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PAGE 1 OF 8

Financings Roundup

Start-Up Ascleitis Taps Chinese Investors for \$100M Series A

By Jennifer Boggs
Assistant Managing Editor

Formed earlier this year to marry U.S. innovation and Chinese capital, start-up Ascleitis Inc. pulled in a whopping \$100 million in committed Series A funding, with the first \$50 million tranche expected to support its dual operation strategy for about five years.

The round was led by Hangzhou Binjiang Investment Holding Co. Ltd., a holding company of Chinese real estate billionaire Jinxing Qi, with investments from other private entrepreneurs in China, the U.S. and other countries. Money also came from co-founder, president and CEO Jinzi J. Wu, who left his position as vice president of global HIV drug discovery at GlaxoSmithKline plc Feb. 1 to start Ascleitis.

Ideas for the start-up had been brewing since last summer, when Wu was vacationing in China and met up with

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Steps Taken to Replace Board

Valeant Puts its \$5.7B Offer to Cephalon's Stockholders

By Catherine Shaffer
BioWorld Today Contributing Writer

As threatened last week, Valeant Pharmaceuticals International Inc. is moving to replace Cephalon Inc.'s board of directors following a rejection of its \$5.7 billion hostile takeover bid. And the big pharma isn't taking "no" as a final answer: It's putting the question to Cephalon stockholders.

Valeant, based in Mississauga, Ontario, has filed a preliminary consent solicitation statement with the SEC to remove each member of Frazer, Pa.-based Cephalon's current board of directors, to replace them with seven new directors that Valeant has already recruited.

If Cephalon's stockholders accept Valeant's proposal, the new board would "remove the impediments to a tender offer," allowing Valeant to carry out due diligence. Valeant

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Another Health Food Claim Bites the Dust

Choline Metabolites From Gut Microbes Increase Heart Risk

By Anette Breindl
Science Editor

In a study published this week, researchers from the Cleveland Clinic's Lerner Research Institute have discovered a strong new risk factor – the gut flora – for developing atherosclerotic heart disease and risk for heart attack, stroke and death.

Starting from choline, the gut flora produces a metabolite that contributes to development of heart disease, and so, the authors have also identified yet another role for gut bacteria, which have taken center stage recently for their involvement in everything from metabolic to infectious disease. (See *BioWorld Today*, March 22, 2011.)

Like everything else, heart disease and stroke are caused by a combination of genetic and environmental factors. Collectively, Stanley Hazen told *BioWorld Today*, the

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Don't Wait on FDA for Social Media Guidance

By Mari Serebrov
Washington Editor

WASHINGTON – Everybody's doing it, even the FDA. Using social media, that is.

But the online community can be hostile territory for biopharma as the FDA has provided little guidance on where drugmakers can go and what they can do in this 21st century neighborhood.

While the agency is making its presence known – through a YouTube channel, Twitter accounts, a Facebook page and co-sponsored websites – it's made it clear in a number of enforcement actions that biopharma shouldn't get too social. However, it has yet to define the boundaries.

After holding a public meeting on the subject in 2009, the FDA said it would release guidance by the end of 2010. Then it was by the end of March. Now the FDA isn't saying when industry can expect the long-promised

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Other News To Note

- **BioTime Inc.**, of Alameda, Calif., and **XenneX Inc.**, of Cambridge, Mass., collaborated to form LifeMap Sciences Inc. to develop and commercialize a database of the cell lineages branching from embryonic stem cells and their molecular markers. LifeMap plans to make certain aspects of the database available for use by stem cell researchers at pharmaceutical and biotechnology companies and other institutions through paid subscriptions or on a fee-per-use basis. The database will permit users to follow the development of embryonic stem cell lines to the purified progenitor cell lines created by BioTime using its ACTCellerate technology.

- **BioWa Inc.**, of Princeton, N.J., and **Oxford BioTherapeutics Ltd.**, of Oxford, UK, entered into a license agreement to provide OBT with access to BioWa's patented Potelligent Technology platform for the development of antibody-dependent cellular cytotoxicity (ADCC) enhanced antibodies. OBT intends to use it to develop, manufacture and commercialize selected ADCC programs from its pipeline of preclinical antibodies for oncology. Terms of the deal were not disclosed.

- The Briscoe Law Firm and the securities litigation law firm of Powers Taylor LLP are investigating potential legal claims against the board of directors of **Inspire Pharmaceuticals Inc.** related to the proposed \$430 million buyout of Inspire by **Merck & Co. Inc.** The firms are investigating the fairness of the proposed transaction to Inspire shareholders and whether its board of directors acted in the shareholders' best interests. (See *BioWorld Today*, April 6, 2011.)

- **Lupin Ltd.**, of Mumbai, India, granted **Salix Pharmaceuticals Ltd.**, of Raleigh, N.C., exclusive global rights outside India for the use of technology developed by Lupin or jointly developed by Lupin and Salix for rifaximin, a gut-selective antibiotic with negligible systemic absorption and broad-spectrum activity in vitro

Stock Movers

04/06/11

Company	Stock	Change
NASDAQ Biotechnology	+\$1.04	+0.10%
Curis Inc.	+\$0.53	+14.36%
Cardiome Pharma Corp.	+\$0.40	+9.76%
Lorus Therapeutics Inc.	+\$0.13	+17.11%
Micromet Inc.	+\$0.54	+10.23%
Myrex Inc.	+\$0.42	+10.91%

(Biotechs showing significant stock changes Wednesday)

Corrections & Clarifications

A clinic item in the April 6, 2011 issue of *BioWorld Today* should have listed Neurotech Pharmaceuticals Inc.'s location as Lincoln, R.I.

Editor's note: The correction has been made in BioWorld Online.

against Gram-positive and Gram-negative pathogens. The agreement expands the collaboration that Salix and Lupin entered in September 2009. Salix will make a \$10 million up-front payment to Lupin along with potential milestone and royalty payments.

- **Medicago Inc.**, of Quebec City, entered a research collaboration with an unnamed global pharmaceutical company to develop a non-influenza vaccine candidate. Medicago will apply its transient expression system to develop a vaccine candidate for the undisclosed target.

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Financings Roundup

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Qi, a long-time friend. "He was in real estate and I was in biotech, so we had never talked business before," Wu said.

But China has become a much-sought-after source of capital, particularly for the cash-strapped global biotech industry. The country has a "lot of cash from real estate and IT, and entrepreneurs are looking for their next investment opportunities," he told *BioWorld Today*.

A few other biotechs have looked East for funding opportunities. Lead Therapeutics Inc., for instance, snagged Chinese venture capital firm Mustang Ventures for its \$17 million Series A round in 2007. The San Bruno, Calif.-based firm was bought out by neighboring BioMarin Pharmaceutical Inc. in a potential \$100 million deal last year. (See *BioWorld Today*, Nov. 6, 2007.)

And 2009 start-up Western States Biopharmaceuticals Inc. found itself looking in China for capital to advance its adaptive immune system modulating compound. The Aurora, Colo.-based firm has since opened a lab in Beijing. (See *BioWorld Today*, July 23, 2010.)

Still, it's been tough for companies outside of China to reach into the Chinese market. A large part of the barrier is cultural, as Chinese investors tend to be suspicious of outsiders. "Trust is important," Wu said. "So is sharing vision and sharing values." Chinese investors also look for firms that have expertise and experience working in the Chinese market.

Wu's friendship with Qi provided a foot in the door. But Qi is more than simply an investor. "He's also a co-founder," Wu said. "He did a lot of due diligence. He liked the team and he liked the strategy."

Asclepis – named after Asclepius, the Greek god of medicine – is taking a two-pronged business approach. The first is aimed at bringing late-stage and commercial programs into the Chinese market, a plan that is expected to bring in near-term revenue. "I'm hopeful we can break even in the next five years," Wu said.

Right now, Asclepis is seeking products for its pipeline – Phase IIb assets and later – looking primarily for oncology candidates to target unmet needs in China such as liver, lung and stomach cancers, as well as candidates for infectious diseases such as drug-resistance tuberculosis, which is "a big issue both in China and globally," he said.

The second part of the business will focus on discovering and developing drugs in the areas of oncology and infectious diseases. Asclepis anticipates advancing those programs through clinical proof-of-concept and then finding a big pharma partner to handle late-stage work and worldwide commercialization. That part of the business should provide the long-term value creation, Wu added.

Asclepis has about eight employees, but Wu expects to have about 50 scientists on board by the end of the first year, and as many as 100 at two years, with the majority to be based in the firm's China headquarters in Hangzhou and

the rest at its facility in Research Triangle Park, N.C. Still, most of the funds from the firm's lucrative Series A will be focused on R&D rather than on infrastructure, he said.

The second \$50 million tranche from the round will kick in as needed. There's no concrete timeline, nor are those funds associated with a specific milestone. And, if all goes according to plan, the firm won't need the money for at least a few years.

Wu described U.S. innovation and Chinese capital as "winning combination," and said he hopes Asclepis' story could signal a positive trend. "I'd like to see more joint ventures happen," he added, "because we do need money in biotech."

In other financings news:

- **Arrowhead Research Corp.**, of Pasadena, Calif., said its majority owned subsidiary, Ablaris Therapeutics Inc., completed a second closing of its Series A financing for gross proceeds of \$1.2 million, bringing the total to \$2.9 million to date. Arrowhead has invested \$1.3 million and holds a 64 percent stake in the obesity company. Proceeds will go toward up-front licensing payments and expenses associated with preparation for a Phase I trial, expected to start in the second half of this year. Ablaris' technology, which was developed at the University of Texas MD Anderson Cancer Center, consists of a series of peptide conjugates designed to specifically target and kill the blood vessels that feed white fat tissue.

- **PolyMedix Inc.**, of Radnor, Pa., priced a \$20 million underwritten offering of 25 million units – each unit comprising one share of common stock and one warrant to purchase one-half of a share – at 80 cents apiece. Net proceeds are expected to total about \$18.6 million. Underwriters Cowen and Co. LLC, Rodman & Renshaw LLC, Roth Capital Partners LLC and Noble Financial Capital Markets have an option to purchase an additional 3.75 million units at the offering price, which would bring in an additional \$3 million. Proceeds primarily will be used to support clinical development of PolyMedix' two lead drugs: PMX-30063, an antibiotic, and PMX-60056, a small-molecule anticoagulant reversing agent active against both heparin and low-molecular-weight heparin.

- **Sagent Pharmaceuticals Inc.**, of Schaumburg, Ill., set the range for its proposed initial public offering (IPO). The specialty pharma firm anticipates selling 5 million shares priced between \$14 and \$16 per share. At the midpoint range, the IPO would bring in about \$75 million in proceeds, which are expected to support general corporate purposes. Upon pricing, Sagent aims to trade on Nasdaq under the ticker "SGNT." ■

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Valeant

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tantalizes Cephalon stockholders with the suggestion that such diligence may result in a higher offer. The Cephalon board has set a record date of April 8 for stockholder consents.

The proposed slate of directors hail from a range of organizations including Quintiles Transnational Corp., CalPERS, Harvard Business School and RadioShack.

Valeant said that it has received positive feedback on its offer from some of Cephalon's largest stockholders, and is prepared to close the transaction swiftly if the stockholders approve. If they don't approve, Valeant plans to walk away and focus on other opportunities.

The drama between Valeant and Cephalon has unfolded in a series of publicly disclosed letters between Cephalon CEO Kevin Buchi and Valeant CEO J. Michael Pearson.

On March 18, 2011, Pearson opened the negotiations with an offer to acquire 100 percent of Cephalon's issued fully diluted common shares for \$73 in cash.

In a meeting that same day, Buchi allegedly told Pearson that he was confident that Cephalon's board would reject Valeant's offer as being too low to warrant engaging in discussions.

Pearson expressed disappointment that Cephalon had announced an agreement to acquire ChemGenex Pharmaceuticals Ltd. for \$231 million in cash. (See *BioWorld Today*, March 30, 2011.)

Valeant's team, however, was not pleased.

"You are quite aware that investments in early stage development programs are inconsistent with our strategy and quite frankly, from our perspective, this move has reduced the value creation potential of the proposed merger," Pearson wrote in a follow up letter on March 25.

Valeant made an alternative offer. For a total consideration of \$2.8 billion, approximately \$37 per share in cash, Valeant would acquire on a cash-free/debt-free basis all of Cephalon's marketed products in the U.S. not related to oncology as well as appropriate sales operations to support those products, all research and development programs associated with Cephalon's CNS and pain businesses, and all assets acquired with Mepha AG.

For 2010, Cephalon reported sales of more than \$1.6 billion for its products in the category of central nervous system, pain, and "other" (excluding oncology).

Provigil faces patent expiration in April of 2012. Cephalon has been working to boost its sleep disorder franchise and transition patients from Provigil to Nuvigil ahead of that date. (See *BioWorld Today*, Dec. 9, 2010.)

The Mepha estate is considerable. At the time of its acquisition by Cephalon in February 2010, for \$590 million, Mepha marketed 120 products, including generic or branded generic versions of amoxicillin, diclofenac, ciprofloxacin, and omeprazole. The company posted \$277.8 million in sales in 2009, and had 50 new products slated for launch

over a five year term, including statins, anti-depressants and several biosimilars.

That alternative offer would leave Cephalon with its oncology-related marketed products and its pipeline of oncology and other candidates not purchased by Valeant, plus Western European operations, manufacturing, and other corporate and administrative operations.

"Again, we were very disappointed that you have chosen not to engage with us and hopefully you are more open to discussions with this second proposal," Pearson closed.

In a response dated March 28, 2011, Buchi addressed Pearson's chastisement regarding Cephalon's movements to acquire ChemGenex, "In your letter you also raised a concern about our continuing to pursue our business strategy while we are considering your letter. While I respect that we may have very different views of the future of our industry and of the best strategy to address that future, I know you will understand that it is incumbent upon me and my management to continue to follow the strategy agreed with our board and which we have laid out for our shareholders."

Cephalon requested more time to consider Valeant's offers.

In his response on March 29, Pearson conveyed an increased sense of urgency.

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Choline

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field has been “pounding away at determining the genetic underpinnings of cardiovascular disease with big-time genomic studies, but only a small portion of attributable cardiac risk has been identified by genetic studies thus far.” The risk factors identified in those studies pale in comparison to the effects that gut flora seems to have.

Previous experiments trying to link microbes and heart disease have had mixed results. Studies looking at antibiotic treatment failed to lower the risk of heart disease.

But, Hazen said, “we weren’t looking for a bacterial connection . . . we started with an unbiased approach aimed at identifying small molecules in plasma that predict cardiac risk, and were surprised to discover that some of them could only be made by bacteria. We fell into it by following the science.”

Hazen and his team began with profiling metabolites in the plasma of patients who experienced a heart attack, stroke or died within three years of the time their plasma sample was collected, versus patients who did not.

In those profiling experiments, the team found 18 metabolites that were predictive of cardiovascular risk. They decided to focus their attention on three metabolites that were highly correlated with one another, suggesting that they might be part of a common metabolic pathway.

The first step was identifying those three metabolites; the team found that they were TMAO (trimethylamine-N-oxide), choline and betaine. All three are metabolites of the lipid phosphatidylcholine (which also goes by the name lecithin).

Gut microbes metabolize choline into TMAO, and so Hazen and his colleagues next looked at whether gut microbes also have the same role in phosphatidylcholine metabolism. When they fed labeled phosphatidylcholine to mice, labeled TMAO soon appeared in the plasma.

But in mice that had no gut bacteria, because they were raised under sterile conditions, or because they had been treated with antibiotics to suppress intestinal flora, such labeled TMAO was nowhere to be found.

The authors also tested whether higher levels of either choline or its TMAO metabolite affected heart disease risk. In a separate study of over 1,800 subjects, they found “a clear dose-response relationship . . . between TMAO levels and clinical atherosclerotic plaque burden.” Then, when they fed either choline or TMAO to mice, diets high in either of the two compounds increased the formation of plaque.

The mechanistic link between TMAO levels and plaque appears to be mediated via an effect on macrophages. TMAO “changes macrophage biology,” Hazen said. “It makes the macrophage really want to hang onto cholesterol” – and cholesterol-laden macrophages are the major component of atherosclerotic plaques.

Gut bacteria are not the only ones metabolizing choline. A family of liver enzymes participates as well. But, Hazen

said, “we think that’s a small piece, especially in humans. The biggest piece is the ability of the intestinal flora to make this metabolite.”

On a practical level, the work describes both a diagnostic biomarker and a possible therapeutic target for heart disease.

“This gut flora metabolite is head and shoulders above current diagnostic tests” for relative risk of developing heart disease, Hazen said – far better than cholesterol or triglyceride levels.

Therapeutically, too, the findings could be exploited. The therapeutic options for atherosclerosis are just about as sclerotic as the disease itself. “There hasn’t really been a new class of anti-atherosclerotic drugs in the past 25 years,” Hazen said, since statins were introduced in the late 1980s. But the pathway his team has identified in their studies, which were published in the April 7, 2011, issue of *Nature*, are “eminently druggable.”

Ironically, choline is marketed as a nutritional supplement, both for brain development and for weight loss. “You can buy tubs of this at the nutrition store,” Hazen said. “And the long-term health risks aren’t known at all.”

A “News and Views” article that was published with the *Nature* paper said the findings “call into question the safety of using choline and lecithin as dietary supplements,” an assessment that Hazen said he agrees with “100 percent.”

Hazen sees choline’s rise as something of a poster child for dietary fads. As part of cell membranes, a minimal amount of choline is clearly essential for brain development. But even before his team’s study, there was no data suggesting that beyond those minimal amounts choline is particularly good for you.

Such use has only become widespread in the past decade, and Hazen attributes it to a herd mentality among supplement makers: “It showed up in one, and then all the other manufacturers said ‘Oh, we’d better put that in, too.’”

As a result, now, “I can show you pictures of Flintstone chewable vitamins where the biggest font, other than ‘Flintstone,’ is ‘complete with choline!’ We really need to determine what are the minimum essential requirements for good health, and whether this is a healthy thing or not to be providing as added supplement to our children beyond a common sense heart healthy diet.” ■

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Social Media

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guide to social media do's and don'ts.

When the agency missed the March 31 target, the Pharmaceutical Research and Manufacturers of America (PhRMA) publically chided it for the delay. "We note that FDA itself is making almost daily use of Twitter, Facebook and other social media," Jeffrey Francer, PhRMA's assistant general counsel, said. "Clearly, social media can be used to discuss new medical advances in appropriate ways that benefit patients and healthcare professionals, and improve the public health."

But Jeffrey Wasserstein, a director at Hyman, Phelps & Phillips LLP, said, "We should not be waiting for FDA." By the time a guidance comes out, it will already be outdated, he predicted Wednesday at the 54th annual Food and Drug Law Institute (FDLI) conference.

"Is it really possible for the FDA to keep up with Steve Jobs and the other tech giants?" he asked.

Even though the virtual community may be fraught with regulatory potholes, biopharma cannot ignore the growing neighborhood while it waits for the FDA to act. Jeffrey Senger, a partner at Sidley Austin LLP and former acting chief counsel at the FDA, pointed out at the conference that 89 million adults in the U.S. turn to the Internet for health care help.

Citing a Pfizer study, he said 1.4 million discussions about drugs take place via social media each year, but the biopharma industry, concerned about the unspoken regulations that guide its online etiquette, generally is not participating in those discussions. Instead, the people providing the answers are unregulated groups such as overseas pharmacies, supplement makers, plaintiff attorneys and spam artists.

Although the FDA has yet to issue a guidance dealing with the newest social media, it has provided some direction through other guidances and enforcement actions, Glenn Byrd, senior director of regulatory affairs at MedImmune LLC, said at the conference.

For the most part, that guidance addresses rules for 20th century media. "They just continue treating the web as if it were the print page. The problem is the Internet has evolved," Wasserstein said.

While the underlying principles of truth, fair balance and disclosure apply whether a company is dealing in social media or print/broadcast media, new technologies have opened opportunities and set restrictions not found in 20th century media.

The FDA sidestepped that fact in a draft guidance it released in May 2009 on presenting risk information. "It's not the medium; it's the message," Senger said in summarizing that guidance. That may be true with misleading or misbranded claims on a YouTube video or sponsored web site, he added, but more direction is needed for using Twitter, widgets and other new media.

"At some point, the medium becomes the message, and

the medium must be dealt with," Senger said.

To help biopharma be a responsible neighbor in the online community, the FDLI panel, which included Stacey Ferguson, a senior attorney at the Federal Trade Commission, made a number of recommendations:

- Transparency is a must. If a message is sponsored, it should say so. If a company gives bloggers a product or any kind of compensation for a mention or review, it should train the bloggers on their responsibility to disclose that information. A tweet or text message can indicate payment or sponsorship by incorporating "#paid" or "#ad."

- Companies are responsible for the content on their sponsored sites or comments made on other sites by their staff or paid endorsers. If they allow comments from third parties on their sites, they should consider moderating them before allowing them to be posted. Wasserstein and Ferguson suggested using a landing page as a disclaimer to explain the monitoring and posting policies.

- Companies probably are not responsible for comments made on third-party sites – as long as those comments are not made by company officials or compensated individuals. However, if a company corrects something on another site, such as Wikipedia, it could be making itself responsible for continued monitoring of that site. "These are the kind of things [where] a guidance from the FDA would be helpful," Senger said.

- Firms should have policies in place for dealing with adverse events discovered on Facebook, in chat rooms or other social media. This is, perhaps, one of the biggest areas in which guidance is needed.

- When discussing communicating or marketing through social media, a firm should have an attorney or regulatory person at the table.

- Given the explosion of phone applications and other mobile devices, companies should be mindful of how an online message will be viewed on those devices. That view could affect the fair balance of risks and benefits.

- Biopharma also should ask whether it needs to use every media available. "Should we be on Twitter?" Byrd asked. If a company answers yes, it must make critical decisions about what's appropriate for that space. ■

Clinic Roundup

- **Avila Therapeutics Inc.**, of Waltham, Mass., reported that it completed two Phase Ia clinical studies for AVL-292, its orally available, selective inhibitor of Bruton's tyrosine kinase. Avila presented summary results from the first-in-human study, AVL-292-001, at the Keystone Symposium on Molecular and Cellular Biology. In the double-blind, placebo-controlled, single ascending dose study in healthy volunteers, AVL-292-001 demonstrated favorable safety, tolerability and pharmacokinetics.

Valeant

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“Following another evening of reflection, my board and I are increasingly concerned that as each day goes by, the value of Cephalon to Valeant shareholders is decreasing. Specifically, Provigil continues to move closer to its patent cliff and your cash is being rapidly spent on what we believe are risky investments. At some point, a potential merger between Cephalon and Valeant will no longer be attractive to us.”

Valeant declined Cephalon’s request for additional time, noting that Cephalon was rapidly frittering away its cash acquiring assets in which Valeant had no interest. “Since the time of our original offer, you have announced two deals that will reduce your cash on hand by over \$400 million, which makes Cephalon a less attractive acquisition from our standpoint. As a result, we are seriously considering the need to reduce our original \$73 per share proposal,” Pearson wrote on March 29, additionally suggesting that Cephalon’s request for additional time may be a tactic to put up additional barriers to Valeant’s offer.

Pearson refers to the recent ChemGenex acquisition as well as a \$225 million acquisition of Gemin X Pharmaceuticals Inc., initiated by Cephalon March 21. (See *BioWorld Today*, March 22, 2011.)

Buchi’s response on March 29 sought to clear up Valeant’s “apparent misunderstanding” of Cephalon’s process, assuring Valeant that it is carefully considering both alternative offers that Valeant has made.

On April 5, Cephalon issued a curt rejection of Valeant’s offer. Cephalon argued that Valeant’s offer undervalues its pipeline, and assumes a “worst case scenario” outcome for an array of business activities including failure of every pipeline product, loss of all patent litigation, and loss of all provisional sales in the coming year.

In an analysis of the deal, ISS Governance analyst Chris Cernich asks “Where’s the fire?” pointing out that Valeant’s move to replace the board by written consent rather than at an annual meeting was highly unusual. “But this fact pattern only underscores the point that VRX likely did not consider the entire chessboard before making its first move: For one reason or another, this was not an offer it believed would go hostile, much less require a sustained public campaign,” Cernich wrote.

Cernich and David G. Buck, of The Buckingham Research Group, both suggested Valeant’s offer was opportunistic, and did not take into consideration the value of Cephalon’s pipeline. Buck wrote, “We believe that using 11.5x our 2012 EBITDA forecast is a reasonable proxy for takeover value and we have discounted this significantly to get to our price target of \$83 per share. We believe that Cephalon’s pipeline should receive some credit.”

The SEC will have 10 days to review Valeant’s consent solicitation and approve it, during which time Cephalon will have the opportunity to make a filing of its own saying that

it does not wish to have its board replaced. Once the SEC approves the consent solicitation, the shareholder voting period will last 60 days. ■

AACR Roundup

The following study data were presented at the annual meeting of the American Association for Cancer Research (AACR) in Orlando this week:

- **Circadian Technologies Ltd.**, of Melbourne, Australia, reported data demonstrating that its lead anti-cancer therapeutic, VGX-100, inhibits tumor growth and spread in a variety of mouse models of human cancer. VGX-100 is a human monoclonal antibody targeting the vascular endothelial growth factor C growth factor. The addition of VGX-100 to bevacizumab (Avastin) plus docetaxel therapy reduced tumor burden in prostate, ovarian and lung cancer models. In an orthotopic mouse model of human prostate cancer, single-agent VGX-100 inhibited primary tumor growth by 59 percent compared to a control antibody. In the same orthotopic model of human prostate cancer, single agent VGX-100 reduced the incidence of metastasis to local lymph nodes by 55 percent. Circadian plans to file an investigational new drug application with the FDA in the third quarter.

- **Curis Inc.**, of Lexington, Mass., reported preclinical data characterizing three drug development candidates that target cancer signaling networks. Erlotinib-resistant cancer cells and cancer cells harboring MET amplification were sensitive to treatment with CUDC-101, a multi-targeted HDAC, EGFR and Her2 inhibitor and the lead drug candidate from Curis’ network-targeted cancer programs. Curis has completed Phase I testing of CUDC-101 in patients with advanced solid tumors and has initiated a Phase Ib expansion trial in breast, gastric, head and neck, liver and non-small cell lung cancer. A second presentation on CUDC-907, designed to inhibit phosphatidylinositol-3-kinase and HDAC for synergistic interaction against cancer cells, showed that CUDC-907 induces apoptosis at low concentrations in vitro and displays high exposure, a long half-life in tumor tissue and oral bioavailability in preclinical models. A third presentation highlighted the discovery of Debio 0932 (formerly CUDC-305), partnered with **Jennerex Inc.**, of San Francisco, and Transgene, of Illkirch, France reported interim results from Phase I dose-escalation trials demonstrating that administration of JX-594 targets tumor vasculature, disrupting the blood supply to the solid tumors and contributing to destruction of the cancer. The engineered oncolytic virus is designed to selectively target and destroy cancer cells. Phase I and II clinical trials in multiple cancer types have shown that JX-594, delivered directly into tumors or systemically, induces tumor shrinkage and/or necrosis and is well tolerated in a variety of cancers, including liver, colon, kidney, lung and melanoma.

Other News To Note

- **Nuron Biotech Inc.**, of Exton, Pa., acquired assets relating to the vaccine HibTiter (haemophilus b conjugate vaccine (diphtheria CRM197 protein conjugate)) from **Wyeth LLC** for the U.S. and other markets, including Japan and Korea. Financial terms were not disclosed. HibTiter is a previously marketed pediatric vaccine that uses glycoconjugate technology. Wyeth discontinued usage several years ago, and Nuron is working with the FDA to finalize a re-launch strategy.
- **Optimer Pharmaceuticals Inc.**, of San Diego, and **Cubist Pharmaceuticals Inc.**, of Lexington, Mass., signed an exclusive two-year co-promotion agreement to market the antibiotic Dificid (fidaxomicin) in the U.S. to treat *Clostridium difficile* infection (CDI). On Tuesday, the FDA's Anti-Infective Drugs Advisory Committee voted unanimously to recommend approval of Dificid, which has a PDUFA date of May 30, 2011. Optimer and Cubist will co-promote Dificid to physicians, hospitals, long-term care facilities and other health care institutions and jointly provide medical affairs support for the product. Cubist will receive service fees of \$15 million per year and is eligible to receive an additional \$5 million in the first year and \$12.5 million in the second year if sales targets are achieved, plus as a portion of gross profits from sales above target levels. (See *BioWorld Today*, Apr. 6, 2011.)
- **Seattle Genetics Inc.**, of Bothell, Wash., reported

data from a case series of 25 Hodgkin lymphoma patients receiving brentuximab vedotin (SGN-35) following allogeneic stem cell transplant at the European Group for Blood and Marrow Transplantation Annual Meeting in Paris. SGN-35 is an antibody-drug conjugate (ADC) directed to CD30, a defining marker of Hodgkin lymphoma. Half of the patients improved, including 38 percent complete remissions, and an additional 42 percent had stable disease. Median progression-free survival was 34 weeks, and median overall survival had not been reached. Adverse effects such as cough, fatigue, fever, nausea and peripheral sensory neuropathy were manageable. Seattle Genetics is jointly developing SGN-35 with Millennium Pharmaceuticals, of Cambridge, Mass., a unit of Takeda Pharmaceutical Co. Ltd., and has filed a biologics license application to the FDA. (See *BioWorld Today*, March 1, 2011.)

- **Shire plc**, of Dublin, Ireland, said subsidiary **Shire LLC**, of Philadelphia, Pa., filed a lawsuit in the U.S. District Court for the Southern District of New York against Watson Pharmaceuticals Inc., of Morristown, N.J., and its subsidiaries for patent infringement and breach of contract. The lawsuit results from an abbreviated new drug application (ANDA) filed by Watson for generic versions of Adderall XR, alleging that Watson's generic strengths infringe Shire's patents. The suit also alleges that Watson violated settlement and license agreements signed in November 2007, arising from an ANDA that Watson filed in 2006 that also sought approval to market generic versions of Adderall XR.

AACR Roundup

• **Pervasis Therapeutics Inc.**, of Cambridge, Mass., reported preclinical data showing positive effects of PVS-30200, the company's investigational cell therapy for the treatment of solid tumors, in controlling tumor growth and inhibiting metastases in an animal model of prostate cancer. PVS-30200, which uses Pervasis' implantable material comprised of healthy allogeneic endothelial cells embedded in a polymer matrix, is designed to treat tumors locally to regulate key processes in tumor growth and metastasis.

• **Teva Pharmaceutical Industries Ltd.**, of Jerusalem, Israel, and **OncoGenex Pharmaceuticals Inc.**, of Bothell, Wash., presented preclinical data on their investigational compound custirsen (OGX-011/TV-1011), which is being investigated in Phase III studies in castrate-resistant prostate cancer. Custirsen is designed to block production of clusterin, a cell survival protein that is over-produced in several cancer types and in response to many cancer treatments. The companies also presented data showing an inhibitory effect of custirsen on heat-shock protein 90 (HSP90) in prostate cancer cells. Inhibition of HSP90 is being investigated as a strategy to treat prostate cancer, and the addition of custirsen may enhance the activity of HSP90 inhibitors.

• **VBL Therapeutics**, of Tel Aviv, Israel, reported preclinical data demonstrating the potential of its

investigational compound VB-III as a targeted cancer treatment. The company presented two studies, one demonstrating the safety and specificity of VB-III and the other demonstrating its promise against glioblastoma. Researchers evaluated the safety and efficacy of VB-III as monotherapy, in combination with bevacizumab and in combination with carboplatin and pemetrexed and found that VB-III induced a dose-dependent tumor reduction of up to 90 percent. The company also evaluated the impact of VB-III on tumor growth in rats with established intracranial xenografts, demonstrating decreased tumor size. VB-III is the first targeted, dual-action, antiangiogenic and vascular disruptive agent to use VTS, the company's platform technology, for cancer therapy.

Clinic Roundup

• **Circadian Technologies Ltd.**, of Melbourne, Australia, said that licensee **ImClone Systems**, of Bridgewater, N.J., a wholly owned subsidiary of Eli Lilly and Co., began the first Phase I clinical trial of its human monoclonal antibody IMC-3C5 as a cancer treatment. ImClone has exclusive rights from Circadian's 100 percent-owned subsidiary Vegenics Ltd. to develop the vascular endothelial growth factor receptor 3 antibody. The Phase I study is examining the safety and tolerability of escalating doses of IMC-3C5 in patients with advanced solid tumors.



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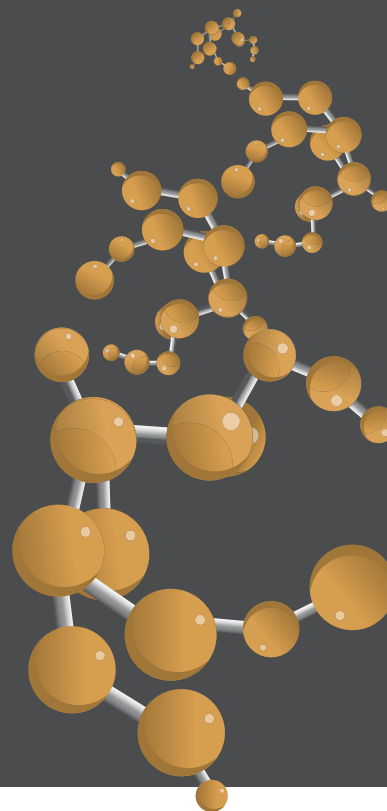
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- A full day Cardiovascular Symposium and seminars focusing on the patient of tomorrow, preventative medicine, oncology, orphan diseases, CNS diseases, and regulation/reimbursement
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