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CMS Dares Critics To Produce ESA Data; Bill Seeks To Vacate Coverage Decision

By Paul Goldberg

The agency that oversees the Medicare program declined to reconsider its coverage decision to restrict payment for erythropoiesis-stimulating agents in oncology.

The oncology and hematology societies as well as US Oncology, a company that operates cancer clinics, had petitioned the Centers for Medicare and Medicaid Services to reopen the decision that could slash the use of ESAs by about two-thirds.

While the agency's National Coverage Decision is on the books and scheduled to take effect on Sept. 30, the agency is yet to send out its

(Continued to page 2)

In the Cancer Centers:

Beck Named Chief Academic Officer At Fox Chase, Joins Leadership Council

J. ROBERT BECK, deputy director of the population science division and vice president for information services and chief information officer at Fox Chase Cancer Center, was named its first chief academic officer. Beck oversees the office of sponsored research, office of business development and institutional review board as well as core research facilities and information technology. He also is chairman of long-term strategic space planning for the center. The new position reflects the expansion of clinical and laboratory research activities and positions at the center, said **Michael Seiden**, president and CEO of Fox Chase. Beck will serve as a member of the center's Leadership Council. Before joining Fox Chase in 2001, Beck was vice president for information, research and planning at Baylor College of Medicine in Houston. He holds grants from NIH, the Commonwealth of Pennsylvania and the NCI Biomedical Informatics Grid. . . . **SMITA PATEL**, professor of biochemistry at the University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, has received a $2.5 million MERIT Award, Method to Extend Research in Time, from NIH. The grant provides Patel, known for her work in the metabolic processes of DNA, long-term funding for research into gene transcription. The research also has implications in infectious diseases and may be used to develop antiparasitic therapies for malaria, and leishmaniais, an infectious disease transmitted by sand flies, said Patel. . . . **SAMUEL WAXMAN** was given the new title of Distinguished Service Professor by Mount Sinai School of Medicine. The award recognizes faculty who have dedicated their careers to Mount Sinai and

(Continued to page 7)

House Bill Would Force CMS To Return To Square One

(Continued from page 1)

instructions to local carriers, who are continuing to make their own decisions on coverage.

Following heavy lobbying by a variety of interests, late on Sept. 27, Rep. Anna Eshoo (D-Calif.) and Mike Rogers (R-Mich.) introduced a bill to vacate the NCD and force the agency to return to square one. In recent weeks, the majority of members of Congress signed letters to the agency, urging it to reconsider the NCD and allow physicians to set higher hemoglobin targets.

Political pressure notwithstanding, CMS is defending its decision. In an unusual move, the agency has challenged its critics in oncology to answer a series of fundamental questions to justify their contention that using ESAs should be used at a level above 10 g/dL, the boundary set by CMS.

"To claim that the agency materially misinterpreted the evidence in this NCD, it would be helpful to identify your specific concerns and the particular evidence that supports a different conclusion," CMS Chief Medical Officer Barry Straube wrote in a Sept. 24 letter to the American Society of Clinical Oncology, the American Society of Hematology, and US Oncology.

The petitioners had presented "no new evidence" to justify reopening the decision, which CMS said was based on a review of over 800 publications and 2,600 comment letters received during the public comment period.

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The questions posed by the agency cannot be answered based on existing data and largely challenge the petitioners to prove the negative:

—"What is the evidence that cancer patients undergoing chemotherapy require hemoglobin levels of above 10 g/dL?

—"What evidence demonstrates that cancer patients undergoing chemotherapy have better outcomes with hemoglobin levels above 10 g/dL? What is the evidence that ESA therapy is superior to transfusion therapy for maintaining that level?

—"What is the evidence that using ESAs intermittently to maintain hemoglobin levels above 10 g/dL results in increased appropriate transfusions or higher adverse outcomes over the current practice of continuous use of ESAs?

—"What is the evidence that cancer patients undergoing chemotherapy have better outcomes from ESA therapy vs. transfusions?

—"What is the evidence that the higher dose of ESAs provided to most patients when using a fixed dose schedule rather than a weight-based schedule does not result in higher adverse outcomes?

—"What is the evidence that patients with comorbidities do better with a hemoglobin above 10 g/dL compared to those without comorbidities?"

Congressional Action Looms

ASCO and ASH officials said to The Cancer Letter that they planned to answer the agency's questions, while US Oncology officials said that they would instead direct the agency to its earlier comments on the NCD.

"The questions that they ask are ones that CMS doesn't have data to address, and neither do we," said Mila Becker, director of government relations and practice at ASH. "We will try to respond in a constructive way."

Joseph Bailes, co-chairman of the ASCO Government Relations Council, said most of the questions have been answered in the society's previous filings.

"It's very disappointing that with all the evidence provided to CMS that CMS elected not to respond positively and affirmatively to the request and reopen the NCD, but instead ask another series of questions, many of which probably have been asked and answered in the request to reopen the NCD," Bailes said. "Obviously, we will have to answer the questions."

ASCO is playing a pivotal role in this debate, as Congressional proponents of reversing the CMS decision point to the professional society's expertise to

counterbalance to that of the agency.

The society's objections were most recently cited in the Eshoo-Rogers bill (H.J.Res.54), which states that "the leading national medical organization representing physicians who treat patients with cancer has noted that the [NCD] hemoglobin level restriction is inconsistent with both the FDA approved labeling and national guidelines."

The CMS coverage decision requires physicians to wait until a patient's hemoglobin drops below 10 g/dL before administering ESAs, then withhold subsequent administration until hemoglobin once again drops to that level. In communications with CMS, ASCO recommended that ESA treatment should begin when a patient's hemoglobin level drops below 10 g/dL, and should be maintained at 10 to 12 g/dL.

ASCO and ASH officials said they are updating their joint guidelines for ESA use, and the new guidelines would be published within the next two weeks.

US Oncology said the agency hasn't clearly laid out its rationale for the NCD. "I can't answer these questions; I don't know what data they used," said Dan Cohen, senior vice president of government relations and public policy at US Oncology. "I just do not know what underpins the NCD. A bibliography of 800 studies is not evidence. It's a bibliography, and we have been unable to connect the dots between the policy and the studies."

The company's response is posted at http://www.legislink.com/site/MessageViewer?em_id=7161.0

Scientists say the questions point to the paucity of data on ESAs.

"The questions asked are fair ones and highlight the need for further studies," said David Steensma, an expert in ESAs at Mayo Clinic. "However, such questions could easily be turned around: e.g., what is the evidence that using a hemoglobin of 10 g/dL as both a starting and stopping point for ESA dosing, as proposed by CMS, is a practical or effective strategy? There isn't any evidence, because there is no experience using the drugs this way."

Steensma, who has no ties with either of the sponsors and who isn't involved in drafting practice guidelines, said he is concerned about patients dropping to hemoglobin levels of less than 10 g/dL.

"What concerns me most about the new rules is it shouldn't take long to document that the transfusion requirements for Medicare beneficiaries are increasing, and we know transfusions can cause harm, whereas there is no convincing evidence that ESAs, when used conservatively and in a manner consistent with the current label, are dangerous in people with cancer," Steensma said.

Michael Henke, a radiation oncologist whose randomized trial data published in 2003 first demonstrated that ESAs could cause tumor promotion, said the agency's questions expose the motivations of all parties involved in this debate.

"Most CMS questions have a simple answer: There are no good data to address these problems with scientific seriousness," said Henke, professor of medicine, radiation oncology in Freiburg University Clinic in Germany. "One wonders what made CMS ask these questions. We might take the liberty to look from outside the debate on the involved industry, on professional societies, health care providers, Wall Street, and politicians, and we might wonder what their real interests are in the current discussion. Isn't it just making or saving money?

"It is no longer the question whether ESAs are harmless. Instead, we should be asking to identify patients who could be given these agents safely," Henke said.

"In that sense, CMS has started the right discussion—*primum nil nocere*!"

Bill Seeks To Overturn CMS Action

The agency's questions could become moot if Congress decides to get involved. Action could be taken under the Congressional Review Act, which allows legislators to review every new federal regulation issued by government agencies, and, by passing a joint resolution, overrule it.

The bill can be sent to the President either separately or as a rider attached to massive omnibus legislation.

In July, House and Senate members representing the majority of both chambers urged CMS to tone down what was then a proposed decision (The Cancer Letter, July 20). Earlier this month, the Senate passed a nonbinding resolution urging the agency to increase the hemoglobin target (The Cancer Letter, Sept. 7).

ESAs were approved based on their ability to reduce the risk of blood transfusions, and questions about their impact on survival and disease progression were not answered at the time of approval and remain unanswered to this day.

Nonetheless, direct-to-consumer advertising and incentives offered by sponsors to physicians helped make ESAs into the single most costly component in cancer care. In 2006, $4.854 billion worth of these agents were used in oncology in the U.S.

Now, this market is at risk. According to Amgen, sales through Medicare account for 40 percent of the company's oncology business. In recent weeks, Amgen and J&J have been laying off staff to adjust to projected declines in the use of the agents.

Earlier this year, FDA issued a "black box" warning urging doctors to use ESAs sparingly and eliminating all references to quality of life from the labels (The Cancer Letter, march 16). The agency is widely believed to be negotiating additional changes in the label.

In these talks, FDA's negotiating position has been enhanced significantly in the past two weeks.

First, the Danish head and neck cancer cooperative group on Sept. 25 reported that its study of Aranesp demonstrated a statistically significant decrease in tumor control on the ESA arm. An earlier report of the finding had triggered FDA's concern about tumor promotion, causing the agency to convene a meeting of the Oncologic Drugs Advisory Committee (The Cancer Letter, Feb. 16, May 11).

The study was presented at the European Cancer Organization meeting in Barcelona.

Also, FDA's position has been strengthened by the passage of a bill that reauthorizes collection of user fees by the agency and enhances its power to regulate drug safety.

The bill, which the President signed on Sept. 27, would allow the agency to require clinical trials and gives it the upper hand in label negotiations.

Under this law, the HHS Secretary would be able to require post-approval studies or clinical trials "on the basis of scientific data deemed appropriate by the Secretary."

Trials could be ordered for the following reasons:

—"To assess a known serious risk related to the use of the drug involved;

—"To assess signals of serious risk related to the use of the drug,

—"To identify an unexpected serious risk when available data indicates the potential for a serious risk."

The law allows companies to appeal, but establishes a tight schedule for resolution of disputes. "For each study or clinical trial…, the Secretary shall require… a timetable for completion" and provide periodic updates to regulators.

Also, HHS would be able "to make such a labeling change as the Secretary deems appropriate to address the new safety information" and assess civil penalties of up to $10 million against sponsors who fail to comply, the document states. The law goes into effect in 180 days.

The law is posted at http://energycommerce.house.gov/FDA%20Amendments/CONF_AGREEMENT_003_xml%20(2).pdf.

Sources said Amgen recently approached the cooperative groups to discuss the prospect of conducting trials of ESAs in non-small cell lung cancer and, potentially, other diseases.

The company also appears to be planning to conduct trials on its own, sources said. Insiders say that if FDA mandates such trials, cooperative groups would be ideally positioned to conduct those trials. However, the level of excitement about such studies would likely be low, considering that ESAs have been in routine use in the U.S. for over 15 years.

Danish Results Show Inferior Tumor Control

The final result of the Danish head and neck cancer study that caused concern about tumor promotion confirms a preliminary finding that Aranesp was associated with loco-regional treatment failure.

The study was conducted in an off-label indication and set hemoglobin targets well above those on label.

The following abstract describes the study's final results:

Randomized study of the importance of Novel Erythropoiesis Stimulating Protein (Aranesp) for the effect of radiotherapy in patients with primary squamous cell carcinoma of the head and neck (HNSCC)- the Danish Head and Neck Cancer Group DAHANCA 10 randomized trial.

Speaker: J. Overgaard, C.M. Hoff, H. Sand Hansen, L. Specht, M. Overgaard, C. Grau, E. Andersen, J. Johansen, L. Andersen, Evensen. Citation: European Journal of Cancer Supplements, Vol 5 No 6, Page 7

Aim: The primary objective of the trial was to evaluate, in an open randomized trial, if the correction of low haemoglobin (Hb) levels by means of darbepoetin alpha (Aranesp) during radiotherapy improves outcome of curative radiation treatment in patients with HNSCC. Following the outcome of a planned interim analysis which showed inferiority of the experimental treatment the trial was stopped on November 28, 2006, and subjected to the following analysis which was performed per July 1, 2007.

Patients and Methods: Pts with HNSCC eligible for primary radiotherapy alone (except those with T1 glottic cancers) and with with Hb values below 9.0 mmol/l (14.0 g/dl) were randomized to receive Aranesp together with accelerated (6 weekly fractions) fractionated radiotherapy (66–68 Gy in 33 to 34

fx). In addition, patients were also treated with the hypoxic radiosensitizer Nimorazole. Aranesp was given subcutaneously in a dose of 150 micrograms. The first dose was administrated the week prior to start of radiotherapy and continued once a week until completion of radiotherapy, or stopped earlier if the Hb exceeded 9.6 mmol/l (15.5 g/dl). Patients were recruited from all Danish oncological centers and from the Norwegian Radium Hospital in Oslo.

Results: In total, 522 patients had been randomized at the time of the interim analysis (of a planned intake of 600) with a median follow-up time since randomization of 37 months (range 8–60). Of these 515 were eligible for analysis (255 pts treated with Aranesp and 260 pts in the control group). Among these, 167 have experienced a loco-regional failure (the primary study endpoint). There have been 218 deaths of which 163 are known to be of the cancer in question. Overall, the patients were evenly distributed according to the stratification parameters (gender, T and N staging, tumor site, institution) which, except the latter, were also found to significantly discriminate prognosis within the material. Aranesp resulted in the expected increase in Hb with more than 91% of the patients obtaining the planned increase. The compliance to Aranesp was good without excess incidence of major serious adverse events. Overall, the results showed a poorer outcome in 5-year actuarial loco-regional control (56% vs. 69% ($p = 0.02$, RR: 1.44 [1.06–1.96]) for the Aranesp vs. control arm. This was also seen for the endpoint of disease-free survival (48% vs. 63% for Aranesp® vs. control, $p = 0.004$, RR: 1.49 [1.13–1.97]). The difference in tumor control resulted in a similar difference in 5-year disease-specific survival (51% vs. 67% for Aranesp vs. control, $p = 0.05$, RR: 1.38 [1.01–1.88]), whereas there was no significant difference in overall survival (38% vs. 51% for Aranesp and control respectively, $p = 0.08$, RR: 1.28 [0.98–1.68]). There was no difference in the risk of developing distant metastases or in non-cancer related deaths, neither was there any enhanced risk of cardio-vascular events observed in the experimental arm. There were no apparent differences in acute or late radiation related morbidity. All univariate analyses were confirmed in a multivariate setting.

Conclusion: Correction of the Hb level with Aranesp in patients with HNSCC resulted in a significantly poorer tumor control after radiotherapy. The treatment principle was abandoned and the difference in outcome is currently being subjected to further examination.

Supported by grants from the Danish Cancer Society and Amgen.

Cancer Statistics:

U.S. Breast Cancer Death Rate Continues to Drop, Study Says

A report from the American Cancer Society finds the breast cancer death rate in the U.S. continues to drop more than two percent per year, a trend that began in 1990 and is credited to progress in early detection and treatment.

But the report says African American women and women of other racial and ethnic groups have benefited less than white women, and that a recent drop in cancer incidence is due in part to fewer women getting mammograms.

The findings are published in Breast Cancer Facts & Figures 2007-2008, available at http://www.cancer.org/statistics. Other highlights of the report:

•In 2007, 178,480 new cases of invasive breast cancer are expected. Excluding skin cancer, breast cancer is the most frequently diagnosed cancer among in U.S women.

•In 2004 (the latest year for which figures are available), approximately 2.4 million women in the U.S. had a history of breast cancer.

•Between 1990 and 2004, the breast cancer mortality rate decreased by 2.2 percent per year. The decline was larger among younger age groups.

•From 1995-2004, female breast cancer death rates declined by 2.4 percent per year in whites and Hispanics/Latinas, 1.6 percent per year in African Americans, and remained unchanged among Asian Americans/Pacific Islanders and American Indians/Alaska Natives.

•In 2007, about 40,460 women are expected to die from breast cancer. Only lung cancer accounts for more cancer deaths in women.

•During 2001-2004, breast cancer incidence rates among white women declined at an average rate of 3.7 percent per year, likely due to lower rates of mammography screening and decreased use of hormone replacement therapy.

•Incidence rates have remained stable for African American women.

•Among women aged 50 and older, incidence rates have been declining sharply (by 4.8 percent per year) since 2001. Among women under age 50, incidence rates have remained stable since 1986.

•Since 2000, the incidence rate of smaller tumors has declined by 3.8 percent per year. In contrast, the incidence rate of larger tumors (>5.0 cm) has increased by 1.7 percent per year since 1992, perhaps due to postmenopausal obesity, HRT use, or both.

NCI Programs:

NCI Funds $15.5M In Grants On Glycobiology Of Cancer

NCI announced awards to seven laboratories in a new $15.5 million, five-year initiative to discover, develop, and clinically validate cancer biomarkers by targeting the carbohydrate (glycan) part of a molecule.

The seven Tumor Glycome Laboratories will search for glycan-based biomarkers for melanoma, and breast, ovarian, lung, prostate, colon, and pancreatic cancers.

"Scientists have long recognized that certain sugar structures, which are attached to protein and lipid molecules, may be important as markers for cancer development," said NCI Director John Niederhuber. "While this area has compelling scientific interest, its biological and chemical complexities have often discouraged investigation. Today, with the advent of advanced technologies to conduct protein and carbohydrate chemistry, research into this intriguing area has experienced renewed interest."

NCI's Tumor Glycome Laboratories are the principle component of the new trans-NIH Alliance of Glycobiologists for Detection of Cancer and Cancer Risk. The other components of the alliance are the Consortium for Functional Glycomics funded by the National Institute of General Medical Sciences and several Glycomics and Glycotechnology Resource Centers supported by the National Center for Research Resources.

NCI's Early Detection Research Network is also an alliance member, providing support for design and statistical analysis, patient accrual, and collection of clinical specimens to facilitate validation studies using EDRN's existing components.

"Looking at different types of biomarkers and new ways to identify them is critically important to both the basic understanding of cancer and the ability to identify early cancer and risk for cancer," said Sudhir Srivastava, chief of the Biomarkers Research Group in the NCI Division of Cancer Prevention. "We believe this new Alliance of Glycobiologists will accelerate the pace of biomarker development and discovery."

The project is headed by Karl Krueger, a program director in the Biomarkers Research Group of DCP.

The seven principal investigators are:

Margaret Huflejt, of Cellexicon Inc., La Jolla, Calif.; Denong Wang, of Stanford University; Milos Novotny, of Indiana University; William Hancock, of Northeastern University; J. Michael Pierce, of University of Georgia; Michael Hollingsworth, of University of Nebraska; and Ajit Varki, of University of California, San Diego.

NIH News:

NIAID's Fauci Wins Lasker Award For Public Service

ANTHONY FAUCI, director of the National Institute of Allergy and Infectious Diseases, was selected for the 2007 Mary Woodard Lasker Award for Public Service for his role in developing two major U.S. public health programs, in AIDS and biodefense. The award will be presented Sept. 28.

Fauci was selected for his role in helping develop the President's Emergency Plan for AIDS Relief, the largest public health program in history devoted to a single disease, as well as Project Bioshield, designed to accelerate the research, development, purchase and availability of medical countermeasures against the effects of biological, chemical, radiological and nuclear agents.

The Albert and Mary Lasker Foundation also will present the 2007 Lasker Award for Basic Medical Research to long-time NIAID grantee **Ralph Steinman** of Rockefeller University for his discovery of dendritic cells, immune system cells that trigger other components of the immune system to thwart microbial invaders.

The Lasker Award for Clinical Medical Research honors **Alain Carpentier**, 74, of Hôpital Europeen Georges Pompidou, Paris, and **Albert Starr**, 81, of the Providence Health System, Portland, Ore., who developed prosthetic mitral and aortic valves. These devices have prolonged and enhanced the lives of millions of people with heart disease, providing treatment where none existed before.

* * *

NIH and NASA have signed a Memorandum of Understanding to help American scientists use the International Space Station to answer questions about human health and diseases.

As part of the agreement, NIH and NASA will encourage space-related health research by exchanging information and providing technical expertise in areas of common interest. The agencies will facilitate and share each other's research and development efforts. Also, NIH and NASA have agreed to coordinate publicity of mutually beneficial activities, publications, and research results.

In late May, NASA sent Congress a plan describing how the U.S. segment of the station can be used as a national laboratory. The report outlined possible partnerships with other government agencies and private companies to conduct research aboard the station. The Sept. 12 signing of the MOU is NASA's first agreement with another agency.

The text of the agreement is available at http://www.niams.nih.gov/ne/highlights/nih_nasa.htm.

In the Cancer Centers:

Beth Karlan Named Editor Of Gynecologic Oncology

(Continued from page 1)

have had a major impact on the educational experience of students, clinical care of patients and quality of research and scholarship, said **Dennis Charney**, dean for academic and scientific affairs at Mount Sinai School of Medicine and senior vice president for health sciences at Mount Sinai Medical Center. . . . **CANDACE JOHNSON** was appointed chairman of the Department of Pharmacology and Therapeutics at Roswell Park Cancer Institute. She is the Robert, Lew and Ann Wallace Chair in Translational Research and has been a senior faculty member in the department and senior vice president of translational research since 2002. Previously, she was deputy director of basic research at the University of Pittsburgh Cancer Institute and professor of pharmacology and medicine at the University of Pittsburgh School of Medicine. . . . **BETH KARLAN**, director of the Cedars-Sinai Women's Cancer Research Institute at the Samuel Oschin Comprehensive Cancer Institute and gynecologic oncologist, was named editor-in-chief of Gynecologic Oncology, the medical journal of the Society of Gynecologic Oncologists. At Cedars-Sinai, Karlan also is director, Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, and director of the Gilda Radner Hereditary Cancer Detection Program. Also, she is professor of obstetrics and gynecology at the Geffen School of Medicine at UCLA. Karlan, who begins her editorship on January 1, succeeds David Gershenson, who was in the position for the past 17 years. . . . **DANIEL HAYES** received the inaugural Gianni Bonadonna Breast Cancer Award and present the first Bonadonna Award lecture at the 2007 Breast Cancer Symposium of the American Society of Clinical Oncology. He is clinical director of the Breast Oncology Program at the University of Michigan Comprehensive Cancer Center, where he is professor of internal medicine. He is known for breast cancer research, which includes the CA15-3 blood test and other tumor markers, such as HER-2. The Gianni Bonadonna Breast Cancer Award and Fellowship, supported by a grant from GlaxoSmithKline Oncology, is a $10,000 annual award that recognizes an active clinical or translational researcher with a distinguished record of accomplishments in advancing the field of breast cancer. The Bonadonna Award is comprised of an endowment, allowing the award to be available for many years to come, and it is accompanied by a one-year, $50,000 Fellowship Grant that will be awarded by The ASCO Foundation to an early-career breast cancer researcher who will work in the lab at the recipient's institution. The fellow will be announced at a later date. . . . **PATRICIA BRANOWICKI**, director of nursing patient care services for pediatric oncology at Dana-Farber Cancer Institute and vice president for medicine patient services at Children's Hospital Boston, was named "Champion in Healthcare" by the Boston Business Journal. This is the second year in a row that a Dana-Farber nurse has received the honor. In 2000, Branowicki became the first single nurse leader of the joint pediatric oncology program at Dana-Farber and Children's Hospital. Since then, she has worked to build a collaborative practice environment between the hospitals. . . . . **MEMORIAL SLOAN-KETTERING** Cancer Center announced recent awards and appointments. **Philip Gutin** was named chairman of the recently established Department of Neurosurgery. Gutin, a neuro-oncologic surgeon and the incumbent of the Fred Lebow Chair in Neuro-oncology, has been chief of the MSKCC Neurosurgical Service for more than 10 years. **Andrei Holodny** was named chief of the Neuroradiology Service in the Department of Radiology. **Gikas Mageras** was appointed chief of the Computer Service in the Department of Medical Physics. **Han Xiao** was appointed chief of medical oncology in the Department of Medicine at MSKCC Basking Ridge. **Jonathan Goldberg** and **Michel Sadelain** were named the incumbents of the newly endowed Stephen Friedman Chairs. **Neal Rosen** was named to the Enid A. Haupt Chair in Medical Oncology. **David Solit** is the Elizabeth and Felix Rohatyn Chair for Junior Faculty. **Jayanta Chaudhuri** is the incumbent of a Frederick A. Adler Chair for Junior Faculty. Also at MSKCC, the Iris and B. Gerald Cantor Foundation has endowed the Iris Cantor Chair in honor of **Sidney Winawer**, gastroenterologist at MSKCC, for his work in digestive cancers. The chair will be held by a yet-to-be-named senior researcher in the field of digestive cancers.

In Brief:

Lectureship Established In Honor Of CTEP's Christian

MICHAELE CHRISTIAN was honored with the establishment of the Michaele C. Christian Lectureship for her 20-year career.

The award recognizes the contributions of individuals, particularly those in mid-career, involved in the development of agents for cancer therapy.

The award consists of a plaque and a lectureship that will be delivered at the annual fall NCI Cancer Therapy Evaluation Program Early Drug Development meeting. The lecture will be published in the journal Clinical Cancer Research.

Christian was appointed associate director of the Cancer Therapy Evaluation Program of DCTD in 1997 after serving as head of the Investigational Drug Branch overseeing the clinical development of anticancer agents.

In 1995, she established the NCI Clinical Trials Monitoring Branch. She received the NCI Director's Award in 1995 and 1999.

The 2007 initial recipient of the award is **Merrill Egorin**, professor of medicine and pharmacology, University of Pittsburgh Cancer Institute. Egorin is co-director of the molecular therapeutics and drug discovery program at the University of Pittsburgh Cancer Institute.

His research is in preclinical and clinical pharmacology studies of investigational and non-investigational antitumor studies with a focus on relating pharmacokinetics and pharmacodynamics of the agents. He is known for using modern analytical chemistry techniques and mathematical modeling approaches to the therapeutic and toxic effects of drugs.

Funding Opportunities:

Lustgarten Foundation Cancer Biomarker Initiative

Mandatory Letter of Intent Due Date: Oct. 1.

Applications Deadline: Nov. 5.

Lustgarten Foundation for Pancreatic Cancer Research announces an RFA for The Lustgarten Foundation Pancreatic Cancer Biomarker Initiative. The RFA is seeking proposals to create mouse monoclonal antibodies to the top ~50 most promising biomarkers for pancreatic cancer. National and international applications will be considered.

Funding will commence January 2008. Inquiries: Lustgarten Foundation for Pancreatic Cancer Research, 1111 Stewart Ave. Bethpage, NY, 11714, 516-803-2304, www.lustgarten.org

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RFP VA-241-08-RP-0017: Tumor Registrar/ Cancer Registrar. Response Due Date: Sept. 27. Full text: http://www.fbodaily.com/archive/2007/09-September/27-Sep-2007/FBO-01420075.htm. Inquiries: Michael Bermes, 802-296-6317.

NOT-CA-07-022: NCI Will Participate in PAR-07-420, Lymphatic Biology in Health and Disease. R01. Full text: http://www.grants.nih.gov/grants/guide/notice-files/NOT-CA-07-022.html. Inquiries: Suresh Mohla, 301-435- mohlas@mail.nih.gov.

RFA-CA-08-503: NCI Limited Competition: Cooperative Human Tissue Network-CHTN. U01. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-08-503.html. Letters of Intent Receipt Date: Sept. 30. Application Receipt Date: Oct. 30. Inquiries: Yaffa Rubinstein 301-496-7147; runinsty@nail.nih.gov.

RFA-CA-08-003: Multidisciplinary Fellowships in Cancer Nanotechnology Research. F32 and F33. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-08-003.html. Application Receipt Date: Dec. 20. Inquiries: Jerry Lee, leejerry@mail.nih.gov., or Piotr Grodzinski, grodzinp@mail.nih.gov.

RFP N02-CO-82403-96: Scientific Library Services at the NCI-Frederick. Full text: http://www.fbodaily.com/archive/2007/09-September/15-Sep-2007/FBO-01406623.htm. Inquiries: Scott Drega, 301-846-1115, sdrega@ncifcrf.gov., or Donald Harne, 301-846-1114, harned@mail.ncifcrf.gov.

RFP N02-CO-82402-92: Computer and Statistical Support Services at the NCI-Frederick. Full text: http://www.fbodaily.com/archive/2007/09-September/15-Sep-2007/FBO-01406622.htm. Inquiries: Patricia White, 301-846-5473, whitep@mail.ncifcrf.gov., or Donald Harne, 301-846-1114, harned@mail.ncifcrf.gov.

RFP N02-CP-71005-53: Mutli-Disciplinary Investigations of Nutrition and Cancer. Full text: http://www.fbodaily.com/archive/2007/09-September/01-Sep-2007/FBO-01391614.htm. Inquiries: Sharon Miller, 301- 435-3783, sm103r@nih.gov., or Kenya Crawford, 301-435-3787, crawfordke@mail.nih.gov.

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Business & Regulatory Report

Product Approvals & Applications:

Roche's Avastin Approved In Europe For Advanced Non-Small Cell Lung Cancer

Roche of Basel, Switzerland, said Avastin (bevacizumab) was approved in Europe for advanced non-small cell lung cancer in combination with platinum-based chemotherapy.

The approval is based on data from the U.S. phase III trial E4599 and the Avastin in Lung, or AVAiL phase III trial, the company said. The approval is for a dose of 7.5 or 15 mg/kg, in combination with platinum-based chemotherapy for unresectable advanced, metastatic or recurrent NSCLC other than predominantly squamous cell histology. The broad label that Avastin has received for NSCLC allows the combination of Avastin

(Continued to page 2)

Clinical Trials:

Genta Begins Phase III Trial Of Genasense Plus DTIC Vs. DTIC Alone For Melanoma

Genta Inc., Nasdaq: GNTA) of Berkeley Heights, N.J., said it has begun enrollment in a confirmatory phase III trial of Genasense (oblimersen sodium) Injection for advanced melanoma.

The trial, known as AGENDA, is a randomized, double-blind, placebo-controlled study of Genasense plus dacarbazine treatment or of darcarbazine treatment (DTIC) alone, the company said. The 300-patient trial will be conducted at 100 sites worldwide, including North America, Europe and Australia.

AGENDA would confirm the safety and efficacy of Genasense when combined with DTIC where chemotherapy has not been used.

Genta said a prior phase III trial of the drug combination had shown that maximal benefit occurred in patients with normal baseline LDH, a blood enzyme that correlates with outcome. The AGENDA study is limited to those whose baseline LDH is less than 0.8 times the upper limit of normal. Analysis of that trial suggested that this group achieved a significantly superior outcome , the company said.

"Genasense plus dacarbazine yielded superior results in a large randomized trial," said Agop Bedikian, professor of medicine at the M.D. Anderson Cancer Center, lead author on the publication of the previous Genasense trial. "We have entered the first patient onto this important new study that seeks to extend those initial results using a biomarker to target novel therapies for melanoma."

"The European Association of Dermato-Oncology will be the lead international cooperative group for AGENDA," said Claus Garbe,

(Continued to page 6)

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Avastin Approved In Europe For Advanced NSCLC

(Continued from page 1)

with any platinum-based chemotherapy regimens at the choice of the physician.

In the 1,000-patient double-blind, randomized, controlled, phase III AVAiL study, treatment consisted of either Avastin at 7.5mg/kg or 15mg/kg + cisplatin/gemcitabine or placebo + cisplatin/gemcitabine, the company said. The results show that by adding Avastin to a cisplatin/gemcitabine regimen progression-free survival was significantly prolonged by 20 to 30 percent compared with chemotherapy alone. No new or unexpected adverse events were observed, the company said.

* * *

Advanced Life Sciences Holdings Inc. (NASDAQ:ADLS) of Woodridge, Ill., said FDA has granted Orphan Drug designation to ALS-357 for metastatic melanoma.

ALS-357 is entering phase I/II development that has demonstrated anti-tumor activity in malignant melanoma, the company said. The drug induces apoptosis in tumor cells.

* * *

ADVENTRX Pharmaceuticals Inc. (AMEX: ANX) of San Diego said FDA has granted Fast-Track designation to ANX-510, or CoFactor injection, which is in a phase III study with 5-fluorouracil and bevacizumab for metastatic colorectal cancer.

The 1,200-patient trial is randomized to two arms containing either CoFactor or leucovorin, each in combination with 5-FU and bevacizumab (Avastin). The primary endpoint is progression-free survival, the company said. Secondary endpoints include response rate, overall survival and incidence and severity of adverse events. The protocol and planned analysis were developed with and accepted by FDA under a Special Protocol Assessment, the company said.

CoFactor is a folate-based biomodulator that replaces leucovorin to enhance the activity and reduce toxicity of 5-FU.

* * *

Cephalon Inc. (NASDAQ:CEPH) of Frazer, Pa., said the FDA Office of Orphan Products Development granted Orphan Drug designation to its investigational therapy, Treanda (bendamustine HCl), for chronic lymphocytic leukemia.

Cephalon said it also is studying the agent for indolent non-Hodgkin's lymphoma, refractory to the monoclonal antibody rituximab.

The drug is the first rationally designed purine analog / alkylator hybrid, combining the moieties of an antimetabolite and an alkylator, the company said.

In a related development, Cephalon said it has submitted a New Drug Application to FDA requesting approval of Treanda (bendamustine HCl) for chronic lymphocytic leukemia.

In August, FDA granted Orphan Drug designation to Treanda for the indication, the company said.

The NDA is based on an international multi-center phase III trial that evaluated the safety and efficacy of bendamustine HCl, the active ingredient in Treanda, compared to chlorambucil.

Chlorambucil is an FDA-approved first- line therapy for CLL. In the trial, bendamustine HCl met both primary endpoints: overall response and progression-free survival, and demonstrated an acceptable tolerability profile, the company said.

Treanda is a rationally designed purine analog/ alkylator hybrid that induces rapid, sustained single- and double-strand DNA damage. This results in apoptosis in the tumor.

* * *

Eli Lilly and Co. (NYSE:LLY) of Indianapolis said it has submitted an application with the European Medicines Agency for centralized review of Alimta (pemetrexed for injection), in combination with cisplatin, for advanced non-small cell lung cancer.

The submission is based on a study that evaluated

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Alimta plus cisplatin versus Gemzar (gemcitabine HCl for injection) plus cisplatin, the company said. The study met its primary endpoint of non-inferiority relative to overall survival in a first-line NSCLC setting.

In 2004, the EMEA approved Alimta as a single agent, second-line treatment for advanced NSCLC, as well as in combination with cisplatin for MPM.

* * *

Genzyme Corp. (NASDAQ:GENZ) of Cambridge, Mass., and **Bayer HealthCare Pharmaceuticals Inc.** (NYSE: BAY) said FDA has approved a supplemental biologics license application for Campath (alemtuzumab) and granted regular approval for single-agent Campath for B-cell chronic lymphocytic leukemia.

Campath was initially approved in 2001 under accelerated approval regulations and the FDA has determined that the study results submitted in the sBLA fulfill the post- marketing commitment to verify clinical benefit. A label expansion is under consideration in Europe.

Data supporting the sBLA were part of an international phase III trial comparing Campath with chlorambucil in untreated B-CLL. The study met its primary endpoint by demonstrating longer progression free survival when treated with Campath versus chlorambucil, with Campath reducing the risk of disease progression or death by 42 percent (p=0.0001), the company said.

Campath exhibited higher overall and complete response rates that were statistically significant in comparison to treatment with chlorambucil.

* * *

Indevus Pharmaceuticals Inc. (NASDAQ:IDEV) of Lexington, Mass., said it has received an approvable letter from FDA for Valstar, its sterile solution of valrubicin for intravesical instillation, for therapy of bacillus Calmette-Guerin-refractory carcinoma in situ of the urinary bladder.

Valstar was removed from the market in 2002 due to impurities in the original formulation and was placed on the FDA Drug Shortages List. The impurity issue was solved and the company said it then submitted a chemistry, manufacturing and controls NDA supplement in May. The approvable letter was in response to the chemistry supplement.

In clinical trials, when administered after transurethral resection, the drug had a median 21 months to documented recurrence of disease.

* * *

Peregrine Pharmaceuticals Inc. (NASDAQ: PPHM) of Tustin, Calif., said it has submitted a clinical protocol with the Drug Controller General of India for an open label phase II safety and efficacy trial of bavituximab in combination with paclitaxel and carboplatin for metastatic breast cancer.

The trial has a two-stage design: up to 15 patients with metastatic breast cancer will be enrolled initially and the study will be expanded up to a total of 46, the company said.

The primary objective is assessment of the overall response rate to the combination of bavituximab with doses of paclitaxel and carboplatin.

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Pharmion Corp. (NASDAQ:PHRM) of Boulder and its collaborator **MethylGene Inc.** (TSX: MYG) of Montreal said FDA has designated its histone deacetylase inhibitor, MGCD0103, as an Orphan Drug for Hodgkin's lymphoma in the U.S.

Preliminary data from a MGCD0103 phase II monotherapy trial in relapsed and refractory Hodgkin's lymphoma demonstrated an objective complete response plus partial response rate of 40 percent and a disease control rate (CR + PR + stable disease for > 6 cycles) of 45 percent in a population of 20 evaluable patients that had relapsed disease or were refractory to previous treatments, including bone marrow transplantation, the companies said. Fatigue and gastrointestinal side effects were the most common adverse events and dose modification was effective.

MGCD0103 is an orally-administered, isotype-selective HDAC inhibitor. The compound is in two phase I/II trials, in combination with Vidaza for hematological malignancies and with Gemzar in solid tumors, and in four phase II monotherapy trials in hematological malignancies, the company said.

* * *

Spectrum Pharmaceuticals Inc., (NASDAQ: SPPI) of Irvine, Calif., said FDA has cleared the Investigational New Drug application for SPI-1620 in recurrent or progressive carcinoma.

SPI-1620 is being developed as an adjunct to chemotherapy. The agent is a selective endothelin-B agonist that has demonstrated in experimental animal models a transient and selective increase in blood flow to tumors by over 300 percent and an increased delivery of anticancer drugs to the tumor while sparing normal tissues and organs, thereby increasing the efficacy and the therapeutic index of the drugs.

* * *

TopoTarget A/S of Rockaway, N.J., said it received approval from FDA for Totect (dexrazoxane hydrochloride for injection, equivalent to 500 mg

dexrazoxane) for extravasation from intravenous anthracycline chemotherapy.

In two studies, the group treated with anthracycline intravenously that experienced extravasation symptoms of pain, burning, swelling and/or redness near the infusion site received Totect. The objective was to reduce surgical interventions for tissue injury following anthracycline extravasation. The protocol required extravasation to be confirmed by fluorescence in tissue biopsies.

The first Totect dose was administered as soon as possible and within six hours following extravasation. After the first dose, treatment was repeated 24 and 48 hours later for a total of three doses. The agent was administered as a one to two hour intravenous infusion through a different venous access location than the extravasation site. The first and second doses were 1000 mg/m2 and the third dose was 500 mg/m2 (maximum daily dose of 2000 mg on Days 1 and 2 and 1000 mg on Day 3.)

Extravasation was confirmed in 57 evaluable patients. The anthracyclines most commonly involved were epirubicin (56 percent) and doxorubicin (41 percent). Peripheral extravasation sites included forearm (63 percent), hand (21 percent), and antecubital area (11 percent). Four patients received the anthracycline via a central venous access device. Most presented with swelling (83 percent), redness (78 percent) and pain (43 percent).

After treatment, only one of the 57 evaluable patients required surgery, while 13 had late sequelae at the event site, including pain, fibrosis, atrophy and local sensory disturbance. All were judged as mild, except the one requiring surgery. None of the four patients with CVADs required surgical intervention.

Deals & Collaborations:

KineMed, Merck To Collaborate On Drug Application Discovery

KineMed Inc. of Emeryville, Calif., said it would collaborate with **Merck Serono**, a division of Merck KGaA of Darmstadt, Germany, to discover applications for drug candidates.

The KineMed proprietary pathway-based drug discovery and development technology identifies compounds that modulate metabolic pathways present in both preclinical animal models and in humans, the company said. By measuring real-time activity of drugs against the targeted pathways, the technology reduces development risk by selecting drug candidates, which best demonstrate clinical efficacy and confirm desired drug activity in clinical trials, the company said.

In the collaboration, KineMed said it would identify therapeutic utility in in vivo preclinical models by applying its proprietary translational medicine technologies. Once a disease target is established for a selected drug candidate, KineMed and Merck KGaA would determine the development and the commercialization path for the candidates.

Under the agreement, KineMed said it would receive from Merck an upfront payment, milestones and royalty payments on products advanced with the KineMed technology.

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GPC Biotech AG (Frankfurt Stock Exchange: GPC; TecDAX index; Nasdaq: GPCB) of Martinsried and Munich said it would implement U.S. staff reductions by 15 percent.

As part of a succession plan that was put into place in 2006, Martine George will succeed Marcel Rozencweig as senior vice president, drug development, and chief medical officer, and will assume leadership of the drug development team, the company said. Rozencweig will remain as senior vice president, clinical science and drug evaluation to identify drug development in-licensing opportunities.

* * *

H. Lee Moffitt Cancer Center and Research Institute of Tampa has selected Azyxxi, the **Microsoft** unified health enterprise platform, to personalize its cancer treatment programs.

Azyxxi will be used to assimilate large quantities of diverse data, including electrocardiograms, magnetic resonance imaging scans, dynamic angiograms, ultrasound images and, ultimately, genomic information, providing a visual gateway for instant access to the information, and allowing researchers to make and prove their hypotheses within minutes instead of months, the center said.

* * *

ImClone Systems Inc. (Nasdaq: IMCL) and **Bristol-Myers Squibb Co**. (NYSE: BMY) said they have amended the terms of their agreement for the co-development and co-promotion of Erbitux (Cetuximab) in North America.

Under the amendment, the companies said they would expand the investment in the ongoing clinical development plan for the agent by up to several hundred million dollars. Development costs, up to a threshold value, will be the sole responsibility of Bristol-Myers Squibb; costs in excess of this threshold will be shared

by both companies according to a pre-determined ratio.

With the additional funding, the companies will add phase II and phase III trials of the drug in therapeutic settings. The clinical program will explore Erbitux in tumor types including brain, breast, bladder, gastric, lung, pancreas and prostate, the company said.

In another development, ImClone said it has signed settlement and sublicensing agreements with the **Massachusetts Institute of Technology** and **Repligen Corp.** to end litigation related to U.S. Patent No. 4,663,281, which is owned by MIT and exclusively licensed to Repligen.

Under the settlement, ImClone said it would pay $65.0 million in cash for full and final settlement of the claims against ImClone, as well as for a royalty-free, irrevocable worldwide sublicense to technology patented under U.S. Patent No. 4,663,281. The lump-sum payment ImClone has made to Repligen represents the full amount the company would pay to settle its litigation with MIT and Repligen, Imclone said.

Repligen also granted to ImClone a royalty-free, irrevocable worldwide sublicense for the future use of other patented technology, including U.S. Patent No. 5,665,578, which is owned by Abbott Laboratories, but to which Repligen has the power to sublicense under an agreement between Abbott Laboratories and Repligen. U.S. Patent No. 5,665,578 is the patent upon which Abbott Laboratories sued ImClone for patent infringement earlier this year.

* * *

Oncology Nursing Certification Corp. of Pittsburgh said its Board of Directors has selected **Pearson VUE**, a leader in the computer-based testing industry, as its new testing partner to develop and administer computer-based OCN, CPON, AOCNP, and AOCNS examinations beginning in January.

Pearson VUE is the electronic testing business of Pearson, and services professional licensing and certification markets in healthcare and other industries.

* * *

Progen Pharmaceuticals Limited (NASDAQ: PGLA) of Brisbane said it will use **Quintiles,** a contract research organization, for clinical development-related projects that include a phase III trial of anti-cancer drug PI-88 for hepatocellular carcinoma.

The primary endpoint is the length of time patients remain disease-free following surgery to remove tumor-affected parts of the liver, the company said.

* * *

Rosetta Genomics Ltd. (NASDAQ: ROSG) of Rehovot, Israel, said it would collaborate with **NYU Medical Center** to develop a microRNA-based diagnostic test for melanoma.

Rosetta Genomics said it would use its proprietary engine to screen more than 700 microRNAs to identify the signature for the melanoma prognostic indicator test. While the diagnostic test is still in the early stages, three diagnostic products in 2008 that include a test for cancer of unknown primary and two differential diagnostic tests related to lung cancer.

"Through our work with microRNAs, which have been shown to hold tremendous potential as biomarkers, we will be able to better understand both the origins and the development of the disease," said Eva Hernando of the Department of Pathology at the NYU School of Medicine. "NYU's extensive experience with melanoma, combined with Rosetta Genomics unmatched knowledge in microRNAs offers an exciting research opportunity."

MicroRNAs are naturally occurring form of RNAi that act as protein regulators and form the basis for a new class of diagnostics and therapeutics.

* * *

Roswell Park Cancer Institute of Buffalo and **AndroBioSys Inc.** said they are entering into a licensing and investment agreement that gives ABS exclusive rights to patented technology held by James Mohler and Gary Smith, co-leaders of the Prostate Cancer Program at RPCI and founders of ABS.

The agreement also provides RPCI with an equity position in the company, the institute said.

* * *

SGX Pharmaceuticals Inc. (NASDAQ:SGXP) of San Diego said it has updated its license and collaboration agreement with **Novartis** to develop and commercialize BCR-ABL inhibitors for both first line and drug resistant chronic myelogenous leukemia.

One of the candidates, SGX393, has a likely application in drug resistant CML, the company said.

Under an amendment to the license and collaboration agreement, SGX said it has obtained the right to develop and commercialize SGX393 outside of the collaboration, subject to a reacquisition right of Novartis that is exercisable at a future date. Also, the amendment gives Novartis responsibility for the selection of all future development candidates as well as responsibility for the clinical development of additional compounds from the collaboration. An IND on SGX393 could be filed is the first half of 2008, the company said.

Clinical Trials:

FDA Allows IND For Genta's G4544, Developed By NCI

(Continued from page 1)

professor of dermatology and head of the Division of Dermatooncology, Department of Dermatology, University Medical Center, Tubingen, Germany. "The use of LDH to pre-select individuals who are disproportionately likely to benefit represents an important innovation for patient treatment."

Genasense blocks the production of Bcl-2. The drug has Orphan Drug designations in Australia and the U.S. for melanoma, along with Fast-Track designation in the U.S.

In the first phase III trial for advanced melanoma, 771 patients were randomly assigned to receive chemotherapy with DTIC alone or in combination with Genasense. They also were prospectively stratified according to blood levels LDH. Further analysis suggested that maximum benefit accrued to patients whose LDH did not exceed 80 percent of the upper limit of normal for LDH. Hazard ratios in this group of 274 patients, who are the focus of the new AGENDA trial, indicate that the addition of Genasense to DTIC was associated with a 42 percent reduction in the risk of disease progression and a 36 percent reduction in risk of death.

In another development, **Genta Inc**. (NASDAQ: GNTA) said FDA has allowed the Investigational New Drug exemption for G4544.

Genta said the first cohort of 6 normal volunteers has been treated with single doses of the treatment without experiencing significant side effects.

G4544 is a new tablet formulation that enables oral absorption of the active ingredient contained in Ganite (gallium nitrate injection), a drug that is marketed by Genta and approved in the U.S. for cancer-related hypercalcemia that is resistant to hydration.

The initial study is a dose-ranging, single-dose evaluation of G4544 that will examine safety and pharmacokinetics.

G4544, developed by NCI, was developed to extend administration of the active ingredient in Ganite, and avoid intravenous pumps or hospitalization.

* * *

Allos Therapeutics Inc. (NASDAQ:ALTH) of Westminster, Colo., said it has begun enrollment in a phase I, open-label, multi-center study of its antifolate PDX (pralatrexate) with vitamin B12 and folic acid supplementation for relapsed or refractory cutaneous T-cell lymphoma.

In the study, treatment will consist of PDX as part of a weekly schedule for two or three weeks followed by one week of rest. Up to 56 evaluable patients will be enrolled to determine optimal dose and safety profile. A total of 20 will be enrolled at the optimal dose and schedule. Steven Horwitz, assistant attending physician, lymphoma service, Memorial Sloan-Kettering Cancer Center, is study chairman.

PDX is a small molecule chemotherapeutic agent that inhibits dihydrofolate reductase, or DHFR, a folic acid-dependent enzyme involved in the building of nucleic acid, or DNA, and other processes.

* * *

Biomira Inc. (NASDAQ:BIOM) (TSX: BRA) of Edmonton said it has begun in a phase I trial of the small molecule compound PX-478 in advanced metastatic cancer.

The compound inhibits the activity of hypoxia inducible factor HIF-1 alpha, a transcription factor that controls the expression of genes in cancer cell growth and survival. Genes regulated by HIF-1 alpha contribute to functions such as angiogenesis, use of glucose for energy, and protection against apoptosis.

The 36 patients with advanced solid tumors or lymphoma who have failed or are intolerant of standard therapy will be given the agent orally on days 1 through 5 of a 21-day cycle.

* * *

Callisto Pharmaceuticals Inc. (Amex: KAL; FWB: CA4) of New York said it has completed enrollment of its phase II trial of Atiprimod in low to intermediate grade neuroendocrine carcinoma. The 40-patient trial has seven clinical sites in the U.S.

The primary objective is to evaluate efficacy of the treatment in low to intermediate grade neuroendocrine carcinoma with metastatic or unresectable cancer and with disease progression despite standard therapy.

Atiprimod is an orally bio-available small molecule drug shown to be antiangiogenic, inhibit secretion of VEGF and IL-6, elicit an apoptotic response, and inhibit phosphorylation of key kinases involved in tumor progression and survival including Akt and STAT3, the company said.

* * *

Kosan Biosciences Inc. (NASDAQ:KOSN) of Hayward, Calif., said it has opened the TIME registration program of its Hsp90 inhibitor, tanespimycin (KOS-953), for multiple myeloma.

The program includes two clinical trials: TIME-1 and TIME-2. TIME-1 is a phase III trial in a first-relapse

population, the company said. TIME-2 is a phase II/III trial in relapsed-refractory disease. TIME-2 also could support registration in a relapsed-refractory setting.

The TIME-2 trial, conducted at clinical sites in the U.S. and in Europe would have an enrollment of 130. The trial would test three different doses of tanespimycin in combination with the approved dose and schedule of bortezomib. Tanespimycin will be administered twice weekly as a one-hour intravenous infusion on a cycle of two weeks of treatment every three weeks.

The primary endpoint is the dose response based on objective response rate after four cycles of treatment.

TIME-1 will be an open-label, randomized, multi-center trial comparing two groups: those treated with bortezomib plus tanespimycin and those treated with bortezomib alone. The trial has a primary endpoint of progression-free survival.

* * *

Genmab A/S (OMX: GEN) of Copenhagen said it has begun a phase III study of HuMax- EGFr (zalutumumab) for head and neck cancer, in cooperation with the Danish Head and Neck Cancer Group.

The study will assess whether concomitant therapy with HuMax-EGFr can improve the efficacy of primary curative radiotherapy, the company said.

In the randomized study, treatment will consist of radiotherapy or HuMax-EGFr plus radiotherapy. Treatment with accelerated radiotherapy plus nimorazole and also cisplatin chemotherapy will also be administered. Those receiving HuMax-EGFr will receive six weekly doses of 8 mg/kg of HuMax-EGFr. They will be followed for five years. The objective is to determine the efficacy of HuMax-EGFr in combination with radiotherapy squamous cell carcinoma of the head and neck. The primary endpoint is loco-regional control.

* * *

Innovive Pharmaceuticals (OTCBB: IVPH) of New York said it has reached a pharmaceuticals agreement with FDA on special protocol assessment for STAR-1, a phase II trial with Tamibarotene for refractory acute promyelocytic leukemia.

The trial will be an open-label, non-randomized, single-arm, multi-national study with an enrollment of 50 patients with relapsed or refractory APL following treatment with all-trans-retinoic acid and arsenic trioxide. Tamibarotene will be self-administered orally via tablets on an outpatient basis.

The primary objective is the rate of durable complete response for Tamibarotene therapy when administered as a single agent.

* * *

Marshall Edwards Inc. (NASDAQ:MSHL) a subsidiary of **Novogen Ltd.,** of Sydney, Australia, and New Canaan said its phase III Ovature trial of phenoxodiol in advanced ovarian cancer resistant or refractory to platinum-based drugs has begun in Europe.

There will be an additional 30 sites in the U.S. Four sites are open in Australia. The 470-patient study would determine the safety and effectiveness of phenoxodiol when used in combination with carboplatin.

In the double-blind treatment arms, one trial arm will receive weekly carboplatin and phenoxodiol, the company said. The other trial arm also will receive weekly carboplatin, but a placebo will be substituted for phenoxodiol.

A change from receiving carboplatin (or cisplatin) in the traditional dose pattern (every two to three weeks) to a weekly carboplatin regimen has been reported to provide a tumor response in some patients with recurrent ovarian cancer, the company said. Therefore, researchers will learn more about the efficacy of weekly carboplatin.

The primary outcome is the assessment of the relative time it takes for the ovarian cancer to progress. An analysis of interim results will be possible after 95 patients have progressed with their disease.

* * *

Millennium Pharmaceuticals Inc. (NASDAQ: MLNM) of Cambridge, Mass., said it has begun a randomized, multi-center phase II trial to evaluate the efficacy of combining Velcade (bortezomib) for injection, lenalidomide / dexamethasone and cyclophosphamide for multiple myeloma.

The EVOLUTION trial will combine Velcade and lenalidomide / dexamethasone and also explore the benefit of cyclophosphamide, an alkylating agent, which has shown synergistic activity with Velcade. The trial would enroll 100 patients.

In another development, the company said interim analysis results of the international phase III VISTA trial for newly diagnosed multiple myeloma showed that Velcade, melphalan, and prednisone demonstrated a statistically significant improvement in all efficacy measures, including time-to-disease progression, complete remission rate, progression-free survival and overall survival, compared to melphalan and prednisone alone.

Based on the recommendation of an independent data monitoring committee, the control arm was stopped early to allow patients being treated with MP to have

Velcade added to their therapy.

"The results position Velcade based therapy as a new standard of care for newly diagnosed multiple myeloma patients," said Paul Richardson, clinical director, Jerome Lipper Multiple Myeloma Center Dana-Farber Cancer Institute, and a lead investigator of the VISTA trial. "The combination of Velcade with melphalan and prednisone surpassed all efficacy endpoints, including time-to-disease progression, complete remission rate, progression-free survival and overall survival, and did so, much earlier than expected."

* * *

Multiple Myeloma Research Consortium of Norwalk, Conn., and **Proteolix Inc.** of South San Francisco said enrollment has begun in a multi-center phase II trial of the Proteolix proteasome inhibitor, carfilzomib (PR-171), for relapsed and refractory multiple myeloma.

Ten MMRC Member Institutions will participate in the study, under the MMRC leadership of Melissa Alsina, of H. Lee Moffitt Cancer Center & Research Institute. The trial will evaluate the overall response rate for two cycles of carfilzomib in multiple myeloma where there has been treatment with specific FDA-approved therapies, with relapse after two or more of such therapies, and where patients are refractory to the most recently received therapy.

MMRC and Proteolix also will begin enrollment for an open-label, single-arm, phase II study of carfilzomib for relapsed multiple myeloma, with stratification by bortezomib (Velcade).

* * *

Spectrum Pharmaceuticals Inc. (NASDAQ: SPPI) of Irvine, Calif., said it has begun enrollment in its second phase III registrational trial for EOquin for non-invasive bladder cancer.

The trial design was reviewed under a Special Protocol Assessment procedure, which calls for two double-blind, placebo-controlled, randomized clinical trials, with randomization in a one-to-one ratio to EOquin or placebo, the company said. The primary endpoint will be the difference in the rate of tumor recurrence between the two treatment groups by year two.

EOquin (apaziquone for intravesical instillation) becomes activated by reductase enzymes found in cancer cells. The product is formulated for administration directly into the urinary bladder. In a phase II pilot study, the agent instilled into the bladder following surgery was well tolerated and was not absorbed in any detectable amount from the bladder wall into the bloodstream.

Spectrum said it completed a multi-center, phase II trial in Europe. The results demonstrated the drug was well-tolerated and produced a 67 percent complete response.

* * *

VION Pharmaceuticals Inc. (NASDAQ:VION) of New Haven, Conn., said it has accrued 85 patients for a phase II trial of Cloretazine (VNP40101M) in untreated elderly with de novo poor-risk acute myelogenous leukemia.

The trial is evaluating the agent in those at least 60 years of age with one of the following risk factors: unfavorable cytogenetics; an ECOG performance status of 2 or greater; or a co-morbid condition that precludes them from receiving cytotoxic therapy with cytarabine and an anthracycline, the company said. Patients over age 70 with de novo AML who do not have favorable cytogenetics are also eligible.

The primary endpoint is the complete response rate, including complete remission, and complete remission with incomplete platelet recovery. The trial had a two-stage min-max design in which if there were at least nine responses in the first 42 patients, the trial was to continue to the second stage. In January, there had been at least nine remissions, allowing the trial to continue. Eighty-five patients were enrolled in order to ensure that at least 77 would be eligible for the trial and included in the full analysis set. At least 22 responses in 77 are required to confirm the 35 percent target response rate with 95 percent confidence. If the full analysis set includes all 85 patients, then at least 24 responses are required for confirmation of the target response rate, the company said.

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YM BioSciences USA Inc. has been cleared by FDA to begin a trial investigating nimotuzumab in pediatric recurrent diffuse intrinsic pontine glioma.

Nimotuzumab is a humanized monoclonal antibody that targets the epidermal growth factor receptor. Eight U.S. pediatric clinical centers will participate. This is the first clinical trial cleared by FDA for a drug of Cuban origin, the company said. Clearance for importation of nimotuzumab into the U.S. was authorized by the U.S. Treasury Department.

The primary endpoint is response rate, with a target of 15 percent. The principal investigatory site is the Hospital for Sick Children in Toronto, where Eric Bouffet, Sylvain Baruchel, and Ute Bartels lead the international program. The U.S. sites include pediatric neuro-oncology centers that are members of the POETIC consortium (Pediatric Oncology Experimental Therapeutics International Consortium).