BioWorld MedTech

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Digital health for COPD

Resmed to pay $225M for Propeller Health

By Liz Hollis, Staff Writer

San Diego-based Resmed Inc. has agreed to buy Propeller Health, a digital therapeutics company that offers connected health solutions for people living with chronic obstructive pulmonary disease (COPD) and asthma. Resmed will acquire Propeller, of Madison, Wisc., for $225 million and fund the buy primarily with its credit facility.

The companies expect to finalize the deal before the end of the third quarter of Resmed's fiscal year 2019 at the end of March, subject to customary closing conditions, including regulatory approvals.

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Inside

Implandata says glaucoma trial patient implanted with Eyemate-SC sensor

By Ned Stafford, Staff Writer

HAMBURG, Germany – The first glaucoma patient in the ARGOS-SC01 clinical trial has been implanted with a suprachoroidally placed Eyemate-SC sensor, which is produced by German start-up company Implandata Ophthalmic Products GmbH and which continually monitors for intraocular pressure (IOP), the only modifiable risk factor in glaucoma treatment.

The prospective, open-label, single-arm clinical investigation, the first in-human validation of Implandata's Eyemate-SC sensor, is intended to generate the safety and performance data

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Amazon enters health care AI fray to make unstructured medical data more useful

By Stacy Lawrence, Staff Writer

The standardization and rigor that was supposed to result from the advent of electronic medical records (EMRs) has failed to materialize. That means that much of the most crucial patient medical information lies in unstructured text relating to everything from diagnosis to treatment to symptoms.

Amazon's latest foray into health care aims to change all that. It has launched Amazon Comprehend Medical, which is a HIPAA-eligible machine learning service designed to process unstructured medical text and identify the

See Amazon, page 5

Wuxi Apptec opens medical device testing center in Suzhou

By Chermaine Lee, Staff Writer

HONG KONG – Chinese contract research organization (CRO) giant Wuxi Apptec Co. Ltd. has expanded into the medical device testing field, establishing a center in East China to match two other centers in the U.S.

The new center in Suzhou, a busy city near Shanghai, opened in late November. Wuxi had earlier launched two similar centers in St. Paul, Minn., and Atlanta, in the U.S.

The Suzhou center is 15,000 square meters and is a new medical device testing unit of the company's laboratory testing division (LTD). The goal of the division is to ensure Wuxi's

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Deloitte, Advamed say diversification is vital to success of med tech

By Mark McCarty, Regulatory Editor

The world of medical technology has never paused for long, but the 21st century has brought digital technologies and value-based care to the forefront for device makers. A new report by the Deloitte Center for Health Solutions and the

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BioWorld MedTech's Cardiology Extra

Staff Writer Liz Hollis on one of med-tech's key sectors

Read this week's edition

Appointments and advancements

Patterson Companies Inc., of Saint Paul, Minn., appointed Tony Pellegrin as vice president of business development, M&A. Patterson connects dental and animal health customers in North America and the U.K. to the latest products, technologies, services and business solutions.

Financings

Fluidic Analytics Ltd., of Cambridge, U.K., raised $31 million to continue developing products for characterizing proteins and their behavior. The proceeds will be used to continue the commercial rollout of the company's lab-tools pipeline and develop clinical applications of its technology. The financing was led by Draper Esprit, which was joined by new investors Delin Ventures and Bgf. Iq Capital and Amadeus Capital Partners also joined Draper Esprit in backing Fluidic Analytics for a third successive time since the company's first financing in 2015.

Merchavia Holdings and Investments, an Israeli investment company specializing in early stage life sciences companies, completed an offering in shares and options. As part of the offering, the company offered 46,000 units including option warrants, 100 shares, 50 series 2 option warrants, at an exercise price of NIS 0.48 (US$0.13), that can be exercised by Jan. 17, 2019, and 50 series 3 option warrants of NIS 0.85, that can be exercised by Nov. 28, 2019. The units were offered through a tender at a price per unit, which was no less than NIS 55 per unit, and the company has given rights to an additional allocation of units in the case of oversubscription. Eli Arad, CEO of Merchavia, said the funds will allow the company to continue to enlarge its portfolio.

Revive Solutions Inc., of San Francisco, completed its $3.4 million seed financing round, which was led by new investor, Greenbox Venture Partners, along with new investors Rock Health, Healthtech Capital, Hippocrates VC, and other medical device executives and health care professionals. Proceeds from this financing will be used to complete the regulatory submission for Revive's product, leading to commercial launch of the product upon FDA approval. To date, the company has raised more than $6 million.

Other news to note

San Francisco-based **McKesson Corp. r**eported the relocation of its corporate headquarters from San Francisco, to Las Colinas, Texas, effective April 1, 2019, expanding upon its presence in the Dallas area. McKesson's Las Colinas campus is already a key hub for the company. Employees at the North Texas location perform vital functions for the company in areas such as operations, information technology, finance and accounting, marketing and sales, administration and support, purchasing and project management. Following the relocation of its headquarters, McKesson will continue to have a strong presence in California, employing more than 1,400 people, primarily in distribution operations and sales. The company opened a new distribution center for its medical-surgical division in Roseville, Calif. earlier this year. McKesson Ventures will remain in San Francisco, along with a technology development team for McKesson's U.S. Oncology Network. As previously reported on April 25, 2018, McKesson launched a multi-year strategic growth initiative, inclusive of plans to optimize the company's operating and cost structures. The company expects these initiatives and actions will generate approximately $300 million to $400 million in annual pre-tax gross savings that will be substantially realized by the end of Fiscal 2021.

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Resmed

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Aiming for growth

"Part of Resmed's growth strategy is to become the leader in out-of-hospital care for millions living with COPD and other respiratory diseases," Richie McHale, Resmed's respiratory care president, told *BioWorld MedTech*. "The acquisition of Propeller establishes Resmed as a leader in this space, with Propeller's connected health solutions for those with stage II and III COPD complementing Resmed's own cloud-connected devices for stages III and IV of the disease."

McHale also expressed enthusiasm that the company's portfolio now includes a connected health solution for those with asthma. "We remain focused, however, on our long-term goal to be the world's leader in out-of-hospital care for those with COPD, improving the quality of millions of lives, and significantly reducing COPD hospitalizations and their associated costs," he added.

When asked what attracted Resmed to Propeller, he noted that the company "is a high-performing standalone business" and serves as a good cultural fit, something Resmed executives have emphasized as an important consideration during buys.

Partnering for digital COPD

"Over the past year, Resmed and Propeller have talked about ways to partner around digital COPD patient management solutions, and Resmed made a small investment in Propeller related to that," McHale replied when asked how long the two had been in talks regarding a deal. "Later, when the opportunity arose to purchase Propeller, Resmed submitted a proposal."

Looking forward, the company is retaining all of Propeller's employees, locations and brand. "Propeller has strong partnerships and positive brand recognition in areas of digital respiratory care and pharma that are complementary to those of Resmed's current offerings in COPD and other lung diseases. Enabling Propeller to operate as a standalone company will help optimize its business opportunities, while Resmed's stability, R&D resources and neutrality with regard to Propeller's customers and partners will enable it to innovate and expand its offerings on a global scale," he added.

When asked about additional M&A, he said Resmed will continue to evaluate other device and software opportunities in out-of-hospital care.

Related to the deal, Safeguard Scientifics Inc., a partner of Propeller Health, said it expects to receive cash proceeds of $41.4 million. Safeguard noted that it deployed $14.3 million in Propeller since August 2014 and has a 20 percent primary ownership position.

Busy with M&A

Word of the buy comes almost a month after Resmed said it would purchase long-term care electronic health record (EHR) provider Matrixcare for $750 million. (See *BioWorld MedTech*, Nov. 6, 2018.) The acquisition marked the latest effort by the company to expand its presence as a software-as-a-service (SaaS) provider outside the traditional hospital setting. It wrapped the acquisition in the middle of that month.

> *"Part of Resmed's growth strategy is to become the leader in out-of-hospital care for millions living with COPD and other respiratory diseases. The acquisition of Propeller establishes Resmed as a leader in this space, with Propeller's connected health solutions for those with stage II and III COPD complementing Resmed's own cloud-connected devices for stages III and IV of the disease.*
>
> Richie McHale
> Respiratory care president, Resmed Inc.

When the deal closed, Margaret Kaczor of William Blair saw positives, noting that it did indeed complement Resmed's U.S. SaaS presence. "Despite the size of the acquisition, we believe the company's balance sheet remains strong though it will suspend its share repurchase program in the near term," she wrote. "We continue to expect management to look for accretive assets in both U.S. and international markets, though these may prove to be more tuck-in in the near term."

The Matrixcare buy followed the pickup of home health and hospice agency EHR provider Healthcarefirst for an undisclosed sum. In 2016, the company bought post-acute care software company Brightree for $800 million.

Quarterly results

Resmed reported Q119 results Oct. 25. During the call, Kaczor noted that the company had mentioned M&A within sales outside the U.S., with a particular emphasis on Europe and Asia. She asked about what kind of attributes Resmed sought in terms of targets. Michael Farrell, acknowledged that the company was looking at opportunities. "As we look at M&A, it's got to meet three criteria: Number one, it's got to fit our global strategy; two, it's got to make sense on the numbers and fit our financial strategy; and three, it's got to be a strong cultural fit. Fit between us and the management team, and that we're going to work together and work better together and provide some growth to each other and sharing across the platform."

At the time, Kaczor noted that Resmed looked impressive. "We believe the company . . . continues to make the appropriate investments to expand its material product and health care informatics differentiation over time. These should allow Resmed to maintain or continue to gain market share. ♦

Implandata

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required to win CE declaration of conformity, which would allow the device to be marketed in the EU. The trial will include a minimum of 20 patients in Germany and Switzerland to be implanted with the sensor and followed up for 12 months.

Max Ostermeier, co-founder and CEO of Implandata, told *BioWorld MedTech*: "We expect the CE mark for the Eyemate-SC sensor and the start of commercialization in 2020."

The Eyemate-SC sensor implant was performed in conjunction with non-penetrating glaucoma surgery by trial principal investigator Peter Szurman, of the Eye Clinic Sulzbach, Knappschaft Hospital Saar, in Sulzbach, Germany. Szurman described the sensor as "pleasantly small and easy to surgically implant."

Easy to surgically implant

"Most patients undergoing glaucoma surgery are likely to be eligible candidates for such a pressure sensor," Szurman said. "This breakthrough product enables glaucoma patients for the first time to monitor their own eye pressure at any point in time. I expect that it will improve therapeutic compliance and also significantly reduce the risk of unnecessary visual field loss or even blindness due to glaucoma."

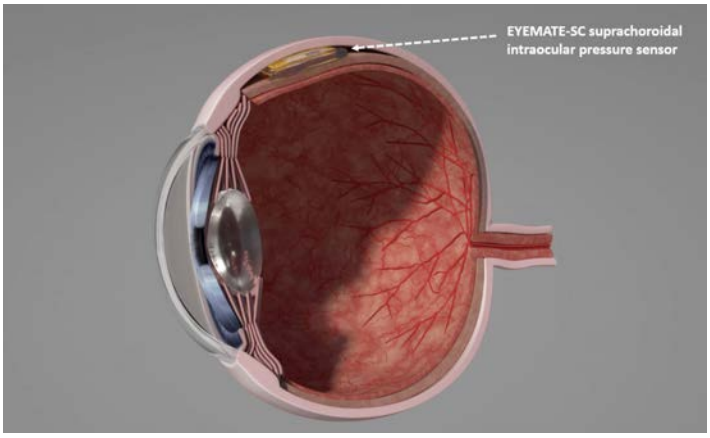
In addition to the Eye Clinic Sulzbach, the ARGOS-SC01 trial will include patients at the Ophthalmic Clinic of Ruhr-University in Bochum, Germany, the Department of Ophthalmology at the University Mainz in Germany, and the Montchoisi Clinique in Lausanne, Switzerland.

> *"Basically, we took this technology then advanced and miniaturized it so that it would also work for measuring intracorporal pressure wirelessly. The biggest challenge was to make it small enough, robust in the long-term, and accurate and precise, which we have been able to accomplish.*
>
> Max Ostermeier
> Co-founder and CEO, Implandata

The study will be observed by an independent data safety monitoring board chaired by Günter Krieglstein, a professor emeritus and former chair of the Department of Ophthalmology of the University of Cologne. The clinical trial is expected to be completed by early 2020.

"The successful inclusion of the first ARGOS-SC01 study patient," Ostermeier said, "is a pivotal milestone for Implandata towards broadening the use of our Eyemate system, eventually also allowing stand-alone implantation of our proprietary eye pressure sensing devices."

Ostermeier said the new Eyemate-SC sensor is based on the same technology as Implandata's Eyemate-IO intraocular sensor, which received a CE mark in 2017 and consists of a tiny micro-sensor chip that is bonded to a gold coil that functions as an RFID antenna.



Eyemate-SC from Implandata Ophthalmic Products GmbH

Biocompatible silicone rubber

"This sensor system is encapsulated in biocompatible silicone rubber for long-term hermeticity," Ostermeier said. "To activate an IOP reading, the sensor implant is powered by means of magnetic RFID coupling via an external patient hand-held device. At the same time the measured IOP data is sent back to the hand-held device, where the IOP value is displayed and stored with a time stamp. By an integrated SIM card, measured data is sent to a safe, web-based database for further data processing and analysis."

The Eyemate-IO implant is for glaucoma patients undergoing cataract surgeries, he said. After surgeons perform standard cataract surgery, the foldable Eyemate-IO sensor can be implanted through the same incision, placing it in the ciliary sulcus between the artificial intraocular lens and the iris.

"So the implant is sitting behind the iris and therefore not visible from the outside," Ostermeier said, adding: "Currently we are preparing for a first market launch of the Eyemate-IO in Germany and Switzerland via direct sales in 2019. Thereafter we will start to address further countries via distribution partnerships."

The new Eyematic-SC, he said, uses the same micro-sensor chip as the Eyemate-IO, but is configured to allow it be placed minimal invasively in the suprachoroidal space between the choroida and the sclera. While the Eyematic-IO is used by cataract surgeons and implanted during cataract surgery, the Eyematic-SC is for patients not yet in need of cataract surgery.

Space in the posterior chamber

"Patients with their natural lens cannot be addressed with the Eyemate-IO, as there would not be enough space in the posterior chamber, as the human lens is much more voluminous than an artificial intraocular lens," he said. "In the final analysis, the Eyemate-IO and the Eyemate-SC are complementary. They address different patient situations and are used by different types of surgeons."

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Amazon

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necessary information within it. Machine learning is a subset of AI that enables a system to automatically learn and improve from its own experience without being explicitly programmed.

Creating comprehension

"Comprehend Medical helps health care providers, insurers, researchers, and clinical trial investigators as well as health care IT, biotech, and pharmaceutical companies to improve clinical decision support, streamline revenue cycle and clinical trials management, and better address data privacy and protected health information requirements," said a recent blog post from Amazon Web Services by Taha Kass-Hout and Matt Wood.

"The majority of health and patient data is stored today as unstructured medical text, such as medical notes, prescriptions, audio interview transcripts, and pathology and radiology reports," the post continued. "Identifying this information today is a manual and time-consuming process, which either requires data entry by high skilled medical experts, or teams of developers writing custom code and rules to try and extract the information automatically. In both cases this undifferentiated heavy lifting takes material resources away from efforts to improve patient outcomes through technology."

Kass-Hout joined Amazon earlier this year and was previously the FDA chief health informatics officer; Wood is the GM of Deep Learning and AI at Amazon Web Services.

Many of the most fruitful early applications of artificial intelligence in health care have been around specific imaging projects, such as in retinal or cardiovascular applications, or in deciphering the vast amount of data generated by personal health technology ranging from diabetes devices to cardiac monitors.

What all these efforts have in common are precisely defined datasets that can be systematically tagged to teach an AI system what kinds of images or events are associated with patient outcomes. That enables the AI to sort this kind of data in ways that may be as good, or better, then human medical practitioners.

Automated structure

But AI has remained largely unsuited to working with vast amounts of unstructured, inconsistent data. However, this is precisely the sort of task that's necessary when it comes to medical information and EMRs that are generated by vast legions of providers and administrators with diverse interests who are using varying systems, approaches and methods. (See *BioWorld MedTech*, Jan. 11, 2018.)

Amazon said that its Comprehend Medical offering addresses all these problems, offering the ability to identify specific kinds of medical information in disparate records with high accuracy, but without having to do elaborate training or rule-setting. It can find common types of medical information including medical conditions, anatomical terms, medications, details of medical tests, treatments and procedures.

> *"Amazon Comprehend Medical will reduce this time burden from hours per record to seconds. This is a vital step toward getting researchers rapid access to the information they need when they need it, so they can find actionable insights to advance life-saving therapies for patients.*
>
> Matthew Trunnell
> CIO, Fred Hutchinson Cancer Research Center

Comprehend Medical is intended as a service in which various customers simply provide unstructured medical text for analysis. The data is then identified, and an analysis returned to the client, who requires no internal machine learning capabilities or training models.

This is expected to facilitate a wide range of health care activities including clinical decision support on a particular patient, revenue cycle management for health care providers, clinical trial management, population health platforms as well as addressing privacy and security assurance.

AWS has already done a few pilot projects with its Comprehend Medical offering including with the high-profile Fred Hutchinson Cancer Research Center, as well as Roche Diagnostics.

For Roche, Comprehend Medical was used to build a comprehensive, longitudinal view of patients for both individualized decision support and population analytics. At Fred Hutchinson, it was used to identify patients for clinical trials for specific cancer therapies by evaluating millions of clinical notes to glean and index information on medical conditions, medications and choice of cancer therapeutic options.

"Curing cancer is, inherently, an issue of time. For cancer patients and the researchers dedicated to curing them, time is the limiting resource. The process of developing clinical trials and connecting them with the right patients requires research teams to sift through and label mountains of unstructured medical record data," said Matthew Trunnell, Chief Information Officer, Fred Hutchinson Cancer Research Center. "Amazon Comprehend Medical will reduce this time burden from hours per record to seconds. This is a vital step toward getting researchers rapid access to the information they need when they need it, so they can find actionable insights to advance life-saving therapies for patients."

Gaining on Google?

Amazon is not new to health care, but this is one of its more ambitious industry-focused efforts to date. Early this year, it formed a partnership with Warren Buffett's Berkshire Hathaway

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Wuxi

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product quality control by offering medical device testing and regulatory services from R&D to commercialization.

"China currently faces massive unmet needs in the medical device testing field," Neil Wang, president of consultancy firm Frost & Sullivan Greater China, told *BioWorld MedTech*. "There are over 17,000 medical device makers in China, with over 15,000 firms producing class I or III medical devices and require testing services."

As of 2017, the medical device market was worth an estimated ¥440.3 billion (US$63.4 billion).

Wang added that in 2017 alone, medical device companies submitted more than 8,900 applications to China's health care watchdog, the National Medical Products Administration (NMPA), for product registration.

"The market concentration of medical device testing in China is extremely low. . . . The news of Wuxi Apptec entering this field is well-received by many medical device companies. It possesses a high competency in research services and extensive experience in overseas cooperation and implementation," he said.

The new center in Suzhou will provide testing services including biomaterials analysis, toxicology, biocompatibility, risk assessment, product aseptic design microbiology, physical testing of packaging and shelf life, and product batch release testing, among other things, Wuxi said.

Asked why Suzhou would have been chosen as the location for the new center, Wang cited favorable policies there for health care companies.

In 2007, China and Singapore collaborated on building a center in Suzhou to cultivate life science innovation. According to Biobay's 2017 report, there are currently a total of 127 companies specializing in drug discovery, and 156 medical device companies, in the designated area.

"Suzhou is one of the most popular choices for biotech, pharmaceutical and CRO companies . . . which is now forming an agglomeration effect. Choosing Suzhou is an unsurprising decision coming from Wuxi Apptec," Wang said.

In April, Wuxi expanded its LTD's drug development testing center in New Jersey to 115,000 square feet, claiming to create more than 200 jobs.

Many health care platforms

LTD and testing services aside, Wuxi has also partnered with other companies for creating different health care platforms.

In October, Wuxi launched a cooperation deal with state-backed big data company China Electronics Data Services Co. Ltd. (CEDS) to start a joint venture, CW Data. The JV utilizes Wuxi's drug discovery expertise and CEDS' sea of data to generate health care big data analytics for pharmaceutical and biotechnology companies. (See *BioWorld MedTech* Oct. 29, 2018.)

This comes after Wuxi launched a technology said to speed up the drug discovery process by allowing easier access to more chemical entities in a shorter time, at a lower cost. The DNA-encoded Library Construction and Screening Platform employs DNA sequences to tag each chemical entity, with the library to enable deconvolution following affinity selection against a target protein, Wuxi said.

Wuxi Diagnostics also launched a joint venture with the nonprofit Mayo Clinic at the start of the year to develop a platform on which scientists can commercialize innovative ideas into clinical tests for complex diseases.

The CRO's active pharmaceutical ingredients maker, Shanghai Syntheall Pharmaceutical Co. Ltd., collaborated with biopharmaceutical company Antengene Corp. in July for chemistry, manufacturing and control development and manufacturing oncology drugs.

The two companies are working together on clinical and commercial projects. They started with the phase II and phase III of ATG-008 from Antegene that targets hepatitis B virus-positive advanced hepatocellular carcinoma. They will then expand their partnership in drugs for treating solid tumor, hematological tumor and viral infection.

Wuxi's Shanghai IPO in May raised $328 million. Previously traded on the New York Stock Exchange, the company was taken private in December 2015 in a $3.3 billion M&A deal with Ally Bridge Group and other investors. Wuxi declined to comment for this story, citing "process of H-share listing" as the reason. Reports have said that Wuxi is eyeing a $1 billion-plus IPO in Hong Kong. ♦

Other news to note

Hilden, Germany; Germantown Maryland; Fort Myers, Florida; November 30, 2018 – Venlo, the Netherlands-based **Qiagen N.V.** and Fort Myers-Fla.-based **Neogenomics Inc.** reported a master service agreement to accelerate the availability of companion diagnostics that enable precision medicine for cancer patients. The partnership between Qiagen and Neogenomics, a provider of cancer-focused genetic testing services, will lead to the introduction of FDA-approved companion diagnostics simultaneously with launch of new therapies.

Product briefs

German pharmaceutical and life sciences company **Bayer AG** reported that the U.S. FDA granted breakthrough device designation to the Chronic Thromboembolic Pulmonary Hypertension (CTEPH) artificial intelligence (AI) pattern recognition software, which Bayer is currently developing jointly with U.S. biopharmaceutical company **Merck & Co. Inc.**, which is known as MSD outside the U.S. and Canada. A rare form of pulmonary hypertension, CTEPH affects an estimated five individuals per million per year globally. Development of the CTEPH pattern recognition AI software will use deep learning methodology to support radiologists by identifying signs of CTEPH in CTPA scans. The software analyzes image findings from cardiac, lung perfusion and pulmonary vessels in combination with the patient's clinical history. If the development is successful, the software could be deployed via Bayer's Radimetrics software, an informatics technology platform that connects contrast medium, injector and scan information to provide important insights.

Regulatory

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Advanced Medical Technology Association (Advamed) says that device makers that do not want to be left behind should key in on three priorities, the most important of which they say is diversification of product portfolios.

The report is the result of a survey of officials with 22 med-tech firms to gain some insight into the priorities in those firms, and the answers were that the emphasis is on driving innovation, improving margins and reducing costs over the next three to five years. The survey took place between April and August 2018, and the respondents were primarily from companies with at least $2 billion of market cap, although most of the concerns expressed are likely felt by smaller device makers as well.

Regulatory picture unlikely to ease

As might be expected, 95 percent of respondents cited the increasingly complex web of global regulatory mandates as a principal concern over that time, an ever-larger consideration given the rising percentage of device makers that do business in multiple regulatory jurisdictions. That picture is unlikely to ease anytime soon as regulatory agencies respond to the so-called Implant Files, a series of reports by the International Consortium of Investigative Journalists to which the Canadian government responded with a suggestion that pre- and postmarket scrutiny of devices is going to elevate in the near term.

As is widely known, digital health is making its presence felt not just in pacemakers and MRIs, but also in the relatively novel field of software as a medical device, the regulatory framework for which still has not crossed the line between revolution and evolution.

All the respondents said they were investing in digital technologies, but more than three in four said the process of integrating the data from those digital technologies is proving difficult. While the novelty of such demands is a source of drag on such efforts, the respondents said they were also struggling to overcome critical funding and skill gaps in their companies, a set of considerations device makers will have to resolve quickly as software continues to expand its footprint in med tech.

Third on the list of concerns at 68 percent is coverage and reimbursement, a concern driven largely by the rush toward non-traditional payment models. Among the possible solutions for this category of concerns are products and services that can improve outcomes, but the surveyed companies also said advances that reduce post-treatment complications and increase procedural efficiency are high on the list of innovations that will help the sponsor persuade payers.

Of the 22 respondents, 15 said they are reorienting their strategic focus because of the emphasis on value-based care, with improved long-term outcomes drawing the most interest. Procedural efficiency was actually one of the lower-rated of the five most commonly cited imperatives in this area, after a reduction in adverse events and reduced total health care costs for patients. More than six in 10 of the respondents say they have at least considered entering into a value-based contract with payers and/or providers, agreements that base payment on device performance and patient outcomes.

Eighty-six percent of the respondents said they are working to meet these headwinds by expand product portfolios. This is assumed to help expand market share and to provide a deeper presence in both geographic markets and in market segments, while 82 percent want to find ways to get their products to market more quickly. The use of real-world evidence (RWE) is an imperative for 77 percent of respondents, although the common understanding of RWE is that the FDA sees it as a way to add indications to an existing approved product, rather than a source of evidence for an entirely novel device type.

One solution to the need to innovate is to partner with organizations that do not fall neatly into the med tech space, and the ratio of companies that intend to adopt that approach will double to 82 percent over the next two years. Much of this collaboration will be undertaken to deal with the difficulty of getting up to speed in the digital space, but there is the hazard that such a collaboration could lead that other party to become a competitor, the report advises.

No net boost in R&D indicated

The report said that respondent companies expect to boost spending on "transformational innovation" by five percentage points in 2019 and 2020, but this would reflect a shifting of emphasis rather than an overall increase in R&D spending. Seven in 10 said R&D accounts for 5-15 percent of revenue, and more than four in five respondents said that rate is going to hold steady for the next few years. This of course will necessitate some difficult choices, and the report said the emphasis on transformational innovation "might explain the prioritization of RWE." The underlying assumption is that such data, which might be provided in part by one or more digital sources, could identify unmet or poorly met needs along with information to boost the case for coverage or higher rates than a payer might otherwise be willing to pay.

Scott Whitaker, president and CEO of Advamed, said the changing landscape of health care "is creating new opportunities for med tech to drive innovation," adding that the association "will continue to promote policies that support this evolution." Glenn Snyder, principal and med tech leader for Deloitte, said device makers are responding to these changes by modifying their operations and investing in future capabilities, but that these new imperatives may force device makers to develop "new processes and operating models." ♦

Implandata

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Implandata was founded in 2010 in Hanover by Ostermeier and Stefan Meyer, who serves as the company's CTO. Ostermeier said the two founders saw a great need for an implantable permanent intraocular pressure (IOP) sensor to continuously monitor eye pressure.

"Current state-of-the-art technologies allow only random and infrequent IOP in-office snapshots, not providing any information about IOP variability over the day and pressure fluctuation between office visits," Ostermeier said. "Imagine if blood pressure of hypertensive patients is checked only once every three to six months and a doctor has to find the right therapy based on this very limited information. That is the situation we have today in glaucoma and the reason why too many glaucoma patients lose their vision and eventually go blind."

Auto tire pressure sensors

To realize the technology platform for continual IOP monitoring, the company accessed similar automotive technologies, he said, specifically auto tire pressure sensors that also need telemetric measurement capabilities.

"Basically, we took this technology then advanced and miniaturized it so that it would also work for measuring intracorporal pressure wirelessly," he said. "The biggest challenge was to make it small enough, robust in the long-term, and accurate and precise, which we have been able to accomplish."

Ostermeier declined to give figures about the company's past funding. However, the company in 2014 issued a statement reporting the closing of a €3 million series B-round. The round included a new investor, Born2grow Venture Partners, a private fund based in Heilbronn, Germany, and previous investors Peppermint Charité Beteiligungsfonds of Berlin; Hannover Beteiligungsfonds, High-Tech Gründerfonds of Bonn, KfW of Bonn, and business angels.

A considerable amount of equity

Ostermeier said the company's investors are diverse, adding: "Most importantly, several ophthalmologists have provided a considerable amount of equity."

In May, the company in a statement reported "a first closing of its series C funding round," saying it had raised "a mid-single digit million Euro amount." The statement said the company "intends to complete the series C-round by raising an upper end single digit million Euro amount by the fall of 2018."

Ostermeier said the series C round funding will be used in part, to begin an IDE pilot study in 2019 as a first step toward winning U.S. FDA approval, which he conceded will not be easy.

"We all know that this is a lengthy process," he said, "but we are dedicated to walk this road given the huge market the U.S. offers for a product like ours." ♦

Amazon

Continued from page 5

and JPMorgan Chase & Co. to try to innovate approaches to providing their U.S. employees with high-quality health care at a reasonable cost.

In June, Amazon also purchased Pillpack, a pharmacy that pre-sorts and delivers medication for patients who are take multiple drugs. It also coordinates prescription refills and renewals. These moves led to some speculation that the consumer giant has long-term plans to try to rationalize an often costly and chaotic U.S. health care system that bears uniquely high drug prices.

Fellow massive tech conglomerate Google also recently advanced its own commitment to the integration of AI into health care. It moved its health care AI unit from its Deep Mind business and into Google, hiring the former head of Geisinger, David Feinberg, to lead it.

At the same time, Google debuted a health care AI product known as Streams, a mobile app designed to keep physicians and nurses current on various kinds of patient data such as test results and vital signs such as heart rate and blood pressure. Streams is being developed in partnership with the U.K.'s National Health Service (NHS). Google parent company Alphabet Inc. also has various AI initiatives housed within its Verily Life Sciences business including retinal image analysis.

Summed up Global Data analyst Edit Kovalcsik on the Amazon Comprehend Medical debut, "While improving health outcomes, Amazon's software could alleviate growing health care costs and insufficient resources brought about by aging populations and increasing prevalence of chronic diseases. Correct interpretation of the abundant data generated through health care services is fundamental to successfully transform the industry to become highly efficient and cost effective and Amazon is right at the edge to achieve this through its AI-integrated software, patient focused online pharmacy, and voice technology." ♦

Regulatory front

The **U.S. Medicare Payment Advisory Commission** said it supports the addition of new durable medical equipment product categories for the Medicare competitive bidding program. The U.S. Centers for Medicare & Medicaid Services has proposed to add items such as off-the-shelf (OTS) back braces and knee braces, and MedPAC said that it believes that the rates paid by Medicare for these and other products are substantially higher than the rates paid by private payers. Medicare and beneficiary spending for OTS orthotics grew from $255 million in 2014 to $678 million in 2017, the commission said, adding that OTS back and knee braces account for roughly 75 percent of that latter sum. Much of the increase is based on "supplier-based demand" and/or fraud and abuse. MedPAC said also that one area of concern is the absence of fitting and adjustment services by DME providers, even when paid to provide those services.

Ginette Petitpas Taylor, Canada's Minister of Health, said in reaction to the Implant Files that she has directed **Health Canada** to draft a plan to tighten both premarket and postmarket scrutiny of class III and IV medical devices. The Implant Files, a series of reports by the International Consortium of Investigative Journalists, had alleged that regulatory entities have not adequately protected patients and consumers from purportedly faulty class III and IV medical devices, and Taylor said Health Canada would consider more extensive premarket data, possibly including "requirements for clinical data," along with more extensive public notification regarding adverse events regardless of the jurisdiction where the adverse event occurred. Approval summaries for class III and IV device may also be more routinely made available to the public, and Taylor said the full details of Health Canada's response to the mandate "will be published in the coming weeks."

The **U.S. Government Accountability Office** said the ongoing overhaul of the Medicare clinical lab fee schedule could result in payment of "billions of dollars more than is necessary." The GAO report said that the use of rates paid in 2017 as a baseline for recalculation of payment rates as modified by data on private payer rates has resulted in higher rates than were previously paid, adding that CMS may pay an excess of more than $730 million in the current and two subsequent calendar years when using rates from CY 2016 as the baseline. The report also cited the cessation of payment for multiple tests via test panel rates as a factor, said to be a consequence of uncertainty regarding the Centers for Medicare and Medicaid Services' authority to pay for test panels under the terms of the Protecting Access to Medicare Act of 2014. GAO recommended that CMS rectify the situation in part by collecting private payer rates from all eligible labs rather than a subset of labs, an argument that has been advanced on several occasions by diagnostic lab associations.

Medtronic plc, of Dublin, said it will appeal a jury decision that the company should pay $112 million in damages to Rick Sasso, a spinal surgeon who sued the company for royalties in connection for spinal implant devices he assigned to the company more than a decade ago. Sasso entered into an agreement with Sofamor Danek of Warsaw, Ind., prior to the company's acquisition by Medtronic, and initially filed the suit in 2013. Sasso lost a trial court case over the matter in 2015, but successfully appealed to a six-juror panel last week after receiving roughly $23 million in royalty payments from the company.

Product briefs

Cellworks Group Inc., of San Jose, Calif., which focuses on precision medicine and Therapy Response Index (TRI) technology, reported that two of its recent studies will be featured as poster presentations at the American Society of Hematology (ASH) Annual Meeting and Exposition held Dec. 1-4 in San Diego. One of the studies, the Cellworks Icare 1 clinical study, demonstrated 90 percent accuracy for predicting response to standard of care treatments in acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) patients. Cellworks' genomics-informed computational biology modeling (CBM) technology was used in the prospective study to understand the mechanisms of relapse after chemotherapy treatment and propose new re-induction treatment options for the 32 percent relapsed patients in this study. For the study, 120 patients with AML or MDS were recruited to assess the predictive accuracy of Cellworks CBM by comparing computer predictions of treatment response to actual clinical outcomes. Of the 120 patients, 96 patients had full genomic testing profiles and 50 were eligible for evaluation based on length of follow-up. In the second study, Cellworks reported that its AI-driven biosimulation technology predicted resistance to Azacitidine (AZA) in newly diagnosed myelodysplastic syndromes (MDS) patients with high accuracy. In a cohort of 37 intermediate and high-risk MDS patients, Cellworks predicted AZA non-responders with 100 percent accuracy.

San Diego-based **Cytori Therapeutics Inc.**, which develops nanoparticle-delivered oncology drugs and autologous adipose-derived regenerative cell therapies within its Nanomedicine and Cell Therapy franchises, reported receiving approval for the Celution Cell Therapy System consumable bundle in Japan as a class III medical device. Furthermore, Cytori reported that the company outsourced an important assembly portion of the production process for its Celution Cell Therapy consumables from San Diego to Viant Medical in San Antonio, Texas. The first consumable lots following this new process were shipped to customers in November 2018.

Product briefs

Edwards Lifesciences Corp., of Irvine, Calif., which focuses on structural heart disease and critical care monitoring, reported that the Hemosphere advanced hemodynamic monitoring platform received FDA clearance for the Acumen suite of intelligent decision-support solutions. The latest Hemosphere platform includes solutions for predictive monitoring of moderate to high-risk surgical patients, which make up the Acumen suite of intelligent decision-support solutions. The solutions include Acumen HPI (Hypotension Prediction Index) software, which introduces artificial intelligence (AI) to hemodynamic monitoring through a machine learning, data-driven algorithm that indicates the likelihood of a hypotensive, or low blood pressure, event before it occurs, and the Acumen IQ sensor, a minimally-invasive sensor that enables the Acumen HPI software and automatically updates advanced hemodynamic parameters every 20 seconds.

Philadelphia-based **Group K Diagnostics Inc.**, (GKD) reported it has started part II of its liver function clinical trial at the University of Pennsylvania Liver Disease Clinic. This next phase of the clinical trial, which will take between one and two months to complete, will allow future patients at the clinic, and other hospitals, to benefit from reliable test results in just 20 minutes, and will give doctors the ability to react quickly and adjust medical treatment based upon the results. The report comes after the company's $2 million series A funding, which is being used to continue GKD's lab expansion and further support the work needed to obtain 510(k) clearance from the FDA.

Jenavalve Technology Inc., of Irvine, Calif., a developer of differentiated transcatheter aortic valve replacement (TAVR) systems, reported U.S. FDA approval of expansion of its investigational device exemption (IDE) feasibility studies for the Jenavalve Pericardial TAVR System with the Everdur transcatheter heart valve (THV) and Coronatix Transfemoral Delivery Catheter. The approval expands eligible patient enrollment from 20 patients at extreme or high surgical risk (10 aortic stenosis [AS], 10 aortic regurgitation [AR]) to 80 patients at extreme or high surgical risk (40 AS, 40 AR) at up to 10 U.S. sites. The prospective IDE studies are part of a larger, ongoing CE Mark clinical program investigating the Jenavalve Pericardial TAVR System for the same indications at centers of excellence in Europe and New Zealand. The Jenavalve system is proprietary and differentiated from currently available TAVR devices due to the Everdur THV locator-based technology, designed to enable anatomically-correct, predictable implantation using the new 18-Fr equivalent Coronatix transfemoral delivery catheter. Enrollment has been completed for the AS CE mark clinical program and is ongoing for the AR CE mark clinical program.

Dublin-based **Medtronic plc**, reported the first patient treated in the TERMINATE AF trial, a multi-center study evaluating two surgical ablation devices – the Cardioblate Irrigated RF (IRF) system and the Cryoflex surgical ablation system – for the treatment of non-paroxysmal (persistent or longstanding persistent) atrial fibrillation (AF) in patients undergoing open-heart surgical procedures. Following investigational device exemption (IDE) approval by the U.S. FDA, the first patient was treated in the study by the heart team led by Ralph Damiano, at Washington University School of Medicine in St. Louis. In the U.S., use for treatment of AF is investigational use only.

Neuropace Inc., of Mountain View, Calif., which recently launched the Next-Gen RNS system for refractory epilepsy, reported complete results from its long-term treatment study that prospectively evaluated 256 patients across 33 epilepsy centers with nearly 1,900 patient implant years of follow-up. Treatment with the RNS System, a brain-responsive neuromodulation system, resulted in significant seizure reduction and improved quality of life for patients, including improved memory and cognition. Drug-resistant epilepsy patients in the study (who had a median of 10 seizures per month) experienced the following long-term clinical outcomes: approximately 3 out of 4 patients responded to therapy, achieving at least 50 percent seizure reduction; 1 in 3 patients achieved at least 90 percent seizure reduction. Some 28 percent of patients experienced seizure-free periods of six months or longer and 18 percent experienced seizure-free periods of one year or longer. Median seizure reduction across all patients was 75 percent at 9 years. Quality of life improvements (including cognition) were sustained through 9 years, with no chronic stimulation-related side effects.

Synchron Inc., of Campbell, Calif., a company developing minimally invasive neural interface technology, reported data demonstrating the feasibility of minimally-invasive techniques to enable focal brain stimulation was published Dec. 3, 2018, in the journal *Nature Biomedical Engineering* under the title "Focal stimulation of the sheep motor cortex with a chronically implanted minimally invasive electrode array mounted on an endovascular stent." The paper reported, for the first time, the delivery of localized stimulation from a permanently implanted device called Stentrode through a blood vessel to the brain, and documents the ability of the device to elicit specific muscle movement. Pre-clinical studies have demonstrated the Stentrode's ability to pick up strong electrical frequencies emitted by the brain, which have previously required invasive surgery through the skull to achieve. Direct electrical stimulation has been demonstrated to alleviate symptoms associated with many neurological conditions and disorders, including Parkinson's disease, depression, and epilepsy. Synchron recently reported plans to initiate clinical trials to evaluate the ability of the technology to aid people with severe paralysis to potentially stream thoughts into a digital output to bypass the damaged nervous system. The technology enables patients to control a mind operating system and in turn directly control assistive technologies, such as computers, vehicles and robotic limbs. The technology utilizes artificial intelligence and machine learning algorithms that directly interface with and predict brain activity.

Cardiology Extra

Keeping you up to date on recent developments in cardiology

By Liz Hollis, Staff Writer

Cancer patients seen as having worse outcomes in PCI

Experts from Keele University in the U.K. say that cancer patients who undergo a common heart procedure have worse short-term clinical outcomes vs. those without the disease. The study, published in the *European Heart Journal* under the title "Percutaneous coronary intervention in cancer patients: a report of the prevalence and outcomes in the United States," reviewed 6.6 million hospital admissions in the U.S. over an 11-year period, in which admitted patients underwent a percutaneous coronary intervention (PCI) procedure. The procedure involves a stent, which is used to open up narrowed or blocked blood vessels in the heart. About 10 percent of those who underwent a PCI procedure during that time period either had a current or historical cancer diagnosis. The study focused on those with common cancers – specifically, prostate, breast, colon or lung cancer, as these were the most prevalent in the dataset. Of note, patients with a current diagnosis of lung cancer were three times more likely to die in the hospital following a PCI procedure, compared with those with no cancer. Colon cancer had the greatest association with major bleeding complications post-PCI, with a threefold increase vs. those with no cancer. Patients with metastatic cancer, irrespective of type, also had poorer outcomes. "Our research found that a concurrent cancer diagnosis during these procedures is not uncommon, and it has an important impact on the clinical outcomes of these procedures, depending on the type of cancer, presence of metastases, and whether the diagnosis is historical or current," said Mamas Mamas, professor of cardiology at Keele University. There are limited data regarding outcomes of patients undergoing PCI with a current or historical diagnosis of cancer, as they are typically excluded from randomized, controlled trials. "Our recommendation is that treatment of patients with a cancer diagnosis should be individualized, recognizing that cancer is associated with a higher risk of complications, and should involve a close collaboration between cardiologists and oncologists," added Jessica Potts, research associate at Keele University and co-author of the study.

Stroke, heart disease remain problem in the U.S.

The battle against heart disease and stroke continues in the U.S., with the former coming in as the leading cause of death and the latter coming in fifth, according to the *National Center for Health Statistics Mortality Data Report for 2017*. "With a slight decrease in deaths from heart disease in 2017 and a slight increase in deaths from stroke this lack of any major movement in these areas has been a trend we've seen the last couple of years," said Ivor Benjamin, president of the American Heart Association. "It is discouraging after experiencing decades when heart disease and stroke death rates both dropped more dramatically. We know there is still much work – new work – to do to turn this trend around." Alzheimer's disease also was high on the list, coming in at number 6, and the association is paying attention with new initiatives. "Due to growing evidence of a strong association with these diseases and heart and brain health, we are making substantial investments to address these conditions. Addressing diabetes and overall brain health are essential to our overall mission to be a relentless force for a world of longer, healthier lives," Benjamin said. In fact, the association has invested millions of dollars to learn more about how the circulatory system affects cognitive impairment. Additionally, there is a push for more resources on the connection between the heart, brain health and stroke prevention. The group also highlighted that research shows people living with diabetes are at least two times more likely to develop and die from cardiovascular disease. In cooperation with the American Diabetes Association, the group launched an initiative – Know Diabetes by Heart – with an eye toward reducing cardiovascular deaths, heart attacks and strokes in people living with type 2 diabetes. The report also revealed that infant deaths from congenital malformations decreased in 2017, possibly reflecting fewer deaths from congenital heart defects (CHD). The association has looked to improve outcomes for children born with CHD through a research initiative with the Children's Heart Foundation.

Cellular gene signatures for heart muscle regeneration

The ability to repair heart muscle could enhance quality of life for the millions of people who suffer from a heart attack or have a chronic heart condition. Now, researchers see human-induced pluripotent stem cells (hiPSC) as a potential way to unlock this regenerative ability. By taking a tiny bit of blood, scientists can generate an individual's specific stem cells and then convert them into any cell type, including cardiomyocytes. The research is in its early stages, and the technique is not yet ready for human heart disease regenerative purposes. With that said, University of Arizona (UA) researchers are gaining ground toward understanding hiPSC cardiomyocytes, as well as how they may be used to repair heart muscles. In a study published in December 2018, in *Nature Communications*, Jared Churko, assistant professor of cellular and molecular medicine at the UA College of Medicine – Tucson, used a systems-based approach encompassing single-cell transcriptomics, single-cell proteomics and CRISPR gene-editing to identify different subpopulations of cardiomyocytes. The research reveals multiple subpopulations of cardiomyocytes expressing specific transcription factors – NR2F2, TBX5 and HEY2 – with different spatial and biological functions as observed in the heart. "Understanding the gene signatures of different populations of hiPSC-CMs will impact our understanding of how to use such cells to discover drugs, model heart disease and repair a damaged heart," Churko said. The article, "Defining human cardiac transcription factor hierarchies using integrated single-cell heterogeneity analysis," appeared Nov. 21, 2018.