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Invitrogen, Applied Biosystems Join Forces in \$6.7B Merger

By Donna Young
Washington Editor

Research and discovery tools firm Invitrogen Corp. has agreed to buy Applied Biosystems Group, a subsidiary of Applera Corp. that develops and markets systems for analyzing nucleic acids, proteins and small molecules, for \$6.7 billion in cash and stocks.

While shares of Foster City, Calif.-based Applied Biosystems (NYSE:ABI) rose 5.3 percent on the news Thursday, Wall Street's reaction was harsh for Carlsbad, Calif.-based Invitrogen (NASDAQ:IVGN), with the firm's stock tumbling 10.6 percent.

Applied Biosystems closed at \$34.16, an increase of \$1.72, while Invitrogen closed at \$38.73, a loss of \$4.62.

Invitrogen will pay \$38 per share for Applied Biosystems, which represents a premium of 17 percent to the

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EpiCept's Phase III Data Shows Promise for AML as Endpoint

By Tiffany Turner
Staff Writer

EpiCept Corp. said Phase III data on Ceplene, its lead product candidate in acute myeloid leukemia (AML) validated leukemia-free survival as a surrogate endpoint for overall survival in AML patients in complete remission.

EpiCept presented data for the 320-patient, pivotal trial at the annual European Hematology Association Congress (EHA) in Copenhagen, Denmark, in hopes of providing additional support for its marketing authorization request in Europe and with the aim of facilitating a pre-new drug application meeting with the FDA.

In March the European Committee for Medicinal Products for Human Use issued a negative opinion regarding marketing authorization for Ceplene. EpiCept has formally requested a re-examination of that opinion, which could

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XBPI: Making the Liver Look Fat Since 2008

Stress Response Protein Plays Role in Synthesis of Liver Fats

By Anette Breindl
Science Editor

With the economy in the tank and prices sky-high, even transcription factors are taking on second jobs.

In the June 13, 2008 issue of *Science*, researchers report that the transcription factor XBPI, which regulates protein synthesis and stress responses in secretory cells, is important for lipid synthesis in the liver.

XBPI had originally been discovered by senior author Laurie Glimcher as a regulator of genes in the major histocompatibility complex. It is also known to regulate the unfolded protein response, "an adaptive mechanism used by many different cells to handle the load of proteins in the endoplasmic reticulum," Glimcher, a professor at the Harvard School of Public Health, told *BioWorld Today*.

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TransPharma Gets \$35M in Osteo Deal with Lilly

By Catherine Hollingsworth
Staff Writer

TransPharma Medical Ltd. said it will receive an up-front payment of \$35 million as part of a deal with Eli Lilly & Co. to develop TransPharma's needle-free ViaDerm-PTH (1-34) for osteoporosis.

Under the deal, TransPharma also is entitled to development and sales milestones, as well as royalties on sales if a transdermal PTH product is successfully commercialized.

The transaction is expected to become effective in either June or July, subject to clearance under U.S. antitrust law. At closing, Lilly said it would expect a 2-cent per share charge to earnings for acquired in-process research and development.

The ViaDerm-PTH product, which is administered trans-

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OTHER NEWS TO NOTE

• **AmVac AG**, of Zug, Switzerland, is starting its first research cooperation program with **Bayer Innovation GmbH**, of Düsseldorf, Germany, on the development of a new influenza vaccine. Joint research and development work is beginning with the Bayer subsidiary **Icon Genetics GmbH** on a novel production approach. Antigens will be produced for the first time in tobacco plants, which along with AmVac AG's adjuvant MALP-2, will be developed into an efficient new generation of flu vaccines.

• **AVI BioPharma Inc.**, of Corvallis, Ore., said preclinical results of a study designed to demonstrate the ability of AVI's NeuGene class of drugs to induce sustained expression of dystrophin in the mdx mouse model of Duchenne muscular dystrophy has been published in the journal *Molecular Therapy*. Treatment with the AVI compound resulted in production of functional dystrophin in numerous appropriate tissues, including the heart, diaphragm and skeletal muscles; key organs for the treatment of the disease.

• **Axelar AB**, of Stockholm, Sweden, said it has received financing from the Foundation for Baltic and East European Studies and Karolinska Development AB to perform a Phase I/II trial with the insulin-like growth factor-I (IGF-I) receptor inhibitor AXLI717 on cancer patients. The amount of the funding was not revealed.

• **Baxter International Inc.**, of Deerfield, Ill., announced publication in the June 12 issue of *The New England Journal of Medicine* of data demonstrating that its candidate avian influenza (H5NI) vaccine, Celvapan, met Phase I/II trial endpoints for safety and immunogenicity.

• **BioNeutral**, of Newark, N.J., said tests using its Ygiene formulation to kill anthrax spores on contact showed it did so in as little as 15 seconds. The test compared results with a 10 percent solution of chlorine bleach which required almost 100 times the contact time to achieve the same test result. Ygiene is being developed for use by the military and first responders in conjunction with

any suspected anthrax exposure.

• **Maxygen Inc.**, of Redwood City, Calif., has received the necessary approvals in the UK to initiate a first-in-human Phase I trial of MAXY-VII in hemophilia patients. MAXY-VII is a Factor VIIa protein for the treatment of hemophilia. Patient dosing is on schedule to begin in the second half of this year.

• **NeoPharm Inc.**, of Lake Bluff, Ill., has received approval from Nasdaq to transfer the listing of its common stock from the Nasdaq Global Market to the Nasdaq Capital Market. The transfer will be effective as of the market opening on Friday. Its trading symbol will remain "NEOL."

• **Proton Laboratories Inc.**, of Alameda, Calif., has formed a business alliance with the principals of BW2Asia, of Pasig City, the Philippines. The principals will exclusively represent Proton Laboratories' four business development priorities in the Philippines.

• **Q Therapeutics Inc.**, of Salt Lake City, said Nicholas Maragakis of Johns Hopkins University received notification of an \$800,000 grant to be awarded from the Maryland Stem Cell Research Fund to enable study of the company's human neural cell product Q-Cells in preclinical models of amyotrophic lateral sclerosis. The study will focus on the ability of Q-Cells to protect motor neurons from degeneration in the SOD-1 rat model of ALS.

Corrections and Clarifications

The CONNECTION study being conducted by Medivation Inc. is a Phase III, placebo-controlled trial of Dimebon. The other Medivation-sponsored trial involving Dimebon and Aricept is a multi-phase I/II study, which will not be part of the company's FDA label submission. Information about the two studies was unclear in a Tuesday news item.

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

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 **AHC Media LLC**

Invitrogen

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stock's closing price on Wednesday.

Invitrogen will pay 45 percent of the purchasing price in cash and the rest in stock, said CEO Gregory Lucier, who will take the reins of the combined company.

The cash portion of the transaction will be paid by cash on hand and about \$2 billion in new debt, he told investors and analysts Thursday during a conference call. Total debt of the combined company will be about \$3.5 billion, Lucier added.

Invitrogen shareholders will maintain a majority ownership of the new company, he noted.

The combined company will generate greater than 70 percent of its revenue from consumables and services. Following the close of the transaction, the combined firm will be named Applied Biosystems Inc., Lucier said.

"But we will maintain and build upon the great brand of Invitrogen for selling and merchandising high-quality reagents," he said, adding that there was a great deal of discussion about the selection of the combined firm's name.

"We believe that Applied Biosystems is a name that best describes a company that we hope to build – a systems company in the biological sciences that has an emphasis on taking technology from the research lab and applying it to commercial applications," Lucier said.

The transaction is expected to close this fall pending regulatory and shareholder approval, he noted.

Tony White, CEO of Applied Biosystems, which reported sales of about \$2.1 billion during fiscal 2007, said his company has been through an extensive deliberative process over the past several months about its strategic options, which he said included continuing to make acquisitions and increasing the firm's portfolio, restructuring and remaining independent or selling to another company.

The merger, he said, is a "hybrid of the second and third options, as we are combining with a very complementary life sciences tools provider to create a new company that will have the strengths of each as well as synergies that will make the combination much more than the sum of its parts."

"I am excited about this powerful combination," White added.

Analyst Doug Schenkel, of Cowen & Co., said the merger was not a surprise, since speculation about a potential strategic sale of Allied Biosystems had been building ever since Applera confirmed its intent to unwind by midyear its tracking-stock structure between that company and its other operating group, Rockville, Md.-based Celera, a firm founded in 1998 by Craig Venter to sequence the human genome. Applera filed in February to separate itself from Celera.

The timing of Applera's plans was right for Invitrogen, which was eager to participate in the high-growth next-generation sequencing market, Schenkel said in a research

note.

In fact, he said, during a first-quarter conference call, Lucier noted that his company had put a dedicated group of R&D and marketing personnel in place to focus solely on the partnership and product opportunities related to next-generation sequencing and that the company planned to be a key player in that area in the coming years.

"These comments led many to conclude that Invitrogen was evaluating ABI as a potential acquisition target," Schenkel said.

Schenkel noted that he had predicted the merger last month.

Moelis & Co. and UBS Investment Bank acted as financial advisors, and DLA Piper US LLP acted as legal counsel to Invitrogen. Morgan Stanley acted as financial advisor, Morgan Stanley and Greenhill & Co. provided fairness opinions to the board of directors and Skadden, Arps, Slate, Meagher & Flom LLP acted as legal counsel to Applera. ■

CLINIC ROUNDUP

• **Arena Pharmaceuticals Inc.**, of San Diego, presented positive Phase IIa trial results of APDI25, an oral selective inverse agonist of the 5-HT_{2A} serotonin receptor, for the treatment of insomnia. The results showed that when compared to placebo, patients treated with APDI25 experienced statistically significant improvements in polysomnographic measurements of sleep maintenance, or the ability to maintain sleep during the night after falling asleep. These improvements were achieved without any next day impairment of cognition or coordination. Arena is currently evaluating the effects of APDI25 on patients' subjective assessment of sleep in a Phase IIb study.

• **BioLineRx Ltd.**, of Jerusalem, Israel, has begun a Phase IIb trial to assess the efficacy, safety and tolerability of BL-1020, a GABA-enhanced antipsychotic for the treatment of schizophrenia. In the six-week, double-blind, parallel group study, patients will be randomized to one of four arms, receiving a low dose or high dose of BL-1020; risperidone, an approved atypical schizophrenia drug; or placebo. The study will also include a blinded six weeks continuation phase. It is expected to include 360 schizophrenia patients and is being conducted under an FDA investigational new drug application.

• **Calando Pharmaceuticals Inc.**, of Pasadena, Calif., said it has entered into a collaboration with City of Hope in Duarte, Calif., to initiate an investigator sponsored clinical trial using Calando's nanoparticle drug candidate, IT-101, in patients with various forms of lymphoma. The trial will be an open-label, Phase II study of IT-101 intended to demonstrate safety and efficacy in patients with relapsed or refractory lymphoma, including B cell, T cell and Hodgkin's lymphoma who satisfy eligibility requirements.

EpiCept

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occur in the third quarter of 2008.

EpiCept CEO and President Jack Talley told *BioWorld Today* that while the drug is still under review by the European Medicines Agency, "the most significant thing is that these data add to the statistical robustness argument in favor of approval." The company conducted the trial not because of an agency requested more information, but rather to provide additional validation of leukemia-free survival (LFS) as a primary endpoint.

And the trial accomplished that mission, he said.

In a poster presentation cancer statistician Marc Buyse showed that while the extension of overall survival (OS) duration is a principal goal of all cancer therapies, leukemia-free is likely to be a better endpoint for AML since overall survival may be confounded by alternative salvage therapies and unrelated events.

In addition, in a weighted linear regression analysis between estimates of LFS and OS at specific time points and between the estimated effects of Ceplene with IL-2 on LFS and OS, researchers found a high correlation between the country-specific Kaplan-Meier estimates of 24-month LFS and 36-month OS in both treated and untreated groups. Similar correlations also were found between 24-month LFS and 48-month and 60-month OS. In addition, country-specific hazard ratios demonstrated that the treatment effect of Ceplene with IL-2 on LFS and OS were found to be highly correlated.

Still, Talley acknowledged that "you can't make a survival claim without a survival outcome." However, he said he thinks the results "certainly lead most clinicians to believe that leukemia-free survival is an appropriate endpoint for them to focus on, and that improving leukemia-free survival will ultimately lead to an improvement in overall survival in their patients."

And he said that the European agency called EpiCept's approach to extended LFS "revolutionary."

"This is the first and the only product that has ever been shown to extend the disease-free period and prevent relapse in AML patients," Talley said. "There are other drugs that are under study, with the goal of improving response rates, meaning the induction of remission, but this is the only drug that has ever been shown to improve the duration of remission."

Talley said that timeline is a factor in developing a drug targeting leukemia-free survival. "Once you decide to do a Phase III trial in this indication, you are committing yourself to a three-year primary endpoint. And we don't believe anyone is close from a competitive standpoint," he added. He said an EMA decision is expected at the end of July, and said the company could meet with the FDA by the end of the year.

In a separate poster presentation at EHA, EpiCept

released new findings from another pivotal Phase III study of Ceplene demonstrating that AML patients maintained their quality of life while undergoing treatment with Ceplene in combination with low-dose Interleukin 2.

Talley said that trial data, which had never before been publicly released, "showed that patients were able to tolerate twice-daily subcutaneous injections of Ceplene and Interleukin 2 with an equivalent quality of life to the untreated control group. In summary, he said "a very high level of patient tolerability was observed in the trial."

Shares of EpiCept (NASDAQ:EPCT) gained 4 cents, or 10 percent, to close at 44 cents. ■

CLINIC ROUNDUP

- **ChemoCentryx Inc.**, of Mountain View, Calif., said it has completed enrollment of 436 patients in PROTECT-1, a Phase II/III clinical trial of Traficet-EN (CCX282-B) in patients with moderate-to-severe Crohn's disease. The trial comprises three discrete phases that allows for evaluation of efficacy and safety of Traficet-EN in inducing a clinical response or remission and maintaining response-remission in Crohn's disease over one year. Traficet-EN is an orally-active inhibitor of the chemokine receptor known as CCR9, which is selectively expressed by inflammatory T cells to migrate to the digestive tract in a process that ultimately results in the persistent inflammation underlying the disease.

- **Cytomedix Inc.**, of Rockville, Md., said it plans to enter the multi-billion dollar anti-inflammatory market with patent protected peptides derived from platelet factor 4 (PF4), a growth factor released when blood platelets are activated. Preclinical studies indicate that the company's CT-112 peptide may be active for the treatment of inflammatory diseases such as rheumatoid arthritis, Crohn's disease, tissue reperfusion injury and other autoimmune diseases, the company said. The studies also indicated that CT-112 may be administered orally, unlike other anti-inflammatory drugs currently on the market which are administered via injection.

- **GenVec Inc.**, of Gaithersburg, Md., announced encouraging results from its Phase I/IIa clinical trial sponsored by the Naval Medical Research Center and the U.S. Military Malaria Vaccine Program showing that its malaria vaccine candidate induced strong T-cell responses against the target antigens in all volunteers. The vaccine is designed to provide protection against both liver and blood stages of the malaria parasite. NMRC is planning to evaluate the protective effects of the vaccine following experimental challenge with *Plasmodium falciparum* parasites that cause malaria in the second half of the study.

Liver Fats

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XBPI is a required transcription factor during development, playing an important role in the liver prenatally. Mice lacking XBPI do not survive to birth. Working under the assumption that a protein that is important during embryonic development likely has a role in the adult liver as well, Glimcher and her team began studying XBPIs function in liver using inducible knockouts.

Their first guess was that its role would be in regulating protein synthesis, similar to its known function in secretory cells. But “to our surprise, we found that the protein synthetic function of the adult liver was largely intact.” Not only that, but “we didn’t see any evidence of endoplasmic reticulum stress, either,” she said.

Which led naturally to the next question: If there’s no endoplasmic reticulum stress and proteins are normal, what else does the liver make? First author Ann-Hwee Lee decided to look at lipids, Glimcher said, “and that’s when we saw that there was a profound absence of cholesterol and triglycerides” in inducible liver-specific XBPI knockouts.

Further studies confirmed that in the liver, XBPI is induced by a high-carbohydrate diet and functions as a transcription factor that controls the synthesis of both triglycerides and cholesterol – though the details of how it does the latter have remained a mystery to date. While XBPI activates at least three genes that are involved in triglyceride synthesis, “we still don’t understand how it controls cholesterol,” Glimcher said.

What is clear is that XBPI does not cause fatty liver; the low plasma lipid levels that Glimcher and her team found were not accompanied by higher lipid levels in the liver, showing that liver fats are not synthesized in the first place, rather than synthesized and retained in the liver instead of making their way into the bloodstream.

Nor does XBPI affect HMG-CoA reductase, the enzyme targeted by statins. This latter finding makes XBPI, Glimcher said, “another pathway to controlling dyslipidemias. So we’re eager to find out” how it works – and whether it can be manipulated therapeutically. Glimcher’s group is currently working, in collaboration with the Broad Institute, to identify small molecules or siRNAs that target XBPI.

Given the factor’s well-known role in secretory cells, whether such targeting will ultimately be a viable clinical option is anyone’s guess at this point. But Glimcher pointed out that like XBPI knockouts, HMG-CoA reductase knockouts die before birth – “and statins are great drugs.”

In the end, Glimcher said, whether targeting XBPI is a viable therapeutic approach will depend on the details. “We know that you need XBPI to generate antibodies. But transient inhibition, or even chronic inhibition at levels that affect lipids, may not affect antibodies,” she said. And, she pointed out, less likely schemes have come to pass: “Who would have thought that you could inhibit the proteasome without massive toxicity?” ■

FINANCINGS ROUNDUP

• **GenVec Inc.**, of Gaithersburg, Md., completed a registered direct offering that raised a total of \$17 million, and also announced encouraging clinical and preclinical data from its malaria vaccine program. The offering consisted of 11,258,279 shares of common stock and warrants to purchase 2,251,653 additional shares. Merriman Curhan Ford acted as lead placement agent, and Boenning & Scattergood, Inc. acted as co-placement agent. The shares of common stock and warrants were offered in units consisting of one share of common stock and a warrant to purchase 0.20 shares of common stock at a per unit price of \$1.51. The warrants have a term of five years and an exercise price of \$2.016 per share.

• **Active Biotech**, of Lund, Sweden, has completed a new share increase, boosting its total shares from 3.9 million to 51.2 million. Nordstjernan AB and MGA Holding AB subscribed for their preferential parts of the new issue. In addition, Nordstjernan AB subscribed for an additional 150,087 shares, or 3.8 per cent of the shares issued. That leaves Nordstjernan and MGA holding 15.3 percent and 30 percent respectively of the shares and votes in Active Biotech. The new issue will provide Active Biotech with approximately SEK 157.7 million (US\$25.8 million) before expenses.

• **Cell Therapeutics Inc.**, of Seattle, said a single institutional investor has agreed to purchase, for \$23 million, newly issued 15 percent convertible senior notes due in 2011, with an initial conversion price of 79-cents per share, and a warrant to purchase approximately 14.6 million shares of common stock with an exercise price of 95-cents per share. The transaction is a partial exercise of a previously granted warrant right for the investor to purchase up to \$67.5 million of securities. The company said it intends to use approximately \$11 million of the net proceeds from this transaction to retire upon maturity the remaining balance of its 2008 convertible notes due June 15, together with accrued interest.

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TransPharma

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dermally using TransPharma's proprietary technology, contains the bone-building parathyroid hormone, or PTH.

Indianapolis-based Lilly already has its own PTH product, Forteo for osteoporosis, but that drug is delivered via an injection. ViaDerm-PTH, on the other hand, is needle-free and is designed to be self-administered by the patient.

TransPharma CEO Daphna Heffetz described the ViaDerm device as "non-intimidating," similar to a pen or marker, requiring no special training by for patient use. She referred questions about the Phase II study to Lilly.

The product currently is in Phase II clinical testing in female patients. This dose-ranging study is still enrolling and no target date for completing enrollment has been set, Mark Taylor, a Lilly spokesperson said. The Phase II study is being jointly funded by the two companies. But after that Lilly would be responsible for further development activities and the potential commercialization of any transdermal PTH products, both companies said.

One question Lilly hopes to find out through the research is "how different this is" from its own PTH product, Taylor said. However, the companies have not yet disclosed which therapies – beyond PTH – are being tested in the ViaDerm-PTH study, he said.

A Phase I study of ViaDerm-PTH showed similarities between Lilly's Forteo and TransPharma's PTH product. According to TransPharma, once-daily transdermal delivery of all doses tested in this trial demonstrated a safety profile similar to the one observed in the Forteo subcutaneous injection. In addition, pharmacokinetic profiles also were similar, the company announced last year, suggesting that ViaDerm-PTH could provide a viable alternative administration route for hPTH.

Lilly also has an oral osteoporosis drug called Evista. However, Evista is bone-maintaining drug – not a bone-building drug like its PTH product Forteo, Lilly's Taylor explained.

Lod, Israel-based TransPharma has other molecules in development using the same pen-like delivery system, Heffetz said. In addition, it also has completed a Phase Ib study for transdermal delivery of human growth hormone (somatropin). ■

OTHER NEWS TO NOTE

- **Viral Genetics**, of Azusa, Calif., has expanded the existing license agreement with the University of Colorado by obtaining two options to acquire rights for treatment and detection of several forms of cancer including lung, breast, leukemia, and others, multiple sclerosis, diabetes, rheumatoid arthritis, malaria and several other diseases.

CLINIC ROUNDUP

- **Geron Corp.**, of Menlo Park, Calif., said newly presented data indicate that GRNCMI, the company's human embryonic stem cell (hESC)-based therapeutic for the treatment of heart failure, evades direct attack by the human immune system in vitro. Unlike whole organ transplants, cell therapies derived from hESCs may provoke only minimal immune reactions suggesting that rejection may be controlled or prevented by short courses of low-dose immunosuppressive drugs, according to data presented at the International Society for Stem Cell Research annual meeting. The work also suggests that patient-specific hESC lines may not be needed to prevent immune rejection.

- **Human Genome Sciences Inc.**, of Rockville, Md., said the results from a long-term Phase II continuation trial showed that LymphoStat-B (belimumab) was associated with sustained improvement in disease activity across multiple clinical measures, decreased frequency of disease flares, potential steroid-sparing activity, and was generally well tolerated through three years on treatment in combination with standard of care in patients with serologically active systemic lupus erythematosus. The overall incidence of adverse events (in general and by system organ class), serious adverse events, infections, malignancies and laboratory abnormalities continued to decrease or stabilize from Week 52 to Week 160.

- **Idenix Pharmaceuticals Inc.**, of Cambridge, Mass., reported positive Phase I/II data for IDX899, a non-nucleoside reverse transcriptase inhibitor being developed for the treatment of HIV-1 confirming potent antiviral activity and favorable safety profile in treatment-naive HIV-infected patients. No treatment-related serious adverse events were reported for any of the patients receiving IDX899 and no patients discontinued the study. Also, there were no discernable patterns in adverse events between treatment groups and there were no laboratory abnormalities during the treatment period.

- **Incyte Corp.**, of Wilmington, Del., presented positive results from a 28-day Phase IIa trial of INCB18424, its orally available janus-associated kinase inhibitor, in patients with rheumatoid arthritis. Results from the first of four treatment groups, involving 12 treated and 4 placebo patients, demonstrated that the 15 mg twice-daily dose was well tolerated and provided ACR20/50/70/90 response rates of 75 percent/50 percent/25 percent/17 percent, respectively, with responses seen as early as one week. These results suggest that INCB18424 has the potential to be more effective than currently available RA therapies, including the widely used injectable biologicals.

CLINIC ROUNDUP

• **Iomai Corp.**, of Gaithersburg, Md., said data from the company's positive Phase II field study of its travelers' diarrhea vaccine were published online and in the June 14, 2008, edition of *The Lancet*. The study analyzed data from 170 travelers and found that those who received the Iomai patch-based vaccine were statistically significantly less likely to suffer from clinically significant diarrhea than their counterparts who received a placebo. The study found that of the 59 individuals who received the patch-based vaccine, only three suffered from moderate or severe diarrhea, while 23 of the 111 who received a placebo suffered from moderate or severe diarrhea, a 75 percent reduction ($p=0.007$).

• **MethylGene Inc.**, of Montreal, said the first patient was dosed in a Phase I trial evaluating MGCD265 in solid tumors (Trial 101). This is the second Phase I trial with the compound which is being evaluated on different dosing schedules. In this dose-escalating Phase I trial, MGCD265 is administered orally to patients at an initial starting dose of 24 mg/m² daily on a continuous basis for a 21-day cycle. The purpose of this trial is to evaluate the safety, pharmacokinetics, pharmacodynamics, and the maximum tolerated dose of MGCD265 in patients with advanced metastatic or unresectable solid tumors that are refractory to standard therapy.

• **Micromet Inc.**, of Bethesda, Md., and **Medimmune Inc.**, of Gaithersburg, Md., said that the first patient has started treatment in a multi-center, Phase II trial conducted in Germany investigating BiTE antibody blinatumomab (MT103/MEDI-538) in patients with adult acute lymphoblastic leukemia (ALL), a very aggressive form of B cell leukemia. Blinatumomab is a T cell engaging antibody targeting the CD19 antigen, which is only expressed on B cells. This Phase II trial recruits ALL patients with low number of residual tumor cells in their bone marrow after chemotherapy and will test whether blinatumomab can eliminate residual tumor cells and prolong the time to relapse.

• **Opexa Therapeutics Inc.**, of The Woodlands, Texas, said data showed that 27.3 percent of patients receiving Tovaxin, an investigational T-cell vaccination therapy for multiple sclerosis, demonstrated sustained improvement, 59.1 percent had no disease progression and 13.6 percent experienced sustained worsening of disability. During the two-year study period, 72.7 percent of patients remained relapse-free. Tovaxin was well-tolerated throughout the two-year study period. The safety profile revealed only mild-to-moderate injection site reactions and no serious adverse reactions related to T-cell vaccination.

• **OPKO Health Inc.**, of Miami, Fla., said it has acquired exclusive worldwide rights to a novel small molecule agent in Phase II clinical development for the treatment of viral conjunctivitis and other viral infections. The agent, CTC-

96, also known as Doxovir, was developed by Redox Pharmaceutical Corp., of New York. It is a member of a novel drug class that has demonstrated potent anti-viral activity and non-steroidal anti-inflammatory properties with good safety in preclinical and human clinical testing. OPKO expects to initiate in the coming months Phase II trials assessing CTC-96 for the treatment of viral conjunctivitis. Financial terms were not disclosed.

• **Panacos Pharmaceuticals Inc.**, of Watertown, Mass., said Phase IIb data in heavily treatment-experienced patients demonstrated that functional monotherapy with bevirimat, its oral HIV maturation inhibitor, resulted in a mean viral load reduction of 1.26 log₁₀ in patients who had these response predictors and a threshold bevirimat concentration of 20 ug/mL. In the study, 44 heavily treatment-experienced patients were given bevirimat for 14 days as functional monotherapy in escalating dose groups. Data were presented at the International HIV Drug Resistance Workshop in Sitges, Spain.

• **Pharmaxis**, of Sydney, Australia, said it has completed a 12-month Phase III trial evaluating the safety of Bronchitol in 100 subjects with bronchiectasis. This 12-month treatment period was an open label extension to a three-month efficacy trial which showed that Bronchitol improved quality of life and mucus clearance. The objective of the open label extension is to determine the adverse event profile of Bronchitol following prolonged use. Results of the trial will be reported in July.

• **PTC Therapeutics Inc.**, of South Plainfield, N.J., said results from an Israeli Phase IIa extension study evaluating three months of oral PTC124 treatment in adult patients with nonsense-mutation-mediated cystic fibrosis demonstrated statistically significant improvements in the function of the cystic fibrosis transmembrane conductance regulator protein CFTR and a statistically significant mean, 28 percent, decrease in the frequency of cough, one of the most prominent and burdensome CF-related symptoms. Separately, results from a European study evaluating 14-day courses of PTC124 in pediatric patients with nonsense-mutation-mediated CF confirmed the CFTR activity observed in previous short-term studies in adult patients.

• **Repligen Corp.**, of Waltham, Mass., said it plans to initiate a Phase IIb clinical trial of RG2417, an oral formulation of uridine, in patients with bipolar disorder later this year. The 150-patient multicenter, parallel arm placebo-controlled, clinical trial will assess the efficacy and safety of RG2417 on the symptom of depression as measured by the Montgomery-Asberg Depression Rating Scale.

• **Rigel Pharmaceuticals Inc.**, of South San Francisco, has begun two Phase IIb trials of its orally bioavailable Syk inhibitor, R788 (fostamatinib disodium), in patients with rheumatoid arthritis. The trials will evaluate the efficacy of R788 compared to placebo in distinct RA patient groups. Results of the clinical trials are expected to be available in late 2009.

CLINIC ROUNDUP

• **Somaxon Pharmaceuticals Inc.**, of San Diego, presented new subset of data from its completed Phase III clinical development program, which comprised four Phase III trials, evaluating SILENOR, a low-dose formulation of doxepin, for the treatment of insomnia. The new analysis showed that elderly subjects with chronic insomnia taking SILENOR experienced consistent symptom improvement beyond the traditional analyses of quantitative nighttime sleep. Doxepin was well-tolerated in both studies, with side effect profiles comparable between groups, no reports of complex sleep behaviors, amnesia or anticholinergic effects and no next-day residual effects.

• **Tengion Inc.**, of East Norriton, Pa., said the results of a preclinical study of its Neo-Bladder Augment will be featured in the July issue of the *Journal of Urology*. Key findings of the preclinical trial show that the Tengion Neo-Bladder Augment restored baseline urodynamics as early as six months after implantation and led to a structurally and functionally complete regenerated bladder wall as early as nine months. In contrast, scaffold implants alone failed to return to urodynamic baseline by the study termination and failed to regenerate a complete bladder wall.

• **Tolerx**, of Cambridge, Mass., said its lead drug otelixizumab showed remission rates of up to 68 percent in non-obese diabetic mice with new onset of Type I diabetes at five separate doses (5-50 mg). The data showed that T-cell receptor modulation levels varied and reflected drug administration, but did not predict efficacy of treatment. Efficacy is likely dependent on initial beta-cell mass present in new onset diabetic NOD mice, Tolerx said. Tolerx also said otelixizumab showed induction of T regulatory cells, characterized as CD4+FoxP3+ in vitro 7 days after antibody treatment. The increase of T regulatory cells seen in vitro was also seen in vivo in subjects dosed with otelixizumab.

• **Transcept Pharmaceuticals Inc.**, of Port Richmond, Calif., said data showed that within 20 minutes of administration, Intermezzo, a low-dose sublingual formulation of zolpidem, delivered overall bioavailability that was significantly greater than that product by a swallowed Ambien tablet containing a zolpidem dose that was nearly three times higher. Results also showed that, despite that higher bioavailability, subjects receiving Intermezzo had significantly lower zolpidem blood levels four hours after administration compared to those who received the 10 mg Ambien dose. The study involved 36 healthy subjects randomized to receive Intermezzo or Ambien following an overnight fast.

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