

Business & Regulatory Report

Deals & Collaborations:

Debiopharm, Moffitt Cancer Center Sign License Agreement For Small Molecule

Debiopharm Group of Lauzanne, Switzerland, and **Moffitt Cancer Center** signed an exclusive license agreement for the development and commercialization of Debio 0928, a small molecule in early preclinical development that inhibits the protein-protein interaction between Raf-1 (key signalling kinase in the MAP kinase pathway) and Rb (retinoblastoma protein).

Rb acts as a barrier to cell division and proliferation. However, when Raf-1 physically interacts with Rb, it triggers a cascade of signals that eventually overcomes this barrier, thus inducing cellular proliferation. By preventing the interaction between Raf-1 and Rb and blocking the cell cycle, (Continued to page 2)

Oncology Management:

US Oncology Launches iKnowMed Electronic Health Record System

US Oncology Inc. of Houston announces the launch of **iKnowMed** to the open market. iKnowMed is an oncology-specific electronic health record system designed for oncologists.

US Oncology acquired iKnowMed in 2004. The comprehensive collaboration between the oncology physicians since the acquisition has led to a technology excellence that is completely focused on the needs of community oncologists and their patients.

iKnowMed goes beyond delivering standard EHR features by leveraging technology that helps physicians focus on clinical excellence and cost effectiveness in community cancer care. iKnowMed facilitates access to powerful new solutions such as US Oncology's Innovent Oncology program, which provides Level I evidence-based medicine pathways to help oncologists realize the benefits of pay-for-performance. For practices participating in the US Oncology Research network, iKnowMed can match patients to appropriate clinical trials, increasing access to the latest treatment opportunities across the nation.

Other features of iKnowMed include oncology-specific terminology, decision support, outcomes reporting, imaging reports, comprehensive patient history, comprehensive cancer regimen library, dictation and transcription, lab results, detailed cancer diagnosis and staging content, and (Continued to page 5)

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Moffitt, Debiopharm Agree To Develop Small Molecule

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Debio 0928 creates a new strategy in the fight against cancer and is thus a potentially promising novel anti-tumour drug.

Under the agreement, Debiopharm will pay Moffitt an up-front fee, as well as predefined advanced milestone payments during the development of Debio 0928.

“This discovery, made by the collaboration between Drs. Srikumar Chellappan, Said Sebt, and Nicholas Lawrence at Moffitt, is a novel approach to the treatment of cancer,” said Rolland-Yves Mauverny, president and founder of Debiopharm Group. “Being able to de-activate a key signaling kinase like Raf-1, known to be involved in many types of cancer, could open the door to more effective oncology treatments in the future.”

Biomodels LLC of Watertown, Mass., a preclinical research organization specializing in cancer support care, said its customized research program allowed **ActoGeniX NV**, a development stage biopharmaceutical company, to rapidly attain FDA approval for phase 1b clinical trials of AGO13 in cancer patients with oral mucositis.

The FDA approval permits ActoGeniX to initiate a phase 1b trial in six major oncology centers in the

U.S. AGO13 could become the first approved therapy for oral mucositis in patients undergoing treatment of solid tumors or head/neck cancers, according to ActoGeniX.

Exosome Diagnostics Inc. and **DxS Ltd.** announced that they will collaborate on the development of blood-based companion diagnostics for key cancer gene mutations, such as KRAS, BRAF and EGFR.

The collaboration will use DxS’ Scorpions real-time PCR Mutation Test Kits in conjunction with ExosomeDX’s xOS technology which harvests high-quality nucleic acids from blood exosomes.

The collaboration will initially focus on developing blood-based measurement of KRAS, BRAF, EGFR and other key mutations for predicting patient response to targeted therapies, the companies said.

Palkion Inc. of San Diego said it has initiated preclinical development studies for its orally available anemia therapeutic candidate that modulates the Hypoxia-Inducible Factor Prolyl Hydroxylase (HIF-PH) enzyme system.

In February 2008, Palkion was founded when a novel drug discovery and development firm, **CrystalGenomics** (KOSDAQ: CRYSTAL [A083790]) and the US-based venture capital firm, **ProQuest Investments**, formed a new joint venture entity.

Under the strategic alliance, CrystalGenomics is receiving upfront and research funding for two years from Palkion, in addition to development and sales milestone payments of potentially more than \$200 million. CrystalGenomics’ role is to use its unique structure-based drug discovery platform to identify novel drug candidates while Palkion oversees the clinical development.

All currently available Erythropoietins are injectables.

Morphotek Inc. of Exton, Penn., announced a research collaboration agreement with **Synageva BioPharma Corp.** to express and develop therapeutic monoclonal antibodies for the potential treatment of various forms of cancer and infectious disease.

Morphotek is a subsidiary of Eisai Corporation of North America.

Under the agreement, Synageva will use its proprietary Synageva Expression Platform technology and its expertise to produce and develop a therapeutic monoclonal antibody. SEP is an integrated platform of proprietary systems for protein production, processing



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and purification.

Through the use Morphodoma technology, Morphotek develops optimized antibodies, including antibodies optimized for affinity and/or titer, for therapeutic applications and high-titer manufacturing cell lines. The company has assembled a portfolio of lead human and humanized antibodies to antigens associated with cancer, neovascular, inflammatory and infectious disease. The antibodies within the company's pipeline are targeted against antigens licensed from its collaborative partners.

Regulatory Approvals & Applications: **CHMP Supports Approval Of Javlor For Urothelial Cancer**

Laboratoires Pierre Fabre of Castres, France, said the Committee for Medicinal Products for Human Use, has issued a positive opinion supporting approval and is recommending to grant marketing authorisation for Javlor as monotherapy in metastatic treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract after failure of a prior platinum-containing regimen.

CHMP is the scientific advisory committee of the European Medicines Agency.

CHMP has issued a positive opinion based on two phase II study results and on the only phase III randomized study ever conducted in the indication of metastatic treatment of bladder cancer after failure of a prior platinum-containing regimen.

After the EMEA will grant the marketing authorization, Javlor will become the first monotherapy approved in Europe for the treatment of adult patients with advanced or metastatic transitional cell carcinoma of the urothelial tract after failure of a prior platinum-containing regimen, where the expectation is important for both oncologists and patients, the company said.

Discovered by scientists at the Pierre Fabre Research Center, vinflunine is a new bi-fluorinated MTI (Microtubule inhibitor) obtained by chemistry exploiting the reactivity of Vinca scaffold in superacidic media. Such strategy, finalized in collaboration with experts at the University of Poitiers (France), enabled the selective introduction of two fluorine atoms in a part of that structure previously inaccessible by classic chemistry, thereby leading to the first bi-fluorinated vinca alkaloid.

Aphera Inc. of Scottsdale, Ariz., said it has reached an agreement with FDA under a Special

Protocol Assessment for its planned phase III clinical trial of the company's lead drug, NeuVax.

The SPA is a written agreement between the trial's sponsor and the FDA regarding the design, endpoints, and planned statistical analysis of the Phase III trial to be used in support of a Biologics License Application.

The multicenter, double-blind, randomized pivotal trial is expected to enroll 700 women diagnosed with HER2/neu-expressing tumors and who have completed standard of care consisting of surgery, chemotherapy and radiotherapy. Women must have a common HLA haplotype (HLA-A2 or -A3) and must agree to be followed for 5-10 years. The primary endpoint of the study is disease-free survival (DFS) as determined by disease recurrence or death from any cause, and the first analysis of the data will occur after 70 recurrence events or approximately 3 years from the start of the study.

Cell Therapeutics Inc. of Seattle (NASDAQ and MTA: CTIC) said it has completed the submission of the New Drug Application to FDA for pixantrone to treat relapsed or refractory, aggressive non-Hodgkin's lymphoma.

CTI requested priority review, which if granted could lead to an approval decision from the FDA in the fourth quarter of 2009. Pixantrone is currently available in Europe on a named-patient basis.

"This is a major milestone for CTI and is the cornerstone of a turnaround strategy for us in meeting our goals of becoming a profitable operating business," said James A. Bianco, CEO of CTI.

CTI's EXTEND clinical trial was a phase III single-agent trial of pixantrone for patients with relapsed or refractory, aggressive NHL who received two or more prior therapies and who were sensitive to treatment with anthracyclines. The trial enrolled 140 patients and patients were randomized to receive either pixantrone or another single-agent drug currently used for the treatment of this patient population as selected by the physician.

CTI previously announced that its pivotal PIX 301 EXTEND trial had achieved its primary endpoint with patients randomized to treatment with pixantrone achieving a significantly higher rate of confirmed (CR) and unconfirmed complete remissions (CRu) compared to patients treated with standard chemotherapy (14 out of 70 patients (20.0%) for the pixantrone arm compared to four out of 70 patients (5.7%) for the standard chemotherapy arm, $p=0.02$). No patient (0%) in the standard chemotherapy arm achieved a confirmed complete remission compared to eight out of 70 (11%)

of pixantrone recipients. Pixantrone treatment also significantly increased the overall response rate (ORR) (26 out of 70 (37.1%) for the pixantrone arm compared to ten out of 70 (14.3%) for the control arm, $p=0.003$). Additionally, pixantrone experienced a statistically significant improvement in median progression-free survival (PFS), compared with other single-agent chemotherapeutic agents (4.7 months vs. 2.6 months, $p=0.007$, respectively). PFS, CR/CRu and ORR were determined by an independent assessment panel that was blinded to the treatment assignments.

The most common grade 3/4 adverse event observed on the pixantrone arm was neutropenia in 41.2% of patients versus 19.4% on the comparator arm. However, the incidence of grade 3/4 febrile neutropenia was only 7.4% versus 3.0% in the comparator arm. Grade 3/4 infections had a similar incidence in both study arms (18% vs. 13%). Although the grade 3/4 cardiac disorder was similar among the two treatment groups (1.5% vs. 1.5%), there was a slightly higher incidence of serious cardiac disorders in patients treated with pixantrone than among patients who received comparator agents (8.8% vs. 4.5%). Events considered cardiac disorders included cardiac arrest, congestive heart failure, myocardial infarction, cyanosis, pericardial effusion, and tachycardia.

Pixantrone (BBR 2778), is a major groove binder with an aza-anthracenedione molecular structure that differentiates it from the anthracyclines and other related chemotherapy agents. Anthracyclines are the cornerstone therapeutic for the treatment of lymphoma, leukemia, and breast cancer. Although they are sufficiently effective to be used as first-line (initial) treatment, they cause cumulative heart damage that may result in congestive heart failure many years later. As a result, there is a lifetime limit of anthracycline doses and most patients who previously have been treated with an anthracycline are not able to receive further anthracycline treatment if their disease returns. It also can be administered through a peripheral vein rather than a central implanted catheter as required for other drugs in this class.

Oncogenex Pharmaceuticals Inc. (NASDAQ: OGXI) of Bothell, Wash., said it has reached an agreement with FDA via the special protocol assessment process on an amendment to the design of a phase III registration trial of OGX-011 for castrate resistant prostate cancer.

FDA has agreed on modifications to the study population of a previously reviewed phase III trial

featuring survival as the primary endpoint. The study population has been modified to evaluate patients receiving first-line chemotherapy, rather than those receiving second-line chemotherapy. FDA agreed that the amended protocol adequately addresses the objectives necessary to support a regulatory submission.

“We are now ready to proceed with two phase III trial designs from the FDA via the SPA process, one in first-line and one in second-line treatment of advanced prostate cancer,” said Scott Cormack, president and CEO. “The trial for first-line treatment evaluates overall survival benefit for OGX-011 while the trial for second-line treatment evaluates for a durable pain palliation benefit. Based on the robustness of the OGX-011 survival benefit observed in the randomized phase II trial for first-line docetaxel treatment, we felt evaluating both of these patient populations, as well as both endpoints, in our phase III trials better positions the availability of OGX-011 treatment to a larger number of men with prostate cancer.”

The revised trial will be a randomized, controlled, international study in 800 men with metastatic CRPC who are in need of first-line chemotherapy. Patients will be randomized to receive treatment with either OGX-011 and docetaxel/prednisone or docetaxel/prednisone alone. The primary endpoint of the study will be overall survival. It is expected that approximately 80 sites, primarily from the U.S. and Canada, will participate in this study.

OGX-011 is designed to inhibit the production of clusterin, a protein that is associated with cancer treatment resistance, and has completed phase 2 clinical trials in prostate, lung and breast cancer.

OGX-011 has received Fast Track designation from the FDA for the treatment of progressive metastatic prostate cancer in combination with docetaxel.

Clinical Trials:

Oncothyreon, Merck Begin Phase III Trial Of Stimuvax

Oncothyreon Inc. (NASDAQ: ONTY) (TSX: ONY) of Seattle said **Merck KGaA** of Darmstadt, Germany, has initiated a global phase III trial of Stimuvax (BLP25 liposome vaccine, L-BLP25) in patients with hormone receptor-positive, locally advanced, recurrent or metastatic breast cancer. Stimuvax is an investigational therapeutic cancer vaccine being developed by Merck KGaA under a license agreement with Oncothyreon.

The phase III trial, named STRIDE (STimulating immune Response In aDvanced brEaSt cancer),

is anticipated to enroll more than 900 patients at approximately 180 sites in over 30 countries including North America, Europe, Asia and Australia.

Patients with estrogen receptor-positive and/or progesterone receptor-positive, non-resectable locally advanced, recurrent or metastatic breast cancer receiving hormonal therapy will be randomized to receive either Stimuvax or a placebo in a 2:1 ratio. The primary endpoint of STRIDE is progression-free survival. Overall survival, quality of life, tumor response and safety will also be assessed in this study.

Stimuvax is an investigational therapeutic cancer vaccine designed to induce an immune response to cancer cells that express MUC1, a glycoprotein antigen widely expressed on common cancers. MUC1 is over-expressed on many cancers such as lung cancer, breast cancer, prostate cancer and colorectal cancer. Stimuvax is thought to work by stimulating the body's immune system to identify and destroy cancer cells expressing MUC1.

In addition to STRIDE, Merck KGaA currently is conducting a global phase III trial of Stimuvax known as START (Stimulating Targeted Antigenic Responses To NSCLC). START is a randomized, double-blind, placebo-controlled study that will evaluate patients with documented unresectable stage III NSCLC who have had a response or stable disease after at least two cycles of platinum-based chemo-radiotherapy. START is expected to enroll more than 1,300 patients in over 30 countries. For more information on the START trial log on to www.nslclstudy.com or www.clinicaltrials.gov.

Lixte Biotechnology Holdings (OTC Bulletin Board: LIXT) announced that investigators of the National Institute of Neurological Disorders and Stroke and the National Cancer Institute and Lixte reported that its novel compound, LB-1.2, enhances the effectiveness of two standard chemotherapy drugs in mouse models of human cancers.

This research is being conducted under a Cooperative Research and Development Agreement between NINDS and Lixte. The report was published online in the early edition (June 29) of the Proceedings of the National Academy of Science. The print version will appear July 14.

John Kovach, president and CEO of Lixte, said "LB-1.2 exerts anti-cancer activity directly on the cancer cell and, more dramatically, by preventing cancer cells from recovering from DNA-damage produced by standard anti-cancer drugs. In mouse models, LB-1.2 plus Temozolomide caused complete regression

without recurrence in 50 % of animals bearing tumors of human glioblastoma multiforme (GBM), the most common and aggressive brain tumor of adults, and also, marked regression of neuroblastoma, the most common cancer of children. Temozolomide, the standard drug for the treatment of patients with GBM, by itself caused regression but with recurrence of all tumors."

Kovach added "that, since LB-1.2 has a biochemical action similar to an older drug used for anticancer treatment for many years in China, we are cautiously optimistic that LB-1.2 will be well tolerated by cancer patients and hopefully, will potentially be as effective as it is in animal models of human cancer. We believe that adding LB-1.2 may be a general method for improving the effectiveness of several standard anticancer drugs not only against tumors of the brain and neural tissue but also against other cancers sensitive to drugs that work by damaging DNA. Safety, of course, must be demonstrated first in animal studies and subsequently in Phase I clinical trials before evaluation of therapeutic effectiveness can be assessed against different cancer types in patients."

Yaupon Therapeutics, a privately held specialty pharmaceutical company based in Radnor, Penn., said it has completed enrollment for a phase II trial of Clearazide in early-stage cutaneous T-cell lymphoma.

The study, which is being conducted under a Special Protocol Assessment with the FDA, has enrolled 260 patients in 13 cancer centers in the US. The study is focused on stages 1-2a. The randomized, double-blind, controlled clinical study is the largest ever undertaken involving patients with cutaneous T-cell lymphoma, the company said.

Clearazide is a topical form of nitrogen mustard.

Oncology Management: **US Oncology Launches iKnowMed Electronic Record**

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practice efficiencies.

"As America's healthcare system moves toward a pay-for-performance environment, in which higher-performing doctors receive preferred compensation, it is essential that oncology practices accurately document and report outcomes while achieving greater efficiency," says Cindy Chavez, vice president of iKnowMed. "iKnowMed provides solutions that will help drive this clinical excellence."

iKnowMed provides physicians with online access

to patient records 24 hours a day, 7 days a week. This allows treatment decisions to be made from anywhere at any time, without the need of a hardcopy patient record. Patient safety is enhanced by eliminating handwritten notes and orders, minimizing misinterpretations, and the system detects possible medication conflicts, generating a safety alert to the attending oncologist and staff. The system also helps practices stay current on billing as charge codes, billable units, primary diagnosis codes and billable drug waste for each visit are calculated, allowing staff to spend more time focusing on patient care.

Community oncologists across the nation are invited to attend a special webinar focusing on the Medicare Health Information Technology Stimulus at 2 pm EDT, July 10. Sponsored by iKnowMed, this webinar will feature a status report of standards for qualified EHRs and meaningful use requirements. To register for the webinar, visit www.opspharmacist.com/HITStimulus.

American Society of Clinical Oncology has commissioned a study, funded by Susan G. Komen for the Cure, to find out how non-physician practitioners, such as nurse practitioners and physician assistants, can provide vital services to cancer patients as part of continued efforts to address projected future oncology workforce shortages.

The study, to be conducted for ASCO by Oncology Metrics, will be a comprehensive analysis of how oncology practices provide patient care, through collaborative care teams made up of oncologists, nurse practitioners, and physician's assistants, ASCO said.

The study of up to 40 private and hospital-based oncology practices will specifically examine the satisfaction, efficiency and productivity of each collaborative care team in order to establish "best practices."

"ASCO and the Workforce Advisory Group continue to explore a variety of solutions to the anticipated oncology workforce shortage," said ASCO President Douglas Blayney. "We believe collaborative practice models will help cancer care professionals cope with the realities of having too many patients and not enough doctors."

The number of Americans aged 65 and older will double by 2030 as baby boomers age. At the same time, people are living longer with cancer, requiring ongoing care. Cancer specialists will struggle to handle the patient load: a 2007 ASCO workforce study said demands for visits will leap by 48 percent by 2020, but the number of oncologists will fall 4,000 short.

ASCO's Workforce Advisory Group identified the increased use of non-physician practitioners in an oncology practice as a possible way to narrow the gap between supply and demand for oncology services. According to ASCO's 2007 Workforce Study, 56 percent of oncologists work with nurse practitioners or physician's assistants, and providers who use nurse practitioners/ physician's assistants have higher visit rates than those who do not.

The practices being included in the survey will vary in size, patient population, and location. "This study will enable us to address the unique problems oncology practices are facing across the country and potentially offer some solutions. Obviously, a small rural practice will have different needs than a large practice in an inner city," said Dean Bajorin, co-chair of ASCO's Workforce Advisory Group.

Some of the services that nurse practitioners and physician's assistants provide in a practice setting include ordering and administering routine chemotherapy, as well as patient education and counseling.

The study results are expected to be released in early 2011, ASCO said. This study is part of a collaboration between the ASCO Cancer Foundation, ASCO and Komen for the Cure, in which Komen is providing \$10 million in support of projects and programs designed to improve the quality of cancer care in the U.S.

Varian Medical Systems Inc. of Palo Alto, Calif., (NYSE: VAR) said it has acquired the assets of Houston-based **IKOEmed** and **IKOEtch**, privately-owned suppliers of software used in the planning of radiotherapy and radiosurgery treatments.

The acquisition enables Varian to offer hospitals and clinics an additional software tool to automate and accelerate the most time-consuming portion of the treatment planning process. Varian is paying approximately \$2.2 million plus an additional amount based on achievement of specified milestones to acquire the IKOE assets.

The software is designed to achieve greater than 50 percent reduction in the contouring portion of the radiotherapy treatment planning process, which typically takes anywhere from 30 minutes to 4 hours. It automates the contouring process by matching patient images with pre-contoured images from an expert database created by renowned radiation oncologists. This eliminates the need for clinicians to manually outline between 10 and 20 organs in each of anywhere from 100 to 200 images of a patient's disease site.