely to benefit from the standard pre-surgical treatment of chemoradiation. The results were reviewed in an oral presentation at the 11th Annual Meeting of the International Society of Gastrointestinal Oncology in Arlington, Virginia. The results suggest that up to 30% of esophageal cancer patients may not benefit from the highly toxic, pre-surgical chemoradiation therapy (CTRT), and instead could have the option of moving directly to surgery and to other treatment options. The DecisionDx-EC test analyzes the localization of three protein biomarkers, NF-kB, Gli1, and SHH, to classify tumors as either responsive to (non-exCTRT) or resistant to CTRT (exCTRT). Testing was performed on formalin-fixed paraffin-embedded esophageal cancer tissue. In this second, multi-center validation study involving 64 patient cases, 67% of whom had been treated with a regimen that included 5-fluorouracil (5FU), researchers reported a 95% specificity, with positive (PPV) and negative (NPV) predictive values of 88% and 83%, respectively. These results confirm a similar analysis of an earlier validation study involving 167 patient cases, all of whom underwent a chemoradiation regimen involving 5FU plus platinum/taxanes. This study showed a specificity of 90% and positive (PPV) and negative (NPV) predictive values of 64% and 98%, respectively. The company also presented data from a parallel study of a gene expression profile (GEP) test in development for esophageal cancer. The study assessed the ability of two preliminary gene signatures to predict responsiveness to chemoradiation therapy in tumor samples from 16 patients. The results from this initial study showed that the GEP test predicted treatment response with high accuracy and specificity of 100% and 100%, respectively. The company plans to further evaluate the GEP test in esophageal and rectal cancer. Castle is a molecular diagnostics and prognostics company dedicated to helping patients and physicians make optimal decisions regarding treatment and follow-up care based on the tumor's unique molecular signature.

• **RedPath Integrated Pathology** (Pittsburgh), a maker of molecular diagnostics, said results from The National Pancreatic Cyst Registry, a multicenter clinical study, were published online in *Endoscopy*. The study concluded that integrated molecular pathology using PathFinderTG more accurately determines malignant potential of pancreatic cysts than current guideline-recommended criteria and, subsequently, can help guide patient management decisions for surgery and surveillance. These conclusions were drawn from a review of disease outcomes in 492 patients who had PathFinderTG testing as part of their standard of care when cytological analysis of cyst fluid was not definitive for the presence of malignancy. The results show that PathFinderTG is the most accurate, clinically validated test available for determining risk of malignancy in pancreatic cysts. PathFinderTG could distinguish patients who had 97% probability of benign disease at 3 years follow-up from those who were at 31-76 fold greater risk of malignancy. This is a marked improvement in risk stratification over that of current guideline-recommended criteria. RedPath's PathFinderTG Pancreas profile uses LOH markers, oncogene mutations, and DNA content abnormalities to evaluate pancreatic cystic lesions and integrate these analyses with clinical features to accurately risk stratify patients for the development of pancreatic adenocarcinoma.

• **X-spine Systems** (Miamisburg, Ohio) reported the addition of a broad line of biologics to their product portfolio. The initial launch of biologics includes Axograft DBM Putty, Axograft Cancellous Crushed Allograft, Axograft Crunch Allograft and Axograft Amniotic Membrane. Axograft says this biological line will complement X-spine's comprehensive line of spinal fixation products. The Axograft products will be used to promote spinal fusion, bone healing and wound treatment in spinal arthrodesis procedures. X-spine is a medical device maker that provides class-leading products for the treatment of spinal disease.

COURT REPORT

ourt dismisses class action lawsuit against Venaxis

Staff Report

Morrison & Foerster reported it won the complete dismissal of a securities class action against medical diagnostics company **Venaxis/AspenBio Pharma** (Castle Rock, Colorado) with the ruling on Oct. 17, at the Tenth Circuit Court of Appeals affirming a district court dismissal in 2012.

San Francisco-based litigation partners Jim Brosnahan, Raj Chatterjee and Mark Foster led the Morrison & Foerster team, which had represented AspenBio (renamed Venaxis in 2012) since the suit, Wolfe v. AspenBio, was filed in 2010.

Plaintiffs alleged that AspenBio and certain officers misled investors about preliminary testing results for an appendicitis diagnostic in development, as well as about the viability, uniqueness, and potential applications of the product and its prospects for approval by the FDA. The diagnostic is initially being developed for children, adolescents and young adults and is designed to assist doctors in ruling out appendicitis without the use of CT scans, particularly in an emergency room setting.

In 2012 Chatterjee and Foster filed a successful motion for dismissal in Colorado district court, and had previously obtained a stay of a parallel shareholder derivative lawsuit. The plaintiffs challenged the dismissal on appeal, and Chatterjee presented oral argument before the Tenth Circuit in September 2013.

"We are thrilled that the Tenth Circuit has upheld the dismissal of this class action against our client Venaxis. We've been challenging these cases since 2010 and have obtained dismissals at every stage, beginning at the trial level and now prevailing at the appellate stage," said Chatterjee. "With the litigation resolved, Venaxis can continue to focus on growing a company and developing a product that could substantially advance the public health." //

NEUROLOGY EXTRA

Keeping you up to date on recent developments in neurology

By Robert Kimball, Staff Writer

Stenting safe and effective for long-term stroke prevention

Using stents to keep neck arteries open is just as effective as invasive neck surgery for long-term prevention of fatal and disabling strokes, reports an international trial led by UCL (University College London) funded by the Medical Research Council and Stroke Association. The research paper, published in the *Lancet*, was authored by researchers from UCL, Basel University, Switzerland, the London School of Hygiene & Tropical Medicine, the University Medical Center Utrecht, the Netherlands, Sheffield Teaching Hospitals NHS Foundation Trust, and Newcastle University.

The brain's blood supply comes from the carotid arteries, two large blood vessels that run through the neck. Carotid artery disease occurs when cholesterol and fatty deposits build up in these arteries, restricting blood flow and increasing the risk of stroke.

In the UK, carotid artery disease is most commonly treated by an invasive surgical procedure called endarterectomy. Patients are put under general or local anaesthetic and surgeons cut open the affected artery to remove the build-up and then sew the wound up. The operation leaves a scar on the neck and can lead to heart attack, short-term facial paralysis from nerve damage, and bleeding, which can prolong hospital stays.

Stenting is an alternative procedure in which a small mesh cylinder, a 'stent', is used to keep the artery open. This is inserted under local anaesthetic through a small nick in the groin and fed up to the neck using a thin wire. The procedure is less invasive, causing only minor bruising in the groin, no risk of nerve damage and a lower heart attack risk than endarterectomy.

The study followed 1,713 patients with carotid artery disease, of whom 855 were assigned to stenting and 858 to endarterectomy, for up to 10 years. The median follow-up was 4.2 years. Both techniques were found to be equally good at preventing fatal and disabling strokes, but stented patients were slightly more likely to have minor strokes without long-term effects. The risk of any stroke in five years was 15.2% in the stenting group compared to 9.4% in the endarterectomy group, but the additional strokes were minor and had no impact on long-term quality of life.

"At the moment, stenting is not widely used in the UK due to historical uncertainty over its long-term effectiveness," says study leader Professor Martin Brown from the UCL Institute of Neurology. "However, we have now shown that stenting is just as good as endarterectomy for preventing fatal and disabling strokes. We have also shown that the risk of stroke during the procedure is no higher for stenting than for endarterectomy in younger patients. The risks of each procedure are different and will vary depending on the patient, but stenting should be offered as an option to many more patients under the age of 70.

Shamim Quadir, Research Communications Manager at the Stroke Association, said: "A transient ischaemic attack, also known as a mini-stroke, can be a warning sign that someone has carotid artery stenosis, and is at risk of having a major stroke. Preventative procedures to treat such carotid artery stenosis are therefore crucial. Carotid endarterectomy is a common, yet invasive surgery used to treat carotid artery stenosis, and is widely used throughout the UK. Previously, far less was known about the long-term effectiveness of stenting as an alternative procedure. These latest research findings suggest that overall, stenting is just as safe, and equally effective for the long-term prevention of fatal and disabling strokes. Both procedures carry their own risks, and these will need to be considered for each individual patient. This research provides a vital step in providing another viable option which will help people significantly reduce their stroke risk."

Let the cardiologists perform carotid stenting.

Several centers in the UK do not currently offer stenting as an option so the patient choice is not there. Worldwide more staff should be trained to carry out the procedure, now that it is known that stenting is effective in the long term. Otherwise there is a vicious cycle where nobody at a center has stenting experience so patients are only offered endarterectomy and staff cannot learn or observe the procedure. In other countries, such as the U.S., stenting is more widespread and the safety of the procedure improves as staff gain experience.

An Article Review in the Incidence and Prevalence Database (IPD), examined national data on elderly Medicare beneficiaries to determine the current specialty composition of operators performing carotid stenting in the United States and the extent to which specialty explains variation in its utilization and outcomes across different health care markets. From the Centers for Medicare and Medicaid Services (CMS), the authors obtained Physician Carrier (Part B), Medicare Provider Analysis and Review (MEDPAR), and Denominator files from January 1, 2005 to December 31, 2007. Each procedure of carotid stenting was mapped to a hospital referral region (HRR) based on the patient's residence zip code. The authors calculated population-based utilization rates for carotid stenting in each HRR over the 3-year study period. For each HRR, the authors also calculated 30-day risk-standardized mortality and 2 30-day risk-standardized mortality or stroke admission.

Physician specialty (U.S.): The authors identified 28,700 carotid stenting procedures performed in 26,938 patients between January 1, 2005, and December

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31, 2007. Of these, 14,919 procedures (52.0%) were performed by cardiologists, 7840 (27.3%) by surgeons, and 5112 (17.8%) by radiologists, with the remaining 829 (3.2%) performed by other specialties that were largely represented by neurology and internal medicine. Of the operators performing carotid stenting, 904 (34.9%) were cardiologists, 864 (33.4%) were surgeons, 719 (27.8%) were radiologists, and 101 (3.9%) were other specialists. Among surgeons, vascular surgeons made up the largest group (n = 539, 62.4%), followed by general surgeons (n = 180, 20.8%), neurosurgeons (n = 68, 7.9%), and cardiothoracic surgeons (n = 68, 7.9%).

Cardiologists were more likely to perform procedures in patients with Elixhauser comorbidities related to cardiovascular conditions but less likely to do so in those with neurological conditions. Rates of cardiac catheterization (including with concomitant carotid x-ray angiography) and coronary intervention in the 180 days prior to carotid stenting were significantly higher in patients undergoing carotid stenting by cardiologists. However, rates of recent diagnosis of acute stroke or transient ischemic attacks (TIAs) in the 180 days prior to carotid stenting were much less in this group.

The overall mean age-, sex-, and race-adjusted rate of carotid stenting was 3.3 per 10,000 enrollees during the study period. Substantial variation existed in its use across HRRs, with adjusted utilization rates varying from 0.3 to 20.2 per 10,000 enrollees.

Cardiologists for carotid stenting: The authors found that cardiologists in the U.S. currently play an important role in carotid stenting. Approximately one-third of the operators performing this procedure in Medicare beneficiaries are cardiologists, and they are responsible for more than half the total procedures. The authors found that cardiologists treat patients substantially different from other specialists. Not surprisingly, procedures by cardiologists more frequently involved patients with cardiac conditions or recent invasive cardiac procedures. Yet these patients also had fewer neurologic conditions, including less evidence of recent acute stroke or TIA. The authors found that HRRs where cardiologists performed most carotid stenting had higher population-based utilization rates than other HRRs with similar outcomes (see Article Review: "Physician Specialty and Carotid Stenting among Elderly Medicare Beneficiaries in the United States" as cited in the IPD).

Neurons can be reprogrammed to switch the emotional association of a memory

Memories of experiences are encoded in the brain along with contextual and emotional information such as where the experience took place and whether it was positive or negative. This allows for the formation of memory associations that might assist in survival. Just how this positive and negative encoding occurs, however, has remained unclear.

Susumu Tonegawa and colleagues from the RIKEN–MIT Center for Neural Circuit Genetics have now discovered that neurons in the hippocampus region of the brain can be artificially switched to encode memories as either positive or negative regardless of the original experience.

Tonegawa's research team used genetic techniques to mark neurons in the dorsal dentate gyrus region of the hippocampus and the basolateral complex of the amygdala (BLA) in male mice. Memories are encoded in both these regions as specific groups of activated cells called 'engrams', but each region encodes the memory in slightly different ways: the BLA encodes positive and negative memory 'valence', while the dorsal dentate gyrus encodes contextual information such as emotion.

The genetic labeling, which involved using a light-sensitive ion channel called channelrhodopsin, was activated by the formation of either a positive memory, in this case exposure to females, or a negative memory associated with a foot shock. The cells that expressed this channel could be subsequently activated by exposure to light; doing so induced aversive responses in mice that had experienced foot shocks, and appetitive responses in those that had experienced female interactions.

The researchers then used light to activate the hippocampal or BLA neurons that had been labeled during the formation of a positive memory while exposing the mice to foot shocks. The next time the animals were tested, light activation of those hippocampal neurons that had initially induced appetitive responses instead led the mice to exhibit aversive responses. However, BLA neurons could not be switched in this way, indicating that only neurons in the hippocampus have plasticity in their encoding of positive or negative memories.

The valence of hippocampal neurons, the researchers found, could be switched from both good to bad and bad to good using this technique, with the switch attributed to a change in the strength of connections between the hippocampal and BLA neurons of each engram.

The findings provide new insight into how memories can be altered after they are formed. The possibility of inducing similar changes to memory valence in humans could also offer hope of a treatment for those suffering from conditions such as post-traumatic stress disorder.