

Business & Regulatory Report

Product Approvals & Applications:

FDA Approves Mozobil With G-CSF For Autologous Stem Cell Transplantation

FDA granted marketing approval for Mozobil (plerixafor injection), used in combination with granulocyte-colony stimulating factor to mobilize hematopoietic stem cells for autologous transplantation in non-Hodgkin's lymphoma and multiple myeloma.

Mozobil is sponsored by **Genzyme Corp.** (NASDAQ: GENZ) of Cambridge, Mass. The product has also been granted orphan drug designation.

"Mozobil is an important advancement in the treatment of patients with certain types of cancer who require a stem cell transplant," said John DiPersio, professor, Washington University, St. Louis. "This product should
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Oncology Management:

Co-Payments To Rise As Access To Drugs Tightens For Patients On Medicare Part D

Cancer patients enrolled in Medicare Part D plans will spend more on co-payments and face increased restrictions on access to these drugs in 2009, a study by **Avalere Health** and the **American Cancer Society** Cancer Action Network shows.

The research found that over the past four years Medicare stand-alone prescription drug plans have been shifting name-brand oral cancer drugs to higher formulary tiers.

In 2009, the large majority of PDPs placed name-brand oral oncology products—including Gleevec, Sutent, Tarceva, Thalomid, and Tykerb—on specialty tiers that require cost sharing of 26 percent to 35 percent for each prescription. For example, 84 percent of PDP enrollees are in plans that put Gleevec on their most expensive tiers (fourth or higher) in 2009, up from 39 percent in 2006.

"This pattern of shifting the costs of branded medications to patients needs to be scrutinized, especially in light of the economic difficulty being experienced by so many seniors," said Valerie Barton, vice president at Avalere Health.

"Shifts in drug coverage can limit access to treatment for people with cancer, significantly reducing their treatment options or even requiring a stoppage of treatment," said Daniel Smith, president of ACS CAN. "We urge policymakers to pay close attention to how these changes impact people with
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Mozobil Approved For NHL, Multiple Myeloma Transplants

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become an integral part of the treatment regimen for transplantation because of the benefits it offers to patients, physicians and transplant centers.”

Mozobil mobilizes hematopoietic stem cells from the bone marrow into the bloodstream where they can be collected, making it more likely for cancers to proceed to transplant, the company said.

In pivotal studies of the agent, 59 percent with NHL who received Mozobil and G-CSF collected the target number of 5 million stem cells/kg of body weight in four or fewer apheresis sessions compared with 20 percent with placebo. The median number of days to reach the target cell count was three days for the Mozobil group and not evaluable in the placebo group. Seventy-two percent with MM who received the drug and G-CSF collected the target number of at least 6 million stem cells/kg of body weight in two or fewer apheresis sessions compared to 34 percent with placebo. The median number of days to reach the target cell count was one day for the Mozobil group and four days for the placebo group. The target numbers of stem cells in the pivotal studies were chosen based on literature that suggests that reaching the targets can help to facilitate engraftment.

Updated 12-month follow-up findings showed that graft durability rates for the Mozobil plus G-CSF

and placebo plus G-CSF arms were comparable, the company said.

In addition to its expected benefits in NHL and MM, Mozobil may offer economic benefits for transplant centers. The product could decrease the number of apheresis days and provide transplant centers with predictable and efficient use of the apheresis center, the company said. The treatment also could reduce the number who require a second mobilization procedure due to a failure to mobilize sufficient numbers of cells with current therapy of G-CSF alone.

Genzyme said it will commercialize Mozobil in the U.S. through a blood and marrow transplant sales force, part of the Transplant and Oncology business unit.

The company said it has submitted an application in Europe for approval of Mozobil and expects approval of the product in the second half of 2009.

Mozobil, a small molecule CXCR4 chemokine receptor antagonist, increases the number of stem cells in circulation in the blood in non-Hodgkin's lymphoma and multiple myeloma.

ImClone Systems Inc. (NASDAQ: IMCL) and **Bristol-Myers Squibb Co.** (NYSE: BMY) said they submitted an application to FDA to broaden the use of Erbitux (cetuximab) to include first-line treatment of advanced non-small cell lung cancer in combination with platinum-based chemotherapy (cisplatin/vinorelbine).

BMS and ImClone, co-owners of Erbitux in North America, said ImClone would be notified in February whether the submission would be accepted.

The submission is based on data from the pivotal, multinational FLEX (First-line in Lung cancer with Erbitux) phase III study which demonstrated that the addition of Erbitux to cisplatin/vinorelbine significantly increased overall survival in the first-line treatment in advanced NSCLC when compared with cisplatin/vinorelbine alone, the companies said. The improvement in overall survival, the primary endpoint, was observed across all histological subtypes, performance status, age, previous smoking history, and gender groups, the companies said.

The FLEX study, conducted by Merck KGaA, of Darmstadt, Germany, enrolled 1,100 Stage IIIB with malignant pleural effusion or stage IV NSCLC with no prior chemotherapy. Treatment with Erbitux in combination with cisplatin/vinorelbine, prolonged median overall survival by 1.2 months when compared to cisplatin/vinorelbine treatment alone (11.3 months vs. 10.1 months) with a hazard ratio of 0.871 [95 percent Confidence Interval (CI) = 0.762-0.996], $p=0.044$.



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Grade 3/4 adverse events were reported in 91 percent in the Erbitux plus cisplatin/vinorelbine arm compared with 86 percent in the cisplatin/vinorelbine alone arm, the companies said. Grade 3/4 adverse events reported in the Erbitux plus cisplatin/vinorelbine versus cisplatin/vinorelbine alone arms included: neutropenia (53 percent vs 51 percent), febrile neutropenia (22 percent vs 15 percent), anemia (14 percent vs 17 percent), grade 3 acne-like rash (10 percent vs <1 percent), diarrhea (5 percent vs 2 percent), and infusion-related reactions (4 percent vs <1 percent).

ImClone also said it has received FDA approval for multi-product biologics production in its BB50 manufacturing facility.

“The multi-product FDA approval of BB50 significantly enhances ImClone’s operational flexibility as we scale up production of our pipeline of proprietary antibodies for the growing number of phase II and phase III trials that will be commencing in the next year,” said Richard Crowley, senior vice president, biopharmaceutical operations at ImClone.

The 250,000-square-foot multi-suite BB50 facility received FDA approval to manufacture Ebitux (cetuximab) in 2007, the company said. Together with the BB36 manufacturing facility, ImClone said it has a total production volume capacity of up to 140,000 liters at its Branchburg, N.J., campus. This is among the largest antibody manufacturing capacities in the biotechnology industry and is a component of the ImClone fully integrated operations supporting the development and commercialization of antibodies, the company said.

Three antibodies in the ImClone pipeline are now entering late stage clinical development, with the first beginning a phase III trial earlier this year. IMC-1121B, which targets the vascular endothelial growth factor receptor-2, is in phase II studies for metastatic melanoma, liver, non-small cell lung, ovarian, prostate and renal cancers. A phase III study of the antibody in metastatic breast cancer is beginning enrollment, and phase III testing in gastric cancer may begin in 2009. IMC-A12 targets the insulin-like growth factor-1 receptor is in phase II studies in breast, prostate, pancreatic, colorectal, liver and head and neck cancers, as well as sarcoma. And IMC-11F8, a fully human IgG1 monoclonal antibody targets the epidermal growth factor receptor. IMC-11F8 is in phase II testing for metastatic colorectal cancer, the company said.

Kiadis Pharma of Amsterdam said FDA has granted Orphan Drug Designations to Reviroc for two

types of Non-Hodgkin Lymphoma: One ODD is for diffuse large B-cell lymphoma and the other one is for follicular lymphoma.

The agent is under development to eliminate blood cancer cells in autologous transplants for end stage blood cancer, the company said.

The Committee for Medicinal Products for Human Use, a unit of the European Medicines Agency has adopted a positive opinion and is recommending to grant a marketing authorization for Firmagon (degarelix), a GnRH receptor antagonist for advanced, hormone-dependent prostate cancer.

The agent is sponsored by **Ferring Pharmaceuticals**, a Swiss biotherapeutics company.

In phase III studies degarelix produced a significant reduction in levels of testosterone, within three days in more than 96% of study patients. Testosterone plays a major role in the growth and spread of prostate cancer cells.

The data show that degarelix provided an extremely fast effect on testosterone levels, close to the immediate effect achieved with orchidectomy, the company said.

The phase III study compared monthly administration of degarelix with monthly luteinizing hormone releasing-hormone agonist leuprorelin’s 7.5 mg in a 12-month randomised, open-label, parallel-group study in prostate cancer patients. In comparison to leuprorelin, degarelix suppressed serum testosterone and Prostate Specific Antigen significantly faster. In addition, degarelix was able to sustain these low levels during the entire 12-month study, the company said.

By day three of the study, testosterone levels were suppressed to 0.5ng/mL in 96.1% of patients in the degarelix arms of the study compared to 0% in the leuprorelin arm. By day 14, 100% of patients in the degarelix arms achieved suppression of testosterone levels at =0.5ng/mL compared to 18.2% in the leuprorelin arm.

After 14 days of treatment, PSA levels had declined in the degarelix treated patients by a median of 64%, while patients who were administered leuprorelin saw an 18% decline. Both treatments were well tolerated and showed similar side effect profiles. The most common side effects are hot flushes, injection site pain, injection site erythema,

increased weight, nasopharyngitis, fatigue and back pain.

Ferring said it plans to launch the agent in Europe in the first quarter of 2009 and is also

awaiting an imminent FDA decision on approval for commercialisation in the US. It is expected that commercialisation in other key global markets will follow during 2009 and 2010 once approval is received from the relevant local regulatory authorities.

Oncology Management: **Medicare Shifting Drug Costs To Patients, Analysis Finds**

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cancer. At the same time, it is critical that people with cancer understand their health coverage and the potential hurdles that may impact their treatment.”

In addition to changing tier placement, PDPs in 2009 are increasing their use of prior authorization to control access to branded cancer drugs. The Avalere-ACS CAN research found that Gleevec had the largest increase in the number of PDPs requiring prior authorization, with 70 percent of plans requiring it, up from 35 percent in 2006. Tarceva had the next highest increase, with 62 percent of plans requiring prior authorization in 2009, up from 35 percent in 2006. Thalomid was next, with 68 percent of plans requiring prior authorization in 2009, up from 43 percent in 2006.

Geography and plan choice influence how much a patient spends out-of-pocket in Medicare Part D. Avalere and ACS CAN modeled hypothetical drug regimens for women with breast cancer and found that total out-of-pocket costs for a woman enrolled in AARP MedicareRx Saver in Florida will be \$1,985, while total out-of-pocket costs for beneficiaries enrolled in Humana PDP Standard in California will average about \$2,551.

Avalere said it continues to analyze Medicare drug benefit data. Since the inception of the Medicare drug program, Avalere has used its proprietary DataFrame database to track trends in drug pricing, plan strategy and structure, and the beneficiary experience.

ACS CAN is an advocacy affiliate of the American Cancer Society.

Clinical Trials: **Merck Gives \$1M To NCCN For Clinical Trials Of Zolinza**

National Comprehensive Cancer Network of Fort Washington, Penn., said it received a \$1 million research grant from Merck & Co. Inc. to conduct clinical trials on combinations of its cancer agent Zolinza

(vorinostat), with radiation/chemoradiation in selected locally advanced non-metastatic cancers and areas of unmet medical need.

Vorinostat, a histone deacetylase inhibitor, is used for cutaneous T-cell lymphoma when the disease persists, worsens, or returns during or after treatment with other systemic therapies, the company said. In preclinical studies, the drug has shown activity in a range of cancers and shows promise when used in combination with chemotherapy and other targeted anti-cancer agents.

The research will focus on combinations of vorinostat in selected locally advanced non-metastatic cancers including non-small cell lung cancer, head and neck cancer, pancreatic adenocarcinoma, and brain metastases from a solid tumor with an emphasis on lung cancer, the company said.

“Vorinostat preferentially enhances the killing of tumor cells induced by radiation therapy,” said Jose Garcia-Vargas, senior medical director, oncology clinical research, Merck Research Labs.

The NCCN Oncology Research Program facilitates all phases of clinical research by identifying clinical investigators and initiating trials at NCCN member institutions.

Aposense Ltd. of Petach-Tikva, Israel, said it has begun a phase II, multi-center study of its [18F]-ML-10 compound for molecular imaging of apoptosis at Memorial Sloan-Kettering Cancer Center, following approval by its Institutional Review Board.

The study would evaluate the safety and efficacy of the compound in early assessment of response of metastatic brain tumors to high-dose, single-fraction radiotherapy, the company said.

“Functional imaging tools can identify biological changes that occur in a tumor as a result of treatment. said Kathryn Beal, radiation oncologist at Memorial Sloan-Kettering Cancer Center and principal investigator. “The changes may act as early surrogate markers, which can significantly improve the way we treat patients.”

The 30-to-60-patient study would detect response to treatment of brain metastases, within several days after treatment, the company said. Apoptosis will be observed by mapping the uptake of [18F]-ML-10 within the tumor by using a PET scan, to be performed prior to treatment and at two other points within one week after treatment. Changes in the [18F]-ML-10 uptake will be compared with changes in tumor size two months after treatment according to MRI. The study end-points include assessment of apoptotic changes occurring

within days after treatment, and the accuracy of these changes in predicting treatment results, the company said.

Cylene Pharmaceuticals of San Diego announced the initiation of a phase II trial of quarfloxin (CX-3543) in patients with carcinoid/neuroendocrine tumors (C/NET), which are malignant cancers arising from neural crest cells.

In the open-label study, quarfloxin will be administered to patients with low or intermediate grade C/NET, including those receiving concomitant treatment with a stable dose of octreotide. This multi-centered study will include an assessment of improvements in patients' symptoms and biochemical markers, in addition to RECIST tumor response measurements, the company said. The study is expected to enroll up to 25 patients at several leading cancer centers.

"Quarfloxin has demonstrated potent in vivo efficacy against a broad range of tumors and a considerable therapeutic window in preclinical antitumor models, and has a unique profile of concentrating in neural crest tissues," said Daniel Von Hoff, Cylene co-founder and vice president, medical affairs.

Quarfloxin is a small-molecule targeted cancer therapeutic derived from the validated fluoroquinolone class of drugs. Rationally designed to selectively inhibit ribosomal RNA biogenesis in cancer cells, quarfloxin disrupts the interaction between the Nucleolin protein and a G-quadruplex DNA structure in the ribosomal DNA template, a critical interaction for rRNA biogenesis and one that is amplified in cancer cells. As a result, quarfloxin selectively induces apoptotic cell death in cancers, the company said.

Eisai Corp. of Woodcliff Lake, N.J., said it initiate the first clinical trial evaluating Dacogen (decitabine for injection) compared to Vidaza (azacitidine) in intermediate-1, intermediate-2 or high-risk myelodysplastic syndromes.

The head-to-head trial will directly compare the agents with a primary endpoint of complete response rate, including marrow complete response, the company said.

"Previous to the introduction of the hypomethylating agents, supportive care was the only treatment option for living with MDS," said Hagop Kantarjian, chairman of the Leukemia Department and professor of medicine, University of Texas M.D. Anderson Cancer Center. "This study, for the first time, will provide physicians with important information to understand how these two

agents compare when treating patients with MDS, who have a generally poor prognosis, with life expectancies shorter than those with lung cancer."

The randomized, multi-center, open-label 228-patient study in intermediate-1, intermediate-2 and high-risk MDS, will be randomized on a 1:1 ratio to either Dacogen or Vidaza, the company said. Each treatment arm will be stratified by IPSS risk group and type of MDS, primary vs. secondary.

"Findings could clarify the fundamental differences between Dacogen and Vidaza and ultimately help clinicians with treatment selection," said Anastasios Raptis, co-director, Myelodysplastic Syndrome Program, attending, Stem Cell Transplant Program and clinical assistant professor of medicine, University of Pittsburgh School of Medicine. "The study takes into account recent data that suggest that treatment should continue for as long as they receive clinical benefit or until their disease progresses."

Dacogen was approved by FDA in 2006 for myelodysplastic syndromes including previously treated and untreated, de novo and secondary MDS of all French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, chronic myelomonocytic leukemia), and Intermediate-1, Intermediate-2 and High-Risk International Prognostic Scoring System groups.

EntreMed Inc. (NASDAQ: ENMD) of Rockville, Md., said it has met the primary endpoint for the efficacy portion of the open label phase I/II study of MKC-1 in combination with pemetrexed (Alimta) in non-small cell lung cancer.

The study was designed to first evaluate a dose of MKC-1 to be used safely in combination with Alimta. Patients were subsequently enrolled into the phase II portion where the primary endpoint was tumor response. The primary endpoint has been met and EntreMed said it is considering options for further studies in NSCLC. Options include the continuation of the current single arm study or a randomized phase II study in the same population.

MKC-1 is an orally-active cell cycle inhibitor with in vitro and in vivo efficacy against a range of solid tumor cell lines, including multi-drug resistant cell lines, the company said. Data from studies with MKC-1 demonstrate broad-acting antitumor effects, showing tumor growth inhibition or regression in multiple preclinical models, including paclitaxel-resistant models.

The agent inhibits mitotic spindle formation, prevents chromosome segregation in the M-phase of the cell cycle, and induces apoptosis, the company said. Furthermore, MKC-1 inhibits the Akt-mTOR signaling pathways, which may occur through inhibition of the mTOR/riCTOR pathway.

ImClone Systems Inc. (NASDAQ: IMCL) of New York, N.Y., said it has begun enrollment in a randomized phase II trial of IMC-A12 in previously treated HER2-expressing locally advanced or metastatic breast cancer.

IMC-A12 is an IgG1 anti-insulin-like growth factor-1 receptor (IGF-1R) monoclonal antibody.

The primary objective is to evaluate the antitumor activity of the combination of capecitabine and lapatinib with and without IMC-A12 in HER2-expressing stages IIB, IIC, or IV breast cancer that has progressed on trastuzumab-containing treatment, the company said. The study is being conducted by the North Central Cancer Treatment Group, sponsored by NCI.

NCCTG, which is comprised of a network of more than 1,000 community-based cancer treatment clinics in the U.S., Canada and Mexico that work with Mayo Clinic, also is working with other cooperative groups to recruit patients through the NCI Cancer Therapy Study Unit. The study is one of 10 phase I and II trials of the drug sponsored by the NCI Cancer Therapy Evaluation Program.

“The study of IMC-A12 is a rationally designed study based on preclinical evidence suggesting that there are interactions between the HER2 and IGF-1R that may be exploited to improve treatment outcome for women with HER2-expressing breast cancer,” said Eric Rowinsky, chief medical officer and executive vice president of ImClone. “The NCCTG is seeking to determine if the anticancer activity of the combination with lapatinib and capecitabine, which is an approved treatment for HER2-expressing breast cancer that is no longer responsive to trastuzumab, can be improved by the addition of IMC-A12.”

The 154-patient study of IMC-A12 will be randomized for either capecitabine and lapatinib (one-third) or the same treatment plus IMC-A12 (two-thirds), the company said. Treatment in both arms will be continued as long as benefit is shown. The primary endpoint is progression-free survival.

“Research asserts that HER2-positive breast tumors may resort to the IGF-1R pathway as an adaptive growth mechanism to therapies that target the HER2 cell proliferation mechanism,” said Paul Haluska,

assistant professor of oncology at Mayo Clinic and lead scientist on the phase II study. “The IGF-1R pathway is a key mechanism of resistance in cancers that adapt to HER2-targeted therapy, as well as chemotherapy. Now that we have a therapeutic agent in IMC-A12 to block IGF-1R, we are able to conduct this study to determine if co-inhibiting IGF-1R and HER2 in combination with the chemotherapy agent capecitabine will benefit patients with HER2-positive breast cancers.”

Light Sciences Oncology Inc. of Bellevue, Wash., said it has completed enrollment in a global phase III trial of Light Infusion Therapy for unresectable hepatocellular carcinoma.

The two-armed, randomized 200-patient trial is taking place at sites in the Philippines, Korea, India, Malaysia, Thailand, Hong Kong, Singapore, Serbia, Poland, Croatia, and Italy, the company said. The primary endpoint is to assess survival with Litx therapy treatment versus standard-of-care therapies.

The single-use, disposable Litx device uses light-emitting diodes to activate LS11 (talaporfin sodium), a light-activated, water-soluble drug, the company said. An LS11 molecule activated by the system results in the production of singlet oxygen, which kills target tissues with minimal side effects. The system uses low-intensity light that causes vascular closure and apoptosis. Illumination with low-intensity light activates each molecule of LS11 many times, resulting in a continuous supply of singlet oxygen molecules, the company said.

There is no evidence that Litx produces the typical side effects from the systemic damage to rapidly-dividing normal cells caused by chemotherapy, radiation, and other cancer treatments, the company said.

Medarex Inc. (NASDAQ: MEDX) of Princeton said it has initiated a phase Ib trial for MDX-1106 (ONO-4538: development code of Ono Pharmaceutical Co. Ltd.), a fully human anti-PD-1 antibody for cancer treatment.

Studies suggest the PD-1 signaling pathway plays a role in tumor evasion and escape from host immune responses and promotes the persistence of chronic viral infections, the company said.

The open label 76-patient trial would evaluate the safety and tolerability of repeated dosing of the agent in solid tumors and will also assess the anti-tumor activity of multiple doses of MDX-1106 (1, 3 or 10 mg/kg).

The tumors to be studied include malignant melanoma, renal cell cancer, castrate-resistant prostate

cancer and non-small cell lung carcinoma.

“Anti-PD-1 antibodies could represent the next stage in immunotherapy with a promising mechanism of action and potential for marked synergy with anti-CTLA4 antibodies,” said Geoffrey Nichol, MBChB, senior vice president of product development at Medarex. “Preliminary results from our single-dose phase I study demonstrated an acceptable safety profile and initial evidence of anti-tumor activity in cancer.”

In May 2005, Ono entered into a collaboration agreement with Medarex to research and develop a fully human anti-PD-1 antibody in cancer.

The companies would share the costs and responsibilities of research and product development up to the completion of a phase II study in each party's territory. Thereafter, each company will be fully responsible for any continued development and any commercialization in its exclusive territory; the Medarex exclusive territory is North America, and the Ono exclusive territory is all areas outside of North America.

MDX-1106/ONO-4538 is a fully human antibody that targets and inhibits the function of PD-1, a receptor expressed on the surface of activated lymphocytes. The binding of PD-1 with one of two ligands (PD-L1 or PD-L2) is a negative regulation pathway that suppresses or inhibits activated lymphocytes. Research has noted increased PD-1 expression levels on antigen specific T-cells in both the oncology and chronic infectious disease settings, as well as a strong correlation between increased PD-L1 expression on tumors and a negative survival prognosis in cancer.

Preclinical studies indicate that antibodies targeting the PD-1 signaling pathway reinvigorate antigen-specific T-cell responses and promote an immune response to fight tumors and infectious diseases, the company said.

PTC Therapeutics Inc. of South Plainfield, N.J., announced the initiation of two clinical trials of the company's product candidate PTC299 in adult patients with solid tumor cancers and Kaposi Sarcoma, a HIV-related cancer.

PTC299 is an orally delivered, investigational new drug that offers an innovative approach to anti-angiogenesis, limiting the formation of new blood vessels for tumors.

Based on the pre-clinical and clinical studies to date, PTC299 has the potential to meet significant unmet medical need for patients with different types of cancer, the company said.

An open-label phase 1b clinical trial will enroll up to 42 patients with locally advanced or metastatic solid tumors in order to evaluate the safety and efficacy of multiple doses of PTC299 alone and in combination with Taxotere (docetaxel) chemotherapy. The primary objective of the study is to determine the maximum tolerated dose of PTC299.

The trial will also assess the overall safety profile of the drug when administered alone and in combination with chemotherapy, evaluate its effect on the production of vascular endothelial growth factor (VEGF), its antitumor activity, and its pharmacokinetics.

The study will be conducted at Memorial Sloan-Kettering Cancer Center.

A second open-label phase I/II clinical trial will enroll up to 45 patients with Kaposi's sarcoma associated with human immunodeficiency virus infection. Kaposi's sarcoma, a cancer that develops from the cells that line blood vessels, is the one of the most common HIV-related cancers.

The primary objectives of the study are to determine the maximum tolerated dose of PTC299 and to evaluate the overall safety and efficacy profile of the drug as therapy for Kaposi's sarcoma. The study will be conducted by the AIDS Malignancy Consortium, a multicenter clinical trials group supported by the National Cancer Institute, and will be conducted at AMC sites in the U.S.

The study will be led by Susan Krown, of the Melanoma and Sarcoma Service, Memorial Sloan-Kettering Cancer Center, who chairs the AMC's Kaposi's Sarcoma Working Group.

PTC299 is an orally administered small-molecule investigational drug that in preclinical models selectively blocked the pathological, or disease-related, production of the protein VEGF in tumors acting upstream of current therapies, while sparing physiological VEGF expression. VEGF plays a critical role in angiogenesis, or the formation of new blood vessels, the company said.

SuperGen Inc. (NASDAQ: SUPG) of Dublin, Calif., said it has received clearance to initiate clinical trials with SGI-1776, an inhibitor of Pim kinases.

The clearance of its original Investigational New Drug Application triggers a \$5.2 million milestone payment to the former stockholders of Montigen Pharmaceuticals Inc, the company said.

The milestone payment will consist of \$2.8 million in cash payments and the issuance of \$2.4 million in equity, representing 1.5 million shares of SuperGen

common stock.

SuperGen said it would begin a phase I trial to evaluate the safety, tolerability and pharmacokinetic profile of the agent, a novel, orally administered, small molecule anticancer compound.

The trial program would target solid tumors with emphasis on hormone refractory prostate cancer and refractory non-Hodgkin's lymphomas, the company said.

The solid tumor types overexpress the Pim kinase family of proteins at a high frequency, the company said. Overexpression of Pim-1 kinase is a marker of poor prognosis. A second phase I/II study is planned in refractory leukemias in which Pim kinases are also overexpressed, and correlated with poor prognosis and drug resistance, the company said.

The clearance of the SGI-1776 IND application represents a validation of our CLIMB technology platform and its ability to generate first-in-class drug candidates," said James Manuso, president and CEO of SuperGen.

Treatment with SGI-1776 produces significant tumor regressions in animal models of acute myeloid leukemia and suppression of solid tumor growth and biomarker modulation in models of prostate adenocarcinoma and non-Hodgkin's lymphoma, the company said.

In non-clinical studies, SGI-1776 has shown good oral bioavailability and sustained inhibition of Pim kinase targets in vivo following both single and repeated oral dosing.

The three Pim kinases, Pim-1, Pim-2 and Pim-3, are conserved serine-threonine kinases that are regulators in signaling pathways implicated in cancer, the company said.

Deals & Collaborations:

BioWa Licenses Technology To GSK For Therapeutics

BioWa Inc. of Japan said it licensed to **GlaxoSmithKline** (NYSE:GSK) its Potelligent Technology in developing and commercializing select GSK antibodies with enhancement of antibody-dependent cellular cytotoxicity.

Under the agreement, BioWa said it would provide GSK with non-exclusive commercial rights to the technology for multiple antibodies. In return, BioWa would receive technology access fees, and milestone payments and royalties from resulting GSK products.

Potelligent Technology improves antibody

therapeutics by enhancing ADCC, one of the mechanisms of action for antibody therapeutics. The technology reduces the amount of fucose in the carbohydrate structure of an antibody using a proprietary fucosyltransferase-knockout CHO cell line as a production cell.

BioWa is a wholly owned subsidiary of Kyowa Hakko Kirin Co. Ltd..

Fujirebio Diagnostics Inc. of Malvern, Penn, and **Roche Diagnostics** of Basel, Switzerland, announced a worldwide license and supply agreement for the HE4 ovarian cancer test. Under the agreement, Roche will develop an assay kit utilizing Fujirebio Diagnostics' HE4 test on its automated immunoassay analyzers.

The HE4 test was developed by Fujirebio Diagnostics to be used in conjunction with the company's existing CA125 biomarker, the current gold standard for monitoring ovarian cancer.

This combination of biomarkers, as published clinical data shows, provides clinicians with a diagnostic tool that can provide higher sensitivity and specificity than CA125 alone. Improved sensitivity and specificity should allow clinicians to distinguish between benign and malignant pelvic masses more accurately, helping to ensure that patients receive appropriate therapy earlier.

HE4 in a manual format is currently FDA-cleared for monitoring recurrent or progressive disease in patients with epithelial ovarian cancer (EOC), and CE-marked in Europe as an aid in estimating the risk of EOC in premenopausal or postmenopausal women presenting with pelvic mass. The HE4 manual test and corresponding Risk of Ovarian Malignancy Algorithm are pending clearance by the FDA for use in women who present with a pelvic mass.

Mylan Inc. (NYSE: MYL) of Pittsburgh said it subsidiary, Mylan Pharmaceuticals Inc., has entered into a settlement agreement with **Novartis Pharmaceuticals Corp.**, Novartis Corp. and Novartis International AG, related to Letrozole Tablets, the generic version of the Novartis drug, Femara.

Under the agreement, Mylan said it would provide a patent license to market Letrozole Tablets, 2.5 mg, prior to its expiration.

Letrozole Tablets, which are used in breast cancer treatment, had U.S. sales of \$470 million for the 12 months ending Sept. 30, the company said.

Mylan said it was the first company to file a complete Abbreviated New Drug Application containing a Paragraph IV certification for the product.