Medical Device Daily™
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The MDD Interview

Dubreuil: Usability playing a larger role in designing products

2nd of 2 parts

By JIM STOMMEN, *MDD* Contributing Writer

Marc Dubreuil is director of business development at **Farm**, a Hollis, New Hampshire-based product development firm that focuses on medical and life sciences. He has held numerous positions within the plastics and manufacturing industries, and has a strong background in the product development process.

Marc's focus in business development activities includes orthopedics, arthroscopy, neurology, robotics, dental, and the venture capital and academic communities. Past clients include most of the Fortune 100 medical companies.

MDD: Doing more with less seems the key rule in healthcare moving forward. Is usability playing a more important factor in medical product design than was true previously?

Dubreuil: In the future, all participants involved in product development are going to be challenged to be much more effective in the design process. That means being both more cost-effective and performance-effective. I think we're going to see more companies, in order to maximize resources, develop second-generation products rather than creating brand-new products, and they'll be looking to their development partners to be more efficient.

Where does usability fit into that? In our experience, it means asking the right kinds of questions of users at the beginning of the process. "What are the products that you want, and what are the features that you need?" and, "Which competitive devices could we benchmark against that are successful and which products have been unsuccessful?" and, "What are the products you're using now, and what are their features and benefits?" The better we are at

See Dubreuil, Page 4

Deals roundup

Covidien in plan to acquire CVI for undisclosed sum

A *Medical Device Daily* Staff Report

Covidien (Dublin, Ireland), a provider of healthcare products, reported a definitive agreement to acquire **CV Ingenuity** (Fremont, California). The companies expect to complete the acquisition in the first calendar quarter of 2013. Financial terms of the transaction were not disclosed.

CV Ingenuity is focused on improving patient outcomes in the treatment of peripheral arterial disease (PAD) by providing solutions to relieve vascular obstructions, inhibit restenosis, and allow natural vessel healing.

The company's core technology, while still in the investigational phase, is a Drug Coated Balloon (DCB) platform with a novel, proprietary, tunable, rapid-release system.

See Deals, Page 5

Washington roundup

Mindray recall followed by FDA warning for monitors

By MARK McCARTY

***Medical Device Daily* Washington Editor**

The last two months of the year are not working out well for everyone, including **Mindray** (Mahwah, New Jersey), which announced a recall of anesthesia systems in mid-November, only to find itself in possession of a Nov. 29 FDA warning letter over the firm's handling of corrective and preventive action for problems with its patient monitoring systems. Among the miscues described in the patient monitors was a software patch intended to update the company logo, but the procedure used to install this patch was blamed for blanking out disclosure and calculator functions. The agency made a point of informing Mindray that a follow-up inspection will be required.

See Washington, Page 6

Don't miss today's MDD Extra: Orthopedics

INSIDE:

Financings roundup

Rotech enters new $25 million credit facility with SilverPoint

A *Medical Device Daily* Staff Report

Rotech Healthcare (Orlando), one of the largest providers of home medical equipment and related products and services, reported that it has entered into a new term loan credit agreement with Silver Point Finance relating to a new term loan credit facility in an aggregate principal amount of $25 million. The company borrowed $23.5 million under the new facility on Dec. 21. The remaining $1.5 million portion of the new facility not yet borrowed may be borrowed on a delayed draw basis on or before Jan. 1, 2014, so long as certain limited conditions as set forth in the credit agreement are satisfied. The facility replaces and repays the company's existing commitments and loans under our prior credit agreement and, assuming the company will borrow the $1.5 million portion of the facility not yet borrowed, increases its available liquidity by about $15 million.

The loans under the new facility will mature on April 30, 2015, at which point the entire principal amount is due. The new credit agreement does not require any amortization payments in respect of the loans. All principal borrowings under the facility participate in a first priority security interest in substantially all of the company's and the subsidiary guarantors' assets with the company's $230 million in aggregate principal amount of 10.75% senior secured notes due Oct. 15, 2015.

"We expect that proceeds from the new credit facility will provide the company with additional flexibility to respond to competitive changes and opportunities in the industry and will support the company's working capital needs as we implement our business plans," said Philip Carter, president/CEO.

Rotech is one of the largest providers of home medical equipment and related products and services in the U.S., with a comprehensive offering of respiratory therapy and durable home medical equipment and related services. The company provides home medical equipment and related products and services principally to older patients with breathing disorders, such as chronic obstructive pulmonary diseases (COPD), which include chronic bronchitis, emphysema, obstructive sleep apnea and other cardiopulmonary disorders. The company provides equipment and services in 49 states through about 420 operating locations located primarily in non-urban markets.

In other financings news:

• **Retractable Technologies** (Little Elm, Texas) reported that its board has declared dividends to holders of its Series I Class B and Series II Class B convertible preferred stock in the amounts of $12,937.50 and $44,675.00, respectively. The dividend amount is $0.125 per share for Series I Class B shareholders and $0.25 per share for Series II Class B shareholders. Dividends have accrued at 10% per annum and cover amounts in arrears from Sept. 30, 2012 through date of conversion or Dec. 31, 2012, whichever is applicable. The dividends will be paid on Jan. 21, 2013 to shareholders of record as of the close of business on Jan. 10, 2013.

Retractable makes VanishPoint and Patient Safe safety medical products. The VanishPoint syringe, blood collection, and IV catheter products are designed to prevent needlestick injuries and product reuse by retracting the needle directly from the patient, effectively reducing exposure to the contaminated needle. Patient Safe syringes are uniquely designed to reduce the risk of bloodstream infections resulting from catheter hub contamination. Retractable's products are distributed by various specialty and general line distributors.

Kips Bay Medical (Minneapolis) along with Manny Villafaña, its founder, chairman/CEO, reported the pricing

See Financings, Page 3

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Court report

Abiomed faces class action lawsuit from securities purchasers

A *Medical Device Daily* Staff Report

The Shuman Law Firm said that a class action lawsuit has been filed in the U.S. District Court for the District of Massachusetts on behalf of purchasers of **Abiomed** (Danvers, Massachusetts) securities between Aug. 5, 2011 and Oct. 31, 2012, inclusive.

The complaint alleges that throughout the Class Period the defendants made materially false and misleading statements regarding the company's business, operations and financial prospects. Specifically, defendants misrepresented and/or failed to disclose that: (1) the company was improperly marketing and/or labeling its Impella 2.5 system; (2) Abiomed's financial results would be materially impacted if the company were either forced to stop or discontinued its improper conduct; (3) the company lacked adequate internal and financial controls; and (4) as a result of the foregoing, the company's statements were materially false and misleading at all relevant times.

On November 1, 2012, prior to the opening of the markets, Abiomed disclosed that the U.S. Attorney's Office for the District of Columbia was conducting an investigation into Abiomed's marketing and labeling of its Impella 2.5 system. As a result of this news, shares of Abiomed declined $6.31 per share, or 31.33%, to close on Nov. 1, 2012 at $13.61, on heavy trading volume.

In other legalities; **Acacia Research** (Newport Beach, California) said that its **Adaptive Sonics** (Frisco, Texas), subsidiary has entered into a settlement agreement with **Cochlear Limited** (Sydney, Australia) and **Cochlear Americas**.

The settlement agreement resolves litigation that was pending in the U.S. District Court for the Eastern District of Texas. ■

Med-Tech Notes

Invacare facility injuntion approved

Invacare (Elyria, Ohio) learned that the U.S. District Court for the Northern District of Ohio, has approved the terms of the previously announced consent decree of injunction with the FDA. The consent decree relates to previously reported inspectional observations at the company's corporate facility and its Taylor Street wheelchair manufacturing facility, both located in Elyria, Ohio.

As the company reported, the decree limits production and design activities at the two Elyria facilities until they are certified to be in compliance with FDA regulations by an independent third-party expert and subsequently approved by the FDA. With certain documentation requirements, the company may continue manufacturing at Taylor Street in cases of existing orders, medical necessity and repair and replacement of products currently in use. All other Invacare facilities remain in full operation.

Invacare manufactures long-term care medical products that promote recovery and active lifestyles.

Financings

Continued from Page 2

of an underwritten public offering of 10 million shares of its common stock for total estimated gross proceeds of $6.5 million. Kips Bay has also granted the underwriters a 45-day option to purchase up to 1.5 million additional shares of common stock. The offering is subject to customary closing conditions and is expected to close on Dec. 27.

The company said it plans to use the net proceeds of this offering to seek regulatory approval to market its eSVS Mesh in the U.S. and abroad, including continuing its human clinical trials for the FDA, to develop and test additional applications of its eSVS Mesh, and for working capital and general corporate purposes.

Sunrise Securities is acting as the sole book-running manager. Aegis Capital is acting as co-manager.

Kips Bay Medical, founded in 2007, is focused on manufacturing its external saphenous vein support technology, or eSVS Mesh for use in coronary artery bypass grafting surgery.

The eSVS Mesh is a nitinol mesh sleeve that, when placed over a saphenous vein graft during CABG surgery, is designed to improve the structural characteristics and long-term performance of the saphenous vein graft. ■

People in the News

▪ **SurModics** (Eden Prairie, Minnesota), a provider of surface modification and *in vitro* diagnostic technologies reported the appointment of Andy LaFrence as the company's VP of Finance and CFO, effective Feb. 12, 2013. He will lead all of the financial activities of SurModics, including controlling, financial planning and analysis, treasury, tax, audit and investor relations. LaFrence will succeed Timothy Arens, who currently serves as interim CFO. Arens will remain with the company and will transition into the role of VP of Corporate Development and Strategy. Most recently, LaFrence served as CFO of CNS Therapeutics, which was recently acquired by Covidien.

Dubreuil

Continued from Page 1

understanding user needs, the more robust and cost-effective our development process is, and this gives us a greater confidence that what we're developing will meet the user's requirements.

So if we do usability well – if we get the right research done and it leads us to creating the right product – then we have a much higher likelihood of giving the user a device they will want to use and meeting our client's business goals.

MDD: Meeting safety requirements always has been an important consideration, but with the FDA's renewed emphasis on that, where does it rank in the product development spectrum? I imagine it's fairly close to the top?

Dubreuil: Meeting safety requirements has to be close to the top when you're doing medical device development. We are all required to address risk analysis and safety, because that's our part of the equation. We can contribute to efficacy, but our job is to make sure that products are safe and they meet the user requirements. So safety plays a critical role in what we do, particularly now, with IEC 62366, Medical Devices – Application of Usability Engineering To Medical Devices, which states that you must address usability engineering and user requirements. We have to comply with this regulation. We have to show the process as well as the results that indicate we have addressed the user requirements and met the users' needs.

MDD: To go back to the new normal in healthcare, "outcomes" are part of the mantra moving forward. Does the ability to measure outcomes have to be built into product design, or is that something that can be handled separately?

Dubreuil: No, the ability to measure outcomes must be built in to the development process. We have to know how each product differs from prior or existing products in terms of those outcomes, how they're going to be measured, and those elements must become a part of the product specifications.

The product must meet whatever the performance criteria is – it has to be twice as fast, or twice as light, or be able to withstand higher temperatures or new sterilization methods. Our team must know those things going into the development process so that we can test those criteria in the verification and validation stages and present that data to payers to assure that they're going to recognize the value of the product.

In talking with some of our European partners, we've determined that designing to outcomes is an extremely critical path to CE marking and approval across the European Union – even more so than with FDA – although the expectation is that it will translate to wider application within that agency as well.

MDD: How prevalent is the use of virtual prototyping and other assessment/simulation practices as tools in product design?

MARC DUBREUIL
Cultivates Medical Products

Dubreuil: If we just look at the dollar revenue against everything that we bill for today, it's a relatively small percentage. But it's a key tool in doing things like computational flow and finite element analysis. It's a critical component for reducing costs, reducing time and reducing risk.

For example, our team just did a design review yesterday for a new orthopedic product, and even in the conceptual phase, they were able to do a quick finite element analysis with the CAD file to determine that the materials they were looking to use would not meet the yield forces that the application would demand. So using these simulation tools allowed the team to be able to reliably make a critical choice in the concept stage, rather than getting to the concept stage and saying, "Yeah, that's a really nice idea, let's refine it and prototype it and test it." We now can effectively test an idea very early in the development process with far less effort and cost than in the past.

The use of these techniques is somewhat isolated at this point, but it's become a critical part of our product development process to know where we can apply them and when. If we can apply these tools early enough, we get great feedback which helps lead us in the right direction.

In another example, we've been working diligently on an orthopedic application where we've been doing analysis on the user's walking gait and the performance of the product as it is being worn. We discovered a clever way to combine inexpensive, off-the-shelf software and optical technology into an analysis tool that's provided us some very valuable feedback, giving us an extremely helpful and very cost-effective method of verifying a design prior to moving into large-scale CAD engineering, prototyping and tool-making.

MDD: It seems like optimization of existing products as they move to second-generation form is another area getting attention. What's involved there?

Dubreuil: Some of what's driving that is that OEMs are reluctant to go back through an FDA submittal and taking a risk that the agency may require PMA-type results versus 510(k) results. The FDA has become much more diligent in

See Dubreuil, Page 7

Deals

Continued from Page 1

"We continue to be focused on technologies that deliver improved patient care, delighting both our physician and hospital system customers," said Stacy Enxing Seng, president, vascular therapies, Covidien. "CV Ingenuity offers a robust DCB portfolio, and offering a DCB technology is something that we believe is necessary to continue to improve care for patients suffering from PAD, as well as ensuring we are a full line partner with our customers today and into the future."

As a result of this transaction, Covidien expects to increase research and development expenditures for the next several years to fund the clinical development of CV Ingenuity technologies. Additional expenditures are expected to be more than $20 million in the second half of fiscal 2013 and more than $30 million in fiscal 2014.

Despite these additional expenditures and the negative impact on selling, general and administrative expenses from the transaction, Covidien is reaffirming all of its prior guidance ranges, which were last updated on Nov. 9, 2012. Also, Covidien does not anticipate receiving FDA approval for a DCB product using the CV Ingenuity technology until fiscal 2017.

In other dealmaking activity:

• **National Health Investors** (Murfreesboro, Tennessee) reported a $20.2 million purchase of Charleston House, a 120-unit assisted living and memory care facility in Beaver Dam, Wisconsin. Charleston House will be leased to Landmark Senior Living Communities for an initial term of 15 years with renewal options, at a lease rate of 7.75% plus annual fixed escalators. The purchase was funded from borrowings on NHI's revolving credit facility.

"This acquisition is illustrative of NHI's commitment to growing our private-pay assisted living portfolio through creating valuable relationships with experienced operators," said Justin Hutchens, NHI's president/CEO.

• **McKesson** (San Francisco), a healthcare services and information technology company, said that it has received notification of early termination of the antitrust waiting period in connection with the proposed acquisition of **PSS World Medical** (Jacksonville, Florida).

The termination of this waiting period satisfies one of the conditions for McKesson's proposed acquisition of PSS World Medical.

The transaction remains subject to other customary closing conditions, including approval by the shareholders of PSS. Subject to satisfaction of these other closing conditions, the acquisition is expected to close in the first calendar quarter of 2013.

As previously reported on Oct. 25, 2012, McKesson and PSS World Medical signed a definitive agreement under which McKesson will acquire all outstanding shares of PSS for $29 per share in cash or $1.4 billion (*Medical Device Daily*, Oct 26, 2012).

• **WellPoint** (Indianapolis) reported the completion of its acquisition of **Amerigroup** (Virginia Beach, Virginia), a managed care company that is focused on meeting the healthcare needs of financially vulnerable Americans.

"The acquisition advances our ability to more effectively and efficiently serve the growing Medicaid population, including the expanding dual eligible, seniors and persons with disabilities, and long-term services and support markets," said John Cannon, WellPoint's Interim president/CEO. "By leveraging our combined clinical capabilities, resources and expertise, WellPoint's competitive position in the Dual Eligible and Medicaid markets will be enhanced and will help create more value for state governments and their program beneficiaries."

With Amerigroup, WellPoint's affiliated Medicaid health plans now serve about 4.5 million beneficiaries of state sponsored health care programs in 20 states, bringing the company's total medical enrollment to approximately 36 million members in all affiliated plans. WellPoint also now has a presence in several states with significant dual eligible managed care opportunities.

Amerigroup will operate as a wholly owned subsidiary within WellPoint and will remain dedicated to effectively managing state sponsored programs and further expanding this business. Amerigroup's management team will lead the combined Medicaid businesses.

• **Becton, Dickinson and Company** (BD; Franklin Lakes New Jersey), a medical technology company, said it has completed its acquisition of **Safety Syringes** (Carlsbad, California), a company that specializes in the development of anti-needlestick devices for prefilled syringes. The financial terms were not disclosed.

The acquisition broadens BD's healthcare worker safety offering to include passive safety technologies for any prefillable syringe customer.

"We believe the Safety Syringes product line is a valuable asset to BD and aligns well with our focus on healthcare worker safety, and offering higher-value products," said Claude Dartiguelongue, President, BD Medical - Pharmaceutical Systems. "We are excited about this acquisition, which expands the Company's presence in safety technologies and further demonstrates BD's commitment to developing innovative solutions that help address our customers' unmet needs. We are pleased to welcome this new product portfolio and these new associates to BD."

BD expects the transaction to be minimally dilutive for fiscal year 2013, and does not expect it to impact BD's previously communicated 2013 earnings guidance.

• **Amarantus BioScience** (Sunnyvale, California), a biotechnology company developing treatments and diagnostics for diseases associated with neurodegeneration and apoptosis, said it has purchased all of the intellectual

See Deals Page 7

Washington

Continued from Page 1

Mindray announced a voluntary recall for its A3/A5 anesthesia delivery system because of the possibility of system leakage triggered by improper seating of the gasket used to seal the CO2 canister to the system (*Medical Device Daily*, Nov. 15, 2012). FDA's Nov. 30 statement indicated this was a class I recall, but Mindray's Nov. 14 statement on the matter indicated the fix was relatively simple. The company said the canisters in question exhibited a small step in the surface – presumably at the interface between the canister and the body of the system – and that the problem could be addressed by unlocking and re-locking the canister. However, a system check would have to be invoked upon this refitting procedure.

The warning letter does not address the anesthesia canisters, focusing instead on the firm's production of patient monitoring systems, chemistry analyzers and ultrasound systems at the firm's plant in Mahwah. However, Mindray may have fallen prey to contract manufacturing issues, a persistent feature in warning letters.

According to FDA, the June-August inspection disclosed that Mindray had "not completed any corrective or preventive actions and had not evaluated the effectiveness of [the firm's] supplier's corrective actions" in connection with the replacement of 17 touchscreens used in Mindray's V series monitors between November 2011 and June 2012.

FDA also alleged that Mindray had distributed more than 100 units of the DPM 6 and Beneview T5 patient monitors with cracked bezels, a problem the supplier is said to have chalked up to the materials used to manufacture the front of the monitor housing. The warning letter states that Mindray had not "completed any corrective or preventive actions for this issue."

The agency says it was unimpressed with Mindray's proposed correction for these and four other issues because while the company indicated it would "implement appropriate corrective actions based on root causes" and "conduct risk analysis, where appropriate," Mindray had not provided "this data for [the agency's] review."

The warning letter states that Mindray's procedures for complaint handling did not mandate an investigation into complaints "involving possible failure of a device," and said that Mindray had not investigated problems with a software upgrade for multi-gas modules associated with the firm's DPM 6 and Beneview T5 Monitor. A similar lapse was said to have taken place with regard to a cooling fan and motor pump with one of the firm's Spectrum series of monitors.

The company's response to this finding was deemed inadequate because of a lack of details regarding the investigation into the gas module issue, and because Mindray did not include details on a recommended update to the label for the Spectrum monitor.

Mindray had better luck in its response to the citation dealing with a lack of requirements for investigations into non-conforming products. According to FDA, the company had updated its procedures with "specific criteria for initiating an investigation of nonconforming product," a fix the agency said it would verify in a subsequent inspection.

The citation dealing with the software intended to upgrade the company logo on displays states that the firm's procedures offered "no assurance that a design transfer procedure has been adequately established" for DPM 6/7 monitors to ensure proper software function following upgrades or device reconfiguration. Mindray proposed to draft a design transfer protocol "for each product" identifying and validating performance requirements as well as a validation of "all active manufacturing procedures using the design transfer protocol." FDA asked for updated information as these efforts are completed.

Mindray did not respond to contacts for comment.

Foster bids CMS adieu

The Office of the Actuary at CMS has found itself dragged into a few contentious issues over the past decade, but Rick Foster, the agency's actuary in chief, is said to have called it quits.

The Centers for Medicare & Medicaid Services did not respond to a query by *Medical Device Daily* on the development, but a Dec. 24 story in *Congressional Quarterly* says that Foster will retire at the end of January 2013 after 40 years in government, 18 of which were at the actuary office at CMS.

Foster was threatened by former CMS administrator Thomas Scully with termination of his employment at CMS if Foster shared data regarding cost estimates of the Medicare prescription drug program with Congress, according to a Sept. 7, 2004, report by the Government Accountability Office. More recently, Foster delved into the data behind the Affordable Care Act and said supporters of reform were double counting the purported savings from healthcare reform to pay for both an extension of the Medicare Part A trust fund and premium assistance for those who will enroll in the state health insurance exchanges in 2014 (*Medical Device Daily*, Sept. 10, 2010).

Foster recently began to hand off the task of presenting some public data to his staff at the Office of the Actuary, including the latest estimate of national health expenditures. CMS's Ann Martin presented the most recent NHE data for the agency at the **National Press Club** (*MDD*, Jan. 10, 2012). It is not clear whether this was a management decision based on employee development or an attempt by Foster to remove himself from the limelight.

According to the *CQ* story, CMS will engage in a national recruitment for his replacement, but nonetheless expects to hire a replacement "within a couple of weeks." ■

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Dubreuil

Continued from Page 4

its reviews. They're requiring more clinical data, and they're saying that there are products that had been approved under the 510(k) process that will not be approved under a 510(k) in the future, and that predicate-device applications will be much more challenging to get approval for, if at all. So it's natural to turn to second-generation products, because they can more likely be approved with 510(k) submissions and the development process may be shorter and less expensive based on simple iterations of the existing design.

As developers, our challenge is to identify what we could do that would improve both the product and the usability, because that's always a big factor given that prior products may not have been designed and developed under best usability practices. To create some differentiation from the prior product and competitors' products we can address usability as well as find components that are going to be lower cost, more robust, more reliable and compliant, and allow the OEM to maintain their presence in the market for the next five to 10 years without having to go through an entire development process. So we're seeing a lot of interest in second-generation products.

MDD: The corollary to buffing up second-generation products is to utilize new technology to create differentiation in the marketplace, particularly in the form of joining the digital generation. Are you finding that to be the case?

Dubreuil: Yes, particularly because medical devices have long product lives; they're typically in the marketplace for 10 years or more. So there are a lot of products that are reaching obsolescence in terms of their technologies, particularly in terms of electronic technologies, a lot of which are not meeting ISO 60601 third edition requirements. So there's a big opportunity to advance these technologies and meet 60601 with a newer product.

There's a place for these upgraded products, although there may not be as big an opportunity in the marketplace as there is for new and innovative products that are using really revolutionary core technologies.

The other technology trend we're seeing is a greater interest in developing remotely controlled electromechanical devices, such as those used in catheterization. We see this as an evolution of value creation and the need for more precise control over the movement of a mechanical device than a human can deliver.

In the area of medical robotics, where Farm has done a lot of work, it's easy to look at a 10-year-old technology and be shocked by the advancement in motors and controllers. But it's also easy to imagine a larger-scale integration of robotic systems into medical products, assuming we can meet all of the strict requirements around patient and operator safety. ■

Deals

Continued from Page 5

property (IP) assets from **Power3 Medical Products** (The Woodlands, Texas). Power3 was in bankruptcy, giving Amarantus the ability to acquire all of Power3's IP for the diagnosis of multiple neurodegenerative diseases and oncology for $40,000.

As part of the transaction, Amarantus took ownership of 20 pending patent applications covering a variety of biomarkers and assays related to the treatment of various diseases including Parkinson's, Alzheimer's, and ALS, as well as patent applications related to breast cancer, neuromuscular disease and chronic myelogenous leukemia (CML). The company also acquired all of the data generated by Power3 while creating its IP portfolio. All of the disease states covered by the intellectual property acquired from Power3 are related to programmed cell death.

• **Humana** (Louisville, Kentucky), said that it has completed its acquisition of **Metropolitan Health Networks** (Boca Raton, Florida) in a transaction valued at about $850 million plus transaction costs. Metropolitan is a Medical Services Organization that provides and coordinates medical care for approximately 87,500 Medicare Advantage, Medicaid, and other beneficiaries, primarily in Florida utilizing a primary care-centric business model. Metropolitan's integrated care delivery systems include approximately 35 state-of-the-art primary care medical centers and a robust network of affiliated physicians serving mainly Humana members.

In connection with the closing of this transaction, Metropolitan stockholders will receive $11.25 per share in cash from Humana for each Metropolitan share held. Humana will also repay all of Metropolitan's outstanding debt.

Humana has financed the transaction primarily through the recent issuance of senior notes. The company continues to anticipate the transaction to be modestly accretive to its earnings for the year ending Dec. 31, 2013. Humana expects to update its earnings guidance for FY13 to reflect the closing of the Metropolitan acquisition in conjunction with its 4Q12 earnings release on Feb. 4, 2013. ■

Grants roundup

Maricopa Medical receives grant for DTT ditto device

A *Medical Device Daily* staff report

Keeping a child comfortable and un-distressed during medical procedures is a difficult feat, but **Maricopa Medical Center** (Phoenix) will now have one of the latest technologies for keeping kids smiling while undergoing very painful procedures to help burns heal. The Dec. 24 announcement by device distributor **Avnet** (New York) says that the Arizona Burn Center, located at Maricopa Medical, is the recipient of the Avnet grant for the ditto device, manufactured by **Diversionary Therapy Technologies** (DTT; New York), which will find a home at the burn clinic.

The ditto is described as incorporating "the latest research that using distraction and educational techniques simultaneously lowers stress and anxiety prior to or during a procedure," and the system, which features a display and input devices, "draws upon augmented reality, a multi-modal sensory-based distraction medium that combines technology and therapy," the statement indicates. The ditto's interactive touch screen, colorful marker keys and automatic response to physical movement allows the device to engage patients sufficiently to averting the patient's attention from what is sure to be a negative experience.

The statement explains that the ditto "looks a lot like a traditional video game console and includes a variety of interactive games, stories and procedural preparation tools." The ditto, a handheld, waterproof device, is backed by several clinical trials that indicate the device can "reduce stress and anxiety, lower treatment times, and improve patient outcomes."

Ruth Rimmer, PhD, a developmental psychologist at the Arizona Burn Center, said the ditto will help doctors as well because the unit "not only help[s] to improve the child's long-term outcome but [is] helpful to clinicians so they can best perform a procedure."

DTT is not sitting still where the device's future development is concerned. The staement indicates that healthcare providers, play specialists, and animation teams collaborated to develop the ditto over six years and subjected the device "to more than eight independent clinical trials that have demonstrated its effectiveness." However, DTT is said to be working on new procedures, games and stories to be added regularly to the device's library as DTT "continues to work with experts to establish fresh content."

CPRIT grants to hold, new hires announced

The **Cancer Prevention Research Institute of Texas** (Austin, Texas) has found itself in the crosshairs in the Lone Star State due to allegations of mismanagement of the agency's resources, which routinely hit hundreds of millions of dollars a year in cancer research grants. A Dec. 19 statement by CPRIT indicates that Texas Governor Rick Perry (R-Texas) has urged the agency to suspend further grant-making, but CPRIT has also announced two new hires for the agency's management team, a move intended to allay some of the concerns expressed by lawmakers in the state.

A Dec. 19 statement at the CPRIT website, titled "Message from CPRIT Leadership," noted that Perry and a member of the legislature sent a letter to the CPRIT oversight committee asserting it is "vital that CPRIT fully address the concerns that have been raised about its process and operations prior to future grants being awarded." The letter from Perry and others adds that among the expectations is that CPRIT cooperate "fully with current reviews" and implement governance reforms to ensure that grant applications are properly processed. The letter also states that CPRIT must fill "key management and peer-review positions."

The Dec. 19 response to the letter, signed by oversight committee chairman Jimmy Mansour and vice chairman Joseph Bailes, MD, said the committee "agrees with and endorses the call . . . for a moratorium on CPRIT grants until concerns about the agency are addressed." The statement adds, "these issues need to be resolved to restore public confidence in CPRIT," but assures that the development "will not affect currently funded grants."

CPRIT says in a Dec. 21 statement, however, that it has selected two to fill a couple of vacancies at the agency. The announcement names Wayne Roberts as interim executive director, a job he will hold until a permanent hire can be made. CPRIT's Mansour is said to have also reported that a former state deputy comptroller, Billy Hamilton, "has agreed to serve as a senior advisor to the CPRIT executive director and CPRIT oversight committee."

Mansour said he was "excited about the appointment of our new interim executive director," noting that Roberts "has strong leadership capabilities as well as a background and experience in state government that will be invaluable to the institute as we move forward." Roberts' experience includes service as the associate vice president for public policy at the **University of Texas Health Science Center** (Houston) from November 2008 onward. He is also said to be a member of the state pension review board and sports extensive experience in public finance and budget, "especially with respect to public higher education," the statement explains.

Hamilton is described as a consultant specializing in taxes, fiscal policy and "related issues," but he also served as the chief deputy controller of public accounts in Texas prior to January 2007.

Mansour said restoring public confidence in CPRIT "is critical, and I believe having two recognized leaders like Wayne and Billy assuming leadership roles will go a long way toward improving the institute's management and restoring confidence in its operations." ■

MDD's Ortho Extra

Additional Developments in One of Med-Tech's Key Sectors

Thursday, December 27, 2012

Keeping you up to date on recent developments in orthopedics

Myopathy in chronic alcoholism and vitamin D deficiency . . . Myopathy refers to a muscular disease in which muscle fibers do not function, resulting in muscular weakness and wasting. Vitamin D deficiency is a well-recognized cause of myopathy, and excessive drinking is often associated with low or subnormal levels of vitamin D. A review of studies of the relationship between alcohol-related myopathy and vitamin D deficiency indicates that vitamin D deficiency might partly explain the occurrence of the frequently observed myopathy in chronic alcoholism. Results will be published in a special online issue of A*lcoholism: Clinical & Experimental Research* and are currently available at Early View. "Myopathy simply means 'muscle disease,'" said Jan Wijnia, a researcher at **Slingedael Korsakoff Center** (Rotterdam, the Netherlands) as well as corresponding author for the study. "Muscle weakness is by far the most frequent symptom of alcoholic myopathy, causing difficulties in rising from a chair or in climbing a staircase. In alcoholic myopathy, improvement of muscle weakness usually occurs six to nine months following alcohol abstinence. "It seems that 40 to 60 percent of alcoholics suffer from alcohol-related myopathy," said Frits A. J. Muskiet, a professor of pathophysiology and clinical chemical analysis at the University Medical Center Groningen. "Many subjects with chronic alcoholism have low vitamin D, which prompted the authors to raise the question whether the well-known muscle weakness might be caused by vitamin D deficiency. The answer is that indeed the symptoms of myopathy in alcoholism and vitamin D deficiency are very similar, but since these symptoms are rather aspecific, this is no more than an association, which is obviously not the same as a proven cause-and-effect relation. There are similarities, but also differences." Study authors reviewed articles on alcoholic myopathy and hypovitaminosis D myopathy (n=93) that were listed on PubMed from January 1985 through to September 2011. They analyzed and compared the pathophysiological findings in order to designate or "chart" possible pathways of vitamin D action in the development of alcohol-related myopathy. "Our review links possible interdependent deficiencies of vitamin D, phosphate, and magnesium with muscle weakness in chronic alcoholism," said Wijnia. "Previous studies had suggested that changes in alcoholic muscle disease were not due to dietary deficiencies, but our review is one of the few to examine the effects of severe vitamin D deficiency in alcoholic myopathy." Muskiet agreed. "They have reviewed the literature to show to us that vitamin D deficiency might - at least in part - explain the occurrence of the frequently observed myopathy in chronic alcoholism," he said. "The paper is important because of this connection, but the real proof of the pudding should now be provided by doing research trials." "The causes of vitamin D deficiencies in alcoholics may include liver dysfunction, lack of sun exposure, malabsorption, and inadequate dietary intake," added Wijnia. "It is well known that chronic alcoholism causes people to have abnormal diets that, in their turn, may cause many mineral and vitamin deficiencies," noted Muskiet. "Alcohol has a high caloric value. The combination of poor appetite and possibly less money to spend on good-quality food contributes to eating a poor diet. Thus, the situation in chronic alcoholism is much more complicated than vitamin D deficiency, which in otherwise healthy people is usually due to insufficient exposure to sunlight." "We recommend future research focusing on possible beneficial effects of vitamin D supplementation and on optimal dosages," said Wijnia. "It is possible that Vitamin D supplementation may assist in prevention and treatment of alcohol-related chronic myopathy, thus, assessment of vitamin D status may help clinicians to early diagnose severe vitamin D deficiency and hence offer appropriate treatment. Further research is needed to determine if this can improve muscle function if alcohol consumption ceases, and what dosages of vitamin D may be optimal." "Diet is more than some assembly of nutrients," said Muskiet. "It is the balance that counts. We need to first correct poor diets and widespread vitamin D deficiency in the general population. For this, medical doctors might have to become educated in nutrition and lifestyle in general. But this is of course not only their responsibility. There is good evidence that 90 percent of Type 2 diabetes, 80 percent of coronary heart disease, and 70 percent of colon cancer and stroke can be prevented if people pay more attention to their weight, physical activity, excessive alcohol drinking, smoking, vegetables/fruits, etc. A small daily amount of alcohol keeps the doctor away. With no alcohol and especially with too much alcohol

there is higher chance of many diseases, including all cause mortality, cardiovascular disease, stroke, cancer, etc. Again, it is a matter of balance."

Bone loss decreased in postmenopausal women with increased calcium intake following community-based nutrition education . . . At the **International Osteoporosis Foundation**'s (Nyon, Switzerland) Asia-Pacific Osteoporosis Meeting, researchers from the National Institute of Nutrition in Hanoi presented a new research study that showed the benefits of educational intervention in increasing calcium intake and retarding bone loss in postmenopausal women. Researchers carried out a controlled trial in the Red River Delta in Vietnam involving a total of 140 women. The women, aged 55 years, had been postmenopausal for at least 5 years, and had low dietary calcium intake (less than 400 mg/day). An intervention group was given nutrition education counselling over 18 months to improve calcium intake. After 18 months, the women in the intervention group had increased their calcium intake significantly. Testing showed that the intervention group's bone mass had remained stable. In comparison, the bone mass of the control group which had not received nutrition education, had decreased by 0.5 % ($p<0.01$). The PTH (parathyroid hormone) values in the intervention group decreased by 12 % ($p<0.01$) whereas in the controls, PTH increased by 32 % ($p<0.001$). In many Asian countries, levels of dietary calcium and vitamin D in the general population have been shown to be below FAO/WHO recommended levels of calcium intake. For pre-menopausal women and men under age 65 the recommended levels are 1000 mg/day and for postmenopausal women and men over age 65 the recommendations are for 1300 mg/day. This study suggests that community-based education programmes to improve intake of dietary calcium could make a difference to bone health and fracture prevention in the postmenopausal population. In Asia, with its growing population of seniors, such interventions could translate into significant health-economic benefits.

In animal model, new hormone therapy shows promise for menopausal symptoms . . . Investigators at **Wake Forest Baptist Medical Center** (Winston-Salem, North Carolina) have concluded research on a new postmenopausal hormone therapy that shows promise as an effective treatment for menopausal symptoms and the prevention of osteoporosis without increasing the risk for heart disease or breast cancer. Traditional forms of hormone therapy (HT) provide the benefits of symptom relief, prevention of osteoporosis and prevention of atherosclerosis, but increase the risk of uterine cancer (with estrogens alone) or breast cancer (with combined estrogens and progestins). Thus, the risk-benefit ratio of traditional HT is not ideal. Less potent plant-derived estrogens are relatively safe, but less effective. Selective estrogen receptor modulators (SERMs) provide both beneficial effects and adverse effects, but the ideal treatment has proven elusive, said J. Mark Cline, PhD, one of the co-authors. The Wake Forest Baptist team worked in partnership with the pharmaceutical company Pfizer to explore a new strategy, termed a Tissue Selective Estrogen Combination (TSEC). Using this strategy, a conventional estrogen (CEE) was combined with a bone-protective SERM-like drug, bazedoxifene acetate (BZA), to produce a complementary pattern of tissue effects that maximize the benefits of HT while avoiding the risk. The study involved a 20-month randomized, parallel-arm trial - which has a comparison group and at least one new or active therapy group - in postmenopausal nonhuman primates, designed to determine the effect of TSEC treatment on the breast, uterus and cardiovascular system. The TSEC strategy has been evaluated in the Selective estrogens, Menopause, And Response to Therapy (SMART) Phase 3 trials involving more than 6,000 women. Cline said the Wake Forest Baptist nonhuman primate trials are important because they can address tissue responses directly, whereas studies in women use clinical outcomes that may require many years to provide conclusive results. The Wake Forest Baptist findings are discussed in separate papers, both published recently in *Menopause*. Prior work by Cline in the 1990s demonstrated the adverse effect of a widely used estrogens and estrogen-progestin combination on the breast, a finding that was predictive of the breast cancer patterns later found in the Women's Health Initiative. In contrast to that finding, the TSEC strategy is anticipated to reduce breast cancer risk. "Remarkably, BZA overrides the adverse effects of CEE at the level of gene expression in the breast, suppressing abnormal tissue growth," Cline said. Lead investigator Thomas Clarkson is hopeful about the promise of this new approach. "The findings are encouraging for postmenopausal women," he said. "We believe that women can be given CEE along with BZA to protect against breast cancer and uterine cancer, without adversely affecting the cardiovascular system, but more research is necessary."

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