THE CANCER LETTER

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Ten Is The New 12: Medicare Lowers Hemoglobin Targets For ESA Use

By Paul Goldberg

CMS earlier this week released the final version of its National Coverage Decision on the use of erythropoiesis-stimulating agents in oncology.

The agency has softened its coverage criteria, compared to the version that was put out for public comment in May. However, compared to current practice, the new payment policy will reduce utilization of the ESA agents.

Under the new coverage policy, which became mandatory for all carriers immediately as it was published on July 30, the Medicare and Medicaid programs will pay for ESAs for cancer patients only when their hemoglobin level drops below10 g/dL. The draft version proposed a 9 g/dL threshold.

Until now, CMS carriers routinely covered ESAs for patients whose

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In Brief:

Otis Brawley To Succeed Harmon Eyre As Cancer Society's Chief Medical Officer

OTIS BRAWLEY will succeed **Harmon Eyre** as chief medical officer of the American Cancer Society as of Nov. 1, the society said.

Brawley, a practicing oncologist and professor of hematology, oncology, and epidemiology at Emory University, serves as medical director of the Georgia Cancer Center for Excellence at Grady Memorial Hospital in Atlanta and deputy director for cancer control at Emory's Winship Cancer Institute.

Before joining Emory in 2001, Brawley served in a variety of positions at NCI, most recently as director of the Office of Special Populations Research. He led the NCI Prostate Cancer Prevention Trial.

"It's a real coup to have secured the commitment of Otis Brawley to join the American Cancer Society as our new chief medical officer," said John Seffrin, chief executive officer of ACS. "Dr. Brawley's extensive experience in health disparities will help us as we work to eliminate disparities in access to quality cancer care and as we continue to make global progress against this disease."

The chief medical officer is the society's most senior clinical staff position, providing management oversight of intramural and extramural research, surveillance, and epidemiology, cancer control science and international programs and activities.

Brawley is a member of the American College of Physicians, the

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Medicare Decision Will Further Decrease ESA Use In Cancer

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hemoglobin dipped under 12 g/dL, a level noted in the FDA package insert and suggested as a threshold in the guidelines of the American Society of Clinical Oncology and the American Society of Hematology. The guidelines of the National Comprehensive Cancer Network recommend initiation of therapy in patients with hemoglobin of under 11 g/dL.

Patients who fail to respond to therapy will now be allowed a single 25 percent increase in the agent's dose. In the past, such patients could be subjected to more aggressive dose escalations. Patients who respond to therapy would not receive another dose until their hemoglobin once again drops below 10 g/dL.

The CMS final decision eliminates some of the more controversial features of the draft proposal.

The agency abandoned its plan to impose conditions of coverage based on expression of erythropoietin receptors by certain cancers. "The scientific understanding of this mechanism is a subject of continuing debate among stakeholders, continues to evolve, and can only be resolved through additional studies," the agency said in the NCD document.

The coverage of ESAs in myelodysplastic syndrome, prohibited in the draft decision, isn't mentioned in the final version of the NCD, and is therefore left to the discretion of local carriers.

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Editor & Publisher: Kirsten Boyd Goldberg
Editor: Paul Goldberg
Editorial Assistant: Shelley Whitmore Wolfe

Editorial: 202-362-1809 Fax: 202-318-4030
PO Box 9905, Washington DC 20016
Letters to the Editor may be sent to the above address.

Subscriptions/Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724
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The final decision covers solid tumors, multiple myeloma, lymphoma and lymphocytic leukemia, limiting the starting dose and dose escalations, and capping the duration of treatment to eight weeks after a chemotherapy session ends.

Also, the agency abandoned its plan to withhold coverage for ESAs used in conjunction with bevacizumab and monoclonal antibodies targeting the epidermal growth factor receptor.

"Coverage with Evidence Development," the mechanism CMS uses to induce sponsors to collect medical utilization data, will not be used in ESA coverage.

"Our goal was to maintain physician autonomy while ensuring the safety of our Medicare beneficiaries in light of the FDA boxed warnings," CMS Acting Deputy Administrator Herb Kuhn said in a statement. "This final NCD is based on the best science to date and consistent with FDA labeling and warnings. We look forward to further reports from FDA, and are prepared to make additional modifications to our policies to ensure that Medicare patients receive the best and most effective treatments."

The document is posted at www.cms.hhs.gov/mcd/viewdecisionmemo.asp?id=203.

In the ESA controversy, science is far from definitive. The drugs were approved based on their ability to reduce the need for blood transfusions, without a rigorous evaluation of their impact on survival and time to progression.

Currently, ASCO and ASH are reconsidering their joint guidelines for ESA use, as is NCCN. FDA, too, is believed to be continuing to revise the label for the agents. The agency's overall approach to this controversy is reflected in a "black box" warning that was placed on the ESA products in March: "Use the lowest dose… that will gradually increase the hemoglobin concentration to the lowest level sufficient to avoid the need for red blood cell transfusion."

The sponsors of the two ESAs marketed in the U.S. said the CMS action isn't based on good science.

"The coverage restrictions placed on the FDA-approved indication have no scientific basis and are incompatible with good clinical practice," Roger Perlmutter, Amgen's executive vice president for global research and development said in a statement. "We are concerned that inappropriately limiting coverage for ESAs at hemoglobin levels less than 10 g/dL will both increase blood transfusions and severely compromise the high quality of cancer care delivered by American physicians. In our view, restricting coverage in this way

is unreasonable, impractical and unworkable. Moreover, through this coverage decision, the CMS has undermined the ability of physicians to decide how best to administer ESA therapy to their patients through carefully defined dosing guidance articulated by the FDA."

Johnson & Johnson said the agency's actions may harm patients. "The NCD directs physicians to use Procrit in a manner that has never been studied in controlled clinical studies," said Stephanie Fagan, a company spokesman. "We will continue our efforts with CMS to identify and minimize potential unintended clinical consequences of this decision for Medicare beneficiaries."

ESA sales have been dropping in recent months, largely as a consequence of alarming study results that emerged since January, and, consequently, increased scrutiny by FDA. Aranesp sales decreased by 19 percent during the second quarter ended June 30, Amgen announced last week. Sales of Johnson & Johnson's Procrit dropped by 14 percent during the same period.

CMS, the world's single largest purchaser of ESAs, bought $5.4 billion worth of these agents in oncology and nephrology use last year. Now, with the agency declining to pay for treatment of patients with higher hemoglobin levels, utilization of these drugs is certain to take another hit.

The impact of new CMS rules is difficult to project based on publicly available data. Merrill Lynch projects that the changes in coverage would decrease the Aranesp market by $900 million, lowering sales from $3.63 billion to $2.78 billion.

According to proprietary data selectively released by Amgen, 98 percent of patients receiving Aranesp were initiated at below 12 g/dL, and 84 percent are initiated at below 11 g/dL.

In subsequent cycles, 97 percent of patients are treated at below 13 g/dL, and 86 percent at below 12 g/dL (The Cancer Letter, March 2). Amgen hasn't responded to multiple requests from this reporter to disclose how many patients getting Aranesp are treated at the hemoglobin level below 10 g/dL either initially or on re-treatment.

Amgen's stock price started to slip from just above $56 at the time the CMS policy was announced on July 30 to a low of about $50.50 on Aug. 1.

As CMS was developing its coverage policy, cancer professional societies, oncologists, patient groups and members of Congress urged it to soften some features of its draft decision. The CMS mailbag last month included a sign-on letter from 224 House members, a letter signed by 46 Senators, as well as letters from individual legislators (The Cancer Letter, July 20).

Next Step: Precertification

On July 31, the day after publishing the coverage decision, CMS answered several questions it received from physicians.

"Neither the proposed nor the final NCD created a target hemoglobin or hemoglobin range," the document states. "This is consistent with the current FDA approved label indication 'to decrease the need for transfusions in patients who will be receiving concomitant chemotherapy for a minimum of 2 months…' We note that the labeled dosing for this population does not in fact include an explicit numerical target range. Rather 'the dose should be titrated for each patient to achieve and maintain the lowest hemoglobin level sufficient to avoid the need for transfusion and not to exceed 12 g/dL.'"

Though the NCD went into effect immediately, instructions for local contractors would become available Sept. 30.

Another change in policy would be made on Jan. 1, when agency claim forms will be altered to include the patients' hemoglobin or hematocrit levels. "Thus, we would not expect to pay ESA claims that are not accompanied by a timely hemoglobin or hematocrit," the Q&A document states. This change would make CMS function like a health insurance plan that requires "pre-certification" of services.

The Q&A document is posted at www.cms.hhs.gov/mcd/viewdecisionmemo.asp?id=203.

"I think the final NCD is clearly an improvement over the initial proposal, which was flawed in a number of important ways," said David Steensma, an oncologist at Mayo Clinic. "I was especially pleased that the proposed ban on using ESAs in myelodysplastic syndrome did not come to fruition—I don't see how it could have remained, frankly, given that the clinical community was unified behind the need to preserve access to ESAs for MDS patients with low-risk disease, there were no new data suggesting safety issues with ESAs in MDS, and one of CMS' own pay-for-performance quality metrics released last year dealt with appropriate ESA use in MDS.

"However, there are still issues with the current guideline. For instance, it is inconsistent with the current FDA-approved label for these products," Steensma said. "Also, no study has shown a particular safety issue for patients treated to a goal of 11 g/dL rather than 10 g/dL, so I would have preferred more flexibility with respect to hemoglobin endpoint. I care for some

patients with cardiovascular disease who need to be kept above a hemoglobin of 9.0 or 9.5 g/dL in order to avoid developing symptoms; having to hold an ESA in them when the hemoglobin is 10.1 or 10.2 g/dL is cutting it pretty close, and may increase their use of blood products. It will be interesting to see if private insurers will follow CMS' lead or if they will devise their own policies."

Jeffrey Crawford, George Barth Geller Professor for Research In Cancer and chief of medical oncology at Duke University, said he is puzzled by the agency's medical rationale.

"I really don't understand the cutoff of 10 g/dL of hemoglobin for both initiation and maintenance," said Crawford, who was involved in Amgen's presentation before the FDA Oncologic Drugs Advisory Committee last May.

"In the first category, there are certainly patients who are symptomatic above 10 who by NCCN and other practice guidelines should be allowed to initiate the drug between 10 and 11," Crawford said. "And if 10 is now a ceiling level for maintenance, patients in essence will remain below 10 through most of their treatment time and likely be symptomatic.

"This is essentially removing the maintenance benefit of ESAs to restore hemoglobin levels to the accepted level of 12 to minimize symptoms and maximize impact on the quality of life. Instead, it converts ESAs to a rescue strategy only and since these agents often do not improve hemoglobin levels for weeks, will result in a marked increase in the need for transfusions for these patients.

"This is like using insulin when a patient's blood glucose is over 500, but withholding all doses for every value below 500. This wouldn't be good strategy for the long-term management of patients with diabetes.

"With ESAs, which don't act as quickly as insulin, it's even a worse idea for our cancer patients," Crawford said.

Fadlo Khuri, Blomeyer Professor of Hematology and Oncology and deputy director of the Emory University Winship Cancer Institute, said the CMS decision should require some adjustments, but is generally "a step in the right direction."

"It makes sense to go to 10 g/dL," said Khuri, who wrote an editorial in the June 14 issue of the New England Journal of Medicine on the overuse of ESAs. "They are pushing for doses where we clearly know that most patients can get symptomatic. They are looking at the patient population where the data are the most convincing."

This limit should probably be increased somewhat for patients who have symptomatic heart disease or a compromised pulmonary system, Khuri said.

The CMS decision is consistent with the reason for FDA's approval of these agents--as an alternative to blood transfusion, Khuri said. ESAs aren't approved for enhancing the quality of life.

"Typically, I use it when patients get below 10, or 9, depending on the patient," Khuri said. "I have never been convinced that pushing someone who has a hemoglobin of 11.5 to to 13.5 makes a difference in quality of life. I don't believe there are many physicians who transfuse patients when the hemoglobin drops below 12 . It's really below 9 that we treat with blood transfusions, and in some cases, below 8.

"What this NCD does is reduce the likelihood of overt indiscretion in the use of ESAs and makes it ultimately impossible for practicing oncologists to ignore the data. Maybe this will potentially lead to consideration of appropriate ESA use in specific diseases."

In the States:

North Carolina Assembly Forms Cancer Research Fund

The North Carolina General Assembly created the state's first University Cancer Research Fund with the passage of the new state budget earlier this week.

The fund, established to accelerate cancer research at the University of North Carolina at Chapel Hill's School of Medicine and its Lineberger Comprehensive Cancer Center, will provide $25 million in 2007-08 and is slated to increase to $50 million per year beginning in 2009.

Gov. Mike Easley signed the budget bill into law July 31.

The research funding will improve the quality of life and treatment of cancer patients and enhance UNC's access to science and technology, university officials said. The funds also will increase Lineberger's ability to discover and disseminate knowledge across the spectrum of cancer research, and make real improvements in prevention, early detection and therapies that will benefit all patients.

"We are extremely grateful to the members of the North Carolina General Assembly and Gov. Easley for providing this groundbreaking funding," said William Roper, dean of the School of Medicine and chief executive officer of the UNC Health Care System. "It will allow our university's great researchers to make significant advancements against a disease that has

touched the lives of nearly everyone."

The fund will create a statewide cancer assessment and prevention program.

"With the support of the General Assembly for construction of the North Carolina Cancer Hospital in 2004, and now this extraordinary cancer research fund, UNC has been provided an opportunity and a challenge—to become the nation's best university cancer center," said Shelley Earp, director of UNC's Lineberger Comprehensive Cancer Center.

"We must and will develop pathways to move prevention, early detection and therapeutic research into the clinic and the community, the outcome of which will be improved cancer care, grounded in the latest research findings," Earp said.

In the Cancer Centers:

Vanderbilt GI SPORE Renewed; Mayo, Holden In Collaboration

VANDERBILT-INGRAM Cancer Center received a $11.8 million, five-year renewal of its NCI Specialized Program of Research Excellence in gastrointestinal cancer, one of five such programs in the country.

"We received the top score in the country in the latest pool of GI SPORE applications," said **Robert Coffey Jr**., director of the GI SPORE and Ingram Professor of Cancer Research.

Vanderbilt's GI SPORE, co-directed by **Mace Rothenberg**, focuses on colorectal cancer. GI SPOREs are located at Vanderbilt, Johns Hopkins University, Harvard University, the University of Arizona and the University of North Carolina at Chapel Hill. Vanderbilt-Ingram has two additional SPOREs, one in breast cancer and one in lung cancer. It is one of seven centers to hold three or more SPORE grants.

The renewal application for the GI SPORE includes continuing projects from the first cycle and a new high-throughput screening strategy that aims to develop drug candidates for treating colorectal cancer.

"We knew that the competition was going to be intense, so we decided to 'roll the dice' and propose high-risk, high-payoff projects," Coffey said. "We are the first SPORE to propose high-throughput screening."

The investigators are using the Vanderbilt Institute of Chemical Biology's high-throughput screening facility under the direction of **C. David Weaver** to screen libraries of synthetic small molecules and natural products. **R. Daniel Beauchamp** is leading a screen for compounds that restore E-cadherin to the cell surface of colorectal cells and could therefore reverse the epithelial-to-mesenchymal transition that is a central event in the development of metastasis. **Ethan Lee** is directing a screen to identify agents that block Wnt signaling, a pathway that becomes deranged in nearly 90 percent of colorectal cancers.

"We already have a number of exciting hits from these screens," Coffey said. One of the "hits" is an FDA-approved drug that "has the potential to advance rapidly to a clinical trial," he said.

The renewal application also included patient advocates as integral members of each project.

* * *

TWO NCI-DESIGNATED comprehensive cancer centers said the institute would renew their jointly held Specialized Programs of Research Excellence grant for lymphoma research. Renewed for an additional five years, this $11.9 million grant supports Mayo Clinic Cancer Center and Holden Comprehensive Cancer Center (University of Iowa) in their translational research into lymphoma, said **Thomas Witzig**, hematologist at Mayo Clinic and co-principal investigator of the lymphoma SPORE. The cancer centers' original five-year lymphoma SPORE grant of $10.6 million was awarded in 2002. . . . **Caryn Lerman**, deputy director of the Abramson Cancer Center of the University of Pennsylvania, was awarded the Alton Ochsner Award Relating Smoking and Health. The award will be presented to Lerman for her work on pharmacogenetic approaches to nicotine dependence treatment at the annual convention of the American College of Chest Physicians Oct. 21, in Chicago. Lerman is the Mary W. Calkins Professor in the Department of Psychiatry and the Annenberg School for Communication. She is also director of the NCI-funded Transdisciplinary Tobacco Use Research Center at the University of Pennsylvania which translates research in neuroscience, pharmacology, and genetics to develop pharmacological therapies for nicotine dependence. . . . **JEFFREY FLIER**, the George C. Reisman Professor of Medicine at Harvard Medical School, will become dean of the Harvard Faculty of Medicine Sept. 1. He also is Harvard faculty dean for academic programs. A member of the HMS faculty since 1978, Flier was chief academic officer of the Beth Israel Deaconess Medical Center for five years. He is known for his work on diabetes and obesity. He succeeds **Joseph Martin**, who stepped down as dean June 30 after a decade of service. Flier is a member of the Institute of Medicine of the National Academy of Sciences. He was a clinical associate at NIH from 1974 to 1978 before joining the HMS faculty.

Barbara McNeil, the Ridley Watts Professor of Health Care Policy and professor of radiology, became acting dean July 1. . . . **FRED SANFILIPPO**, a transplant immunologist, will succeed Michael Johns as executive vice president for health affairs, CEO of the Woodruff Health Sciences Center and chairman of the board of Emory Healthcare. Sanfilippo is senior vice president and executive dean for health sciences at Ohio State, and CEO of the Ohio State University Medical Center. The appointment is effective Oct. 1, at which time Johns will assume the position of chancellor of Emory University. . . . **FOX CHASE CANCER CENTER** made three recent appointments. **Crystal Denlinger** was named attending physician in the Department of Medical Oncology. Denlinger, who has a special interest in breast cancer, was chief hematology-oncology fellow at Fox Chase. **Kristin Edwards** joined the Department of Radiology. Edwards, whose interest is abdominal imaging, was clinical instructor in radiology at Jefferson Medical College and a body-imaging fellow at Thomas Jefferson University Hospital. **Sameer Patel** joined the center's department of surgical oncology. Patel specializes in plastic and reconstructive surgery and was a fellow in microvascular reconstructive surgery and a clinical specialist in the department of plastic and reconstructive surgery at M. D. Anderson Cancer Center.

In Brief:

Brawley To Succeed Eyre As ACS Chief Medical Officer

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National Medical Association, the American Society of Clinical Oncology and the American Association for Clinical Research. He has received numerous awards throughout his career, including in 2006 the U.S. Public Health Service Crisis Response Service Award, the U.S. Public Health Service Distinguished Service Commendation and the Key to St. Bernard Parish for his work in New Orleans after Hurricane Katrina.

He is chairman of the NIH Consensus Panel on the treatment of Sickle Cell Anemia, and a member of the Centers for Disease Control and Prevention Breast and Cervical Cancer Early Detection and Control Advisory Committee. He previously served as a volunteer member of the ACS Prostate Cancer Committee and co-chairman of the Surgeon General's Task Force on Cancer Health Disparities.

Brawley is a graduate of University of Chicago Pritzker School of Medicine, and completed his internship at University Hospital of Cleveland, Case-Western Reserve University, his residency at University Hospital of Cleveland, and his fellowship at NCI.

"I am both humbled and extremely honored to have this remarkable opportunity to follow in the footsteps of a great leader," Brawley said. "Dr. Eyre's tenure was extraordinarily effective, and I am committed to continuing those successful efforts to ensure the American Cancer Society remains a leader in cancer science."

Eyre has served as chief medical officer since 1993 and has been a volunteer with the organization for more than 22 years, including serving as its national volunteer president in 1988.

Prior to joining ACS, Eyre was a medical oncologist at the University of Utah where he served as associate chairman of internal medicine and deputy director of the Huntsman Cancer Institute.

"It has been a privilege to have Dr. Eyre as my friend and colleague for many years, starting with our volunteer service together for the society, and for the last 14 years as he served as the organization's chief medical officer," Seffrin said. "Dr. Eyre is globally recognized as a cancer expert, and will be remembered for his tireless efforts in cancer control and research, and more specifically in helping the society make progress towards reducing the incidence and mortality of cancer and improving quality of life for the 10.5 million cancer survivors alive today."

* * *

AMERICAN SOCIETY for Therapeutic Radiology and Oncology announced the recipients of its 2007 Gold Medals. **Jay Harris** and **Larry Kun** will be honored for their dedication to radiation oncology, service to the society, and community cancer work. Harris is professor and chairman, Department of Radiation Oncology, Dana-Farber Cancer Institute and Brigham and Women's Hospital, Harvard Medical School. He also is residency program director for oncology for the Harvard Radiation Oncology Program. Kun is chairman, Department of Radiological Sciences, St. Jude Children's Research Hospital. Kun, a pediatric oncologist and former NCI clinical associate, is chairman of the NCI Pediatric Brain Tumor Consortium. Also, ASTRO announced that **Randal Weber** was named honorary member of the society. An otolaryngologist and the Hubert L. and Oliver Stringer Distinguished Professor and chairman of the Department of Head and Neck Surgery at M.D. Anderson Cancer Center, Weber was selected for promoting and supporting the multidisciplinary approach, especially in treating

patients with head and neck cancers in Houston, said **K. Kian Ang**, chairman of the ASTRO board and radiation oncologist at M.D. Anderson Cancer Center. The gold medals and Weber's award will be presented at the society's annual meeting Oct. 28- Nov. 1 in Los Angeles. . . . **HMO CANCER RESEARCH NETWORK** received a five-year, multi-site, cooperative grant of more than $20.2 million from NCI to continue research into cancer prevention, treatment, clinical trials recruitment research and health literacy activities. Group Health Center for Health Studies, of Seattle, will provide scientific and administrative leadership, said Ed Wagner, director of the MacColl Institute, senior investigator at the center and principal investigator at CRN. Funding was distributed among 13 research centers based in integrated health care delivery organizations that are collaborating with CRN. In this third round of NCI funding, research studies include electronic records to improve cancer prevention and educational methods for prevention and screening. HMO Research Network, of which CRN is a part, is a consortium of health care delivery organizations that have formal recognized research capabilities and a shared commitment to public-domain research. Group Health is a nonprofit health care system that coordinates care and coverage. Group Health Center for Health Studies conducts research related to prevention, diagnosis, and treatment of major health problems. . . . **KARIN REMINGTON**, a genomics researcher and developer of computational tools, was named director of the Center for Bioinfomatics and Computational Biology at National Institute of General Medical Sciences. Before joining NIH, Remington was project manager for the National Ecological Observatory Network, a $300 million effort supported by the National Science Foundation to construct ecological data collection facilities across the contiguous U.S., Hawaii, Alaska, and Puerto Rico. As vice president of bioinformatics research at The Venter Institute from 2002 to 2006, she led an NIH-supported large-scale genome sequencing production center and spearheaded a traveling laboratory-based educational program for public school students in Washington, D.C. . . . **JOYCE HUNTER**, cardiovascular physiologist and administrator at NIH, was named deputy director of the National Center on Minority Health and Health Disparities. Prior to joining NCMHD, she was deputy director, Division of Extramural Activities at the National Institute of Diabetes and Digestive and Kidney Diseases, where she coordinated scientific program policies that governed clinical research. She began her NIH career at the National Heart, Lung, and Blood Institute where she progressed from program officer to chief of the vascular research training and career development group, a scientific review administrator, and later, section chief of the contracts, clinical studies and training scientific review section. . . . **ALEX'S LEMONADE STAND** Foundation has awarded $3.4 million in grants for pediatric cancer research at 28 hospitals and universities in North America. In 2007, the foundation will fund 21 new grants and renew 22 of its 2006 awards to develop and test treatments, improve availability of clinical trials, and fund research into childhood cancers. During the nationwide 2007 Lemonade Days weekend, June 8-10, supporters raised over $1 million. "This grant is particularly important at this time because federal funding for cancer research has been cut in recent years." said Linda Resar, associate professor of medicine, oncology and pediatrics, Johns Hopkins University School of Medicine and a 2006 grant recipient. . . . **ONCOLOGY NURSING Certification Corp.** said it will offer a Certified Breast Care Nurse examination in 2009. Nurses who are successful in completing the multiple-choice examination will be awarded the CBCN credential, which will be valid for four years.

FDA, DoD To Share Data For Medical Safety Reviews

FDA and the Department of Defense said they have signed an agreement to share data and expertise related to the review and use of FDA-regulated drugs, biologics, and medical devices.

General patient data such as prescriptions, lab results and patient weight will be used by the FDA to spot trends, which may identify potential concerns as well as recognize benefits of products.

The two agencies will protect all personal health information exchanged under the agreement, in accordance with federal law.

The partnership, which will operate under a memorandum of understanding, is part of the FDA's Sentinel Network, a medical product safety initiative to explore linking private sector and public sector information to create a virtual, integrated, electronic network.

Funding Opportunities:

NOT-CA-07-020: NCI-Supported Ruth L. Kirchstein Institutional National Research Service Award Programs for Transdisciplinary Training in the Chemical Biology of Cancer. T32. Full text: http://www.grants.nih.gov/grants/guide/notice-files/NOT-CA-07-020.html. Inquiries: 301-496-8580.

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Business & Regulatory Report

Product Approvals & Applications:

GPC Biotech Withdraws Satraplatin NDA Following ODAC's Unanimous No Vote

GPC Biotech AG (Nasdaq: GPCB) said it has withdrawn the satraplatin New Drug Application filed for accelerated approval for the treatment of hormone-refractory prostate cancer patients whose prior chemotherapy has failed.

The company based its decision on the vote by the FDA Oncologic Drugs Advisory Committee July 24, that the agency should wait for the final survival analysis of the SPARC trial before deciding whether satraplatin is approvable.

Overall survival results from the SPARC trial are expected to be

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Clinical Trials:

Avalon Begins Phase II Trial Of Oral Small Molecule For Pancreatic Cancer

Avalon Pharmaceuticals Inc. (NASDAQ:AVRX) of Germantown, Md., said it has begun a phase II trial for pancreatic cancer.

The first active center is the Yale Cancer Center. The company it would conduct enrollment at 15 sites.

The trial will be conducted in two parts, both using an open-label, non-controlled design, the company said. Part A, with 15-20 patients, is a dose- escalation study to determine the maximum tolerated dose or effective biologic dose of AVN944 in combination with gemcitabine. Part B would establish the efficacy and safety of AVN944/gemcitabine combination with an enrollment of 110-120 patients. An initial treatment cycle of AVN944 and gemcitabine will be given and additional cycles of treatment every 28 days may be given at the discretion of the investigator and with the agreement of the patient.

AVN944 is an oral small molecule drug candidate that inhibits inosine monosphospate dehydrogenase, an enzyme that enables cells to synthesize guanosine triphosphate, a molecule required for DNA synthesis and cellular signaling.

* * *

Cell Genesys Inc. (NASDAQ:CEGE) of South San Francisco said it has recruited 600 patients into VITAL-1, the first of two phase III trials of GVAX immunotherapy for advanced prostate cancer.

The multi-center, randomized, controlled study will compare the immunotherapy to Taxotere (docetaxel) chemotherapy plus prednisone in hormone refractory prostate cancer with metastatic disease, the company said.

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PO Box 9905
Washington DC 20016
Telephone 202-362-1809

SPARC Data To Be Available Within Six Months, GPC Says

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available within six months, the company said. However, this timing is based on an extrapolation of death rates in the trial and may change.

"While we were very surprised and disappointed by last week's ODAC outcome, we need to move forward," said Bernd Seizinger, CEO of GPC Biotech. "Thus, we are focusing our efforts on the overall survival results from the satraplatin SPARC trial and integrating these data into the strongest possible NDA submission. If these data are positive, we plan to submit an NDA to the FDA as quickly as possible."

SPARC, a phase III registrational trial, called SPARC, is evaluating satraplatin plus prednisone versus placebo plus prednisone in 950 patients with hormone-refractory prostate cancer whose prior chemotherapy has failed. Patients who have not progressed continue to be treated and all patients are being followed for overall survival.

* * *

Biomira Inc. (NASDAQ:BIOM) of Edmonton said it has submitted an IND to FDA for PX-478.

PX-478, in preclinical studies, inhibits hypoxia-inducible factor (HIF)-1 alpha, the company said. In addition, the agent has produced tumor regression and growth delay in cancers, including cancers of the lung, breast, prostate, colon, kidney, pancreas and ovary.

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Publisher: Kirsten Boyd Goldberg
Editor: Paul Goldberg
Editorial Assistant: Shelley Whitmore Wolfe

Editorial: 202-362-1809 Fax: 202-318-4030
PO Box 9905, Washington DC 20016

Customer Service: 800-513-7042
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Genta Inc., (Nasdaq: GNTAD) of Berkeley Heights, N.J., said the requested re-examination by the Committee for Medicinal Products for Human Use of European Medicines Agency has reaffirmed a negative approval opinion of its marketing authorization application for Genasense (oblimersen).

The MAA proposed the use of Genasense plus dacarbazine for advanced melanoma, the company said. In its review, the EMEA indicated that positive findings in the phase III trial of Genasense should be confirmed in an additional study. Genta said it would conduct the study, known as AGEND.

"The re-examination affirmed the safety profile of Genasense," said Loretta Itri, president of pharmaceutical development at Genta. "We will continue to supply Genasense on a named patient and compassionate use basis outside the U.S., while we continue the late-stage clinical research that we hope will lead to formal EU approval."

* * *

GlaxoSmithKline (NYSE:GSK) of London and Rixensart, Belgium, said its cervical cancer candidate vaccine received a positive opinion from the European Committee for Human Medicinal Products for the prevention of precancerous lesions (high grade cervical intraepithelial neoplasia - CIN grades 2 and 3) and cervical cancer causally related to human papillomavirus types 16 and 18.

The proposed indication is based on data generated in girls and women aged between 10 and 25, the company said.

CHMP reviewed data from clinical trials in 30,000 females, including data from the largest phase III cervical cancer vaccine efficacy trial to date, which demonstrated that the candidate vaccine showed an excellent efficacy profile and was generally well tolerated, the company said.

* * *

Northwest Biotherapeutics Inc. (OTC Bulletin Board: NWBO; AIM: NWBS and NWBT) of Bothell, Wash., said it has received authorization for use from the Swiss Institute of Public Health to make DCVax-Brain commercially available for brain cancer patients in Switzerland.

DCVax, a platform technology applicable to most cancers, mobilizes the immune system to function normally, the company said.

Treatments are made by combining dendritic cells with cancer biomarkers derived from or displayed by the tumor, the company said. Precursors of the master

immune cells are continuously circulating in the blood and are obtained through a blood draw. The master immune cells are then matured and activated through a series of proprietary steps, then educated by exposure to the tumor biomarkers, and injected back through a simple intradermal injection in the arm or thigh, consisting of just a few drops, the company said.

NWBT also said it is conducting a phase II 14-patient trial in the U.S.

Clinical trial data for brain cancer have shown that DCVax-Brain delays disease recurrence from 6.9 months to 18.1 months for the newly diagnosed, the company said. Survival also was extended from 14.6 months to more than 33 months.

* * *

Spectrum Pharmaceuticals Inc. (NASDAQ: SPPI) of Irvine, Calif., said its IND application was filed with FDA for SPI-1620 for recurrent or progressive carcinoma as an adjunct to chemotherapy.

The product is a highly selective endothelin-B agonist, the company said. In experimental models, it has demonstrated a transient and selective increase in blood flow to tumors by over 300 percent and an increase in delivery of anticancer drugs to the tumor while sparing normal tissues and organs, the company said.

* * *

Veridex LLC of Warren, N.J., said it has received FDA approval for GeneSearch Breast Lymph Node Assay, its intra-operative and gene-based test that detects the spread of breast cancer into the lymph nodes.

"With this molecular pathology test, we have an opportunity to improve the standard of care for women with this disease," said Pat Whitworth, director of the Nashville Breast Center and a principal investigator in the GeneSearch BLN clinical trials. "Patients and physicians now have a higher degree of confidence in their lymph node test results and, as a result, make more informed decisions about their treatment."

The GeneSearch BLN Assay is the first in vitro diagnostic test approved in the U.S. for the rapid detection of metastases greater than 0.2 mm in sentinel lymph node tissue, the company said.

In clinical trials of 300 patients that compared performance of GeneSearch with commonly performed intra-operative test procedures, GeneSearch correctly identified 95.6 percent of metastases in lymph nodes, the company said. The accuracy of the test was statistically superior to the most commonly performed intra-operative test procedure, the company said.

The gene-based technology allows for the analysis of 50 percent of the sentinel node, versus five percent of tissue typically examined under a microscope for evidence of cancer cells, the company said. Test results from GeneSearch can be produced in 35 to 40 minutes during the initial surgical procedure versus two to three days with tissue pathology, the company said.

"Too often, women who have had breast cancer surgery are forced to return for a second operation to remove lymph nodes," said Peter Blumencranz, medical director, Breast Health Services, Morton Plant Mease Healthcare, Clearwater, FL. "The GeneSearch BLN test could change that by more accurately guiding decisions during surgery, in real-time, thereby reducing the risks, stress, emotional trauma and costs of second surgeries."

Clinical Trials:

Cell Genesys Begins Phase III Trial In Prostate Cancer

(Continued from page 1)

The primary endpoint is an improvement in survival.

The trial is supported by the median survival results from two, independent, multi-center phase II 15-patient trials, the company said. The subset that received the doses comparable to the phase III study dose showed median survival of 34.9 months and 35.0 months, respectively. The results also exceeded the predicted survival of 22.5 months and 22.0 months, respectively, as determined by a seven point disease characteristic nomogram. Results from both studies compare favorably to the median survival of 18.9 months for metastatic HRPC treated with Taxotere chemotherapy plus prednisone. Moreover, the safety profile observed in the phase II of GVAX immunotherapy for prostate cancer compares favorably with that reported for chemotherapy, the company said.

* * *

Cell Therapeutics Inc. (Nasdaq: CTIC; MTAX) of Seattle said interim results of RAPID, its phase II/III trial for aggressive non-Hodgkin's lymphoma, resulted in both arms achieving a major objective anti-tumor response.

The Replacing Adriamycin with Pixantrone to Improve Safety in NHL Disease trial is a 280-patient randomized controlled combination study investigating whether the substitution of pixantrone for doxorubicin in first-line treatment for advanced aggressive NHL can provide a comparable major response rate while reducing known doxorubicin-related toxicities.

The multi-center international trial randomizes the newly diagnosed to either the standard of care regimen

CHOP-R (cyclophosphamide, doxorubicin, vincristine, prednisone, and rituximab) or an investigational regimen, which replaces doxorubicin with pixantrone, CPOP-R (cyclophosphamide, pixantrone, vincristine, prednisone, and rituximab) monthly for six cycles, the company said. Response to therapy is evaluated every two cycles and evaluated every two months following completion of therapy.

Preliminary results demonstrated that treatment with pixantrone had a reduction in severe (grade 3/4) side effects when compared treatment with standard doxorubicin-based therapy, the company said.

Despite more treatment cycles with pixantrone, a three-fold reduction in the incidence of severe heart damage (LVEF decline >15 percent) was seen as well as clinically significant reductions in infections and thrombocytopenia, the company said. In addition, a reduction in febrile neutropenia was also observed.

* * *

Cylene Pharmaceuticals of San Diego said it has initiated a single-agent phase II trial of quarfloxin (CX-3543), its lead Ribosomal RNA Biogenesis Inhibitor, for chronic lymphocytic leukemia.

In the 25-patient open-label trial, the product will be administered in leukemia that has progressed with a purine analog and a monoclonal antibody treatment, the company said. Study centers include Tower Oncology Group of Los Angeles; South Texas Accelerated Research Therapeutics of San Antonio and Mayo Clinic.

Quarfloxin, a small-molecule targeted cancer therapeutic, is derived from the validated fluoroquinolone class of drugs, the company said.

* * *

EpiCept Corp. (Nasdaq and OMX Nordic Exchange: EPCT) of Tarrytown, N.Y., said it would begin the ATTRACT-CPN trial, a phase III study for EpiCept NP-1, its patented topical cream formulation of two FDA-approved drugs, 4 percent amitriptyline and 2 percent ketamine, for chemotherapy induced peripheral neuropathy.

The Assessment of Topical Treatment Response with Amitriptyline and Ketamine: Combination Trial in Chemotherapy Peripheral Neuropathy, or ATTRACT-CPN study, will be conducted within a network of 25 sites under the direction of the NCI funded Community Clinical Oncology Program, the company said.

The double-blind, 400-patient randomized placebo-controlled study for CPN will be 12 weeks in duration, with the primary endpoint being the change in average daily pain intensity scores from baseline to the end point, the company said. The secondary endpoints include the percentage whose pain intensity decreases greater or equal to 30 percent from baseline and other measures.

* * *

Expression Genetics Inc., of Huntsville, Ala, said a phase Ia study evaluating EGEN-001, in combination with standard chemotherapy is underway at the University of Alabama at Birmingham for recurrent epithelial ovarian cancer.

The product, formulated utilizing the EG proprietary TheraPlas delivery technology, is composed of interleukin-12 gene expression plasmid and a bio-compatible delivery polymer and is designed to increase the local concentration of IL-12, an anti-cancer cytokine, the company said. TheraPlas is a polymeric-based system for delivery of nucleic acids to cells.

* * *

Genzyme Corp. (NASDAQ:GENZ) of Cambridge, Mass., said it has successfully completed its phase III trial of Mozobil (plerixafor) in non-Hodgkin's lymphoma, and that the trial has met its primary and secondary endpoints.

The randomized, double-blind, placebo-controlled trial included 298 patients undergoing hematopoietic stem cell transplant for NHL at medical centers in the U.S. and Canada, examined the effectiveness of the drug in increasing the number of hematopoietic stem cells collected for a transplant, the company said. The study compared the hematopoietic stem cell yield from treatment with Mozobil in combination with G-CSF to treatment with G-CSF in combination with placebo.

In the primary efficacy endpoint, 59 percent treated with a combination of Mozobil and G-CSF achieved the target threshold for collection of at least 5 million CD34+cells/kg from the peripheral blood with four or fewer days of apheresis sessions, compared with 20 percent in the G-CSF/placebo group. The three-fold increase was highly statistically significant in favor of the Mozobil-treated patients ($p<0.0001$). The 40 percent absolute difference between the two treatment groups was nearly double the target that Genzyme prospectively defined in the protocol, which was reviewed by FDA as part of the Special Protocol Assessment process, the company said.

In the secondary efficacy endpoint, 87 percent treated with Mozobil and G-CSF achieved the minimum level of stem cells associated with a successful transplant (2 million CD34+cells/kg) in four or fewer days of apheresis sessions, compared with 47 percent in the placebo arm. The result also was statistically significant

in favor of the Mozobil treatment ($p<0.0001$), the company said.

The other secondary efficacy endpoints were supportive of the findings, including analysis of the number of days needed to reach target ranges for stem cell mobilization, the success of engraftment, the number of days needed to engraft, and the durability of the engraftment for the first 100 days, the company said.

The drug was well tolerated, with the most common adverse events being mild gastrointestinal effects and redness at the site of injection, the company said. There were two related serious adverse events seen in the Mozobil plus G-CSF arm, and one in the G-CSF plus placebo arm.

"These are very impressive results with far-reaching clinical importance for patients undergoing a stem cell transplant for lymphoma," said John DiPersio, professor, Washington University, St. Louis and principal investigator. "Literature suggests that increasing the number of stem cells in circulation and the number collected at the time of apheresis may improve the outcomes of patients undergoing a stem cell transplant, reduce the costs associated with stem cell collection and, more importantly, broaden the pool of patients for whom transplantation is an option."

* * *

Kiadis Pharma B.V. of Amsterdam said NIH would begin a phase II trial with the Kiadis Pharma ATIR product for conventional HLA matched transplants.

ATIR was selected after a pre-clinical research program and will be investigated as a treatment option for terminally ill blood cancer patients, the company said.

NIH investigators leading the trial are Stephan Mielke and John Barrett of the Hematology Branch of the National Heart, Lung, and Blood Institute, who have been approved by the NHLBI Institutional Review Board and FDA to conduct the study, the company said.

* * *

Kinex Pharmaceuticals of Buffalo, N.Y., said it has received FDA approval for its IND and will begin phase I trails with KX2-391, for lymphoma or solid tumors.

The studies would look at safety and at using biomarkers, the company said.

KX2-391 is an orally active Src kinase inhibitor the first non-ATP competitive kinase inhibitor to enter human trials, the company said.

* * *

Maxygen Inc. (NASDAQ:MAXY) of Redwood City, Calif., said it has begun a phase IIa trial to evaluate the efficacy, safety and tolerability of MAXY-G34 in chemotherapy-induced neutropenia.

MAXY-G34 is a pegylated granulocyte colony stimulating factor shown in preclinical and phase I studies to have superior properties compared to the PEG- GCSF therapy, the company said.

The 30-patient phase IIa trial will be conducted at centers in Eastern Europe in stage I-III breast cancer. TAC (docetaxel, adriamycin and cyclophosphamide) chemotherapy treatment will be followed by next-day administration of either MAXY-G34 or Neulasta to the control population, the company said. The trial is designed as a multiple ascending dose study, with planned doses at 10, 30, 60, or 100 micrograms per kilogram of MAXY-G34 compared to 6mg of Neulasta. Both MAXY-G34 and Neulasta will be administered as a single subcutaneous injection once per chemotherapy cycle, the company said.

* * *

Millennium Pharmaceuticals Inc. (NASDAQ: MLNM) of Cambridge, Mass., said it has begun UPFRONT, a randomized, multi-center, company-sponsored phase III trial to determine a Velcade based combination therapy with approved agents for newly diagnosed multiple myeloma, ineligible for stem cell transplantation.

"Velcade has delivered some of the highest complete remission and survival rates, rarely seen with the exception of high-dose therapy and stem cell transplantation," said Ruben Niesvizky, of New York Presbyterian Hospital and Weill-Cornell Medical Center, and principal investigator.

The UPFRONT, or Untreated Patients receiving therapy For multiple myeloma in a Randomized trial Of three novel regimens for patients Not intending to receive Transplant Therapy trial, will evaluate the safety and efficacy of Velcade and dexamethasone; Velcade, thalidomide and dexamethasone; and Velcade, melphalan and prednisone, the company said. The primary endpoint is progression-free survival with secondary endpoints including duration of response, overall survival and overall safety and tolerability, the company said. Target enrollment is up to 500 and participants will remain in the trial on treatment for up to one year.

The trial has an adaptive design, providing flexibility to modify the therapies, following an interim analysis, should a new standard of care be established in the marketplace, the company said.

* * *

OncoGenex Technologies Inc. today announced enrollment of the first patient in an open label, dose-escalation, multi-center phase I clinical study evaluating a new investigational drug, OGX-427, in patients with breast, ovarian, bladder, prostate or lung cancer.

OGX-427 blocks production of Heat Shock Protein 27 (Hsp27), a cell-survival protein that inhibits apoptotic cell death through multiple pathways. The study, which will enroll up to 54 patients with cancers known to overexpress Hsp27, will evaluate the safety, pharmacokinetics and biological activity of OGX-427 alone and in combination with docetaxel. All patients who enter the trial have failed therapies that are potentially curative or failed/refused other standard therapy. Clinical sites in Canada and the U.S. will participate in the study. Kim Chi, medical oncologist at the BC Cancer Agency, is the study's principal investigator.

* * *

Poniard Pharmaceuticals Inc. (NASDAQ: PARD) began a phase II trial of intravenous picoplatin in combination with docetaxel (Taxotere) and prednisone in patients with metastatic hormone-refractory prostate cancer.

Picoplatin, the company's lead product candidate, is a new generation platinum chemotherapy agent designed to overcome platinum resistance and to prolong the time to relapse after chemotherapy in the treatment of solid tumors, and to have an improved safety profile compared with existing platinum-based chemotherapeutics.

Picoplatin is also being studied in a phase III trial, known as SPEAR (Study of Picoplatin Efficacy After Relapse), in small cell lung cancer.

* * *

Progen Pharmaceuticals Ltd. (NASDAQ: PGLA) of Brisbane, Australia, said it has designed its phase III trial of PI-88 for liver cancer to allow it to be faster, more cost effective, and with a higher likelihood of success than reported.

Disease-free survival is the primary endpoint. Recruitment for the double-blinded, placebo controlled study will begin later in the year in 14 countries in North America, Europe and Asia, the company said. A maximum of 800 patients with hepatocellular carcinoma will be recruited.

Results of the 48-week data of the phase II trial of PI-88 in patients who had undergone surgical removal of liver cancer, demonstrated that 160 mg of PI-88 showed an improvement in disease-free rate of 25 percent and prolonged the time to tumor recurrence from 27 to 48 weeks, or by 78 percent, building on the 30-week results.

* * *

Rigel Pharmaceuticals Inc. (NASDAQ:RIGL) of South San Francisco said its partner **Merck Serono**, a division of Merck KGaA of Darmstadt, Germany, has begun enrollment in a phase I study to evaluate R763/AS703569 in combination with a standard of care therapy in advanced malignancies.

* * *

SuperGen Inc. (NASDAQ:SUPG) of Dublin, Calif., said collaborators at **Translational Genomics Research Institute** and **TGen Clinical Research Services** at Scottsdale Healthcare in Scottsdale, Ariz., have begun dosing in a phase I trial of MP470, an oral, multi-targeted tyrosine kinase inhibitor in advanced-stage solid tumors.

The study also is open to accrual at South Texas Accelerated Research Therapeutics of San Antonio, Texas. The trial is an accelerated titration dose-escalation study to assess the safety and tolerability of MP470, and to determine the maximum tolerated dose of the compound. Additionally, the company said it would assess pharmacokinetic and biomarker data.

MP470 suppresses c-MET, c-RET and the mutant forms of c-KIT, PDGFR and FLT3, the company said. The agent also suppresses Rad51 protein, a component of double-stranded DNA repair in cancer cells.

* * *

Threshold Pharmaceuticals Inc. (NASDAQ: THLD) has begun a phase I clinical trial evaluating the safety of TH-302, the company's first hypoxia-activated prodrug, in patients with advanced solid tumors.

About 50 patients with advanced solid tumors are planned to enroll in the open-label, dose-escalation clinical trial to be conducted in the U.S. Up to six patients per dose level will participate in the dose escalation phase of the trial. Once a maximum tolerated dose has been established, six additional patients will be enrolled at the MTD level.

Patients who have received one or more regimens of chemotherapy, or for whom no effective therapy is available, are eligible for the trial. Patients will not receive any additional chemotherapy while receiving TH-302. The primary objectives of the study are to determine the MTD and dose- limiting toxicities of TH-302 in patients with advanced solid tumors and to establish the appropriate dose for testing in potential phase II clinical trials.

* * *

Tracon Pharmaceuticals Inc. (TRACON) of

San Diego and **Micromet Inc**., (NASDAQ:MITI) of Bethesda, Md., said Tracon has begun a phase I trial of TRC093 for advanced cancer.

TRC093 is a humanized monoclonal antibody that inhibits angiogenesis and tumor cell growth by binding cleaved collagen, a component of the extracellular matrix of tumors, the company said. The agent has shown activity, as monotherapy or when combined with chemotherapy, in pre-clinical studies of melanoma, breast and pancreatic cancer.

The trial would assess the safety, tolerability and pharmacokinetics, as well as preliminary anti-tumor activity, of the product, the company said.

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YM BioSciences Inc. (AMEX:YMI) enrolled the first five patients within the 50-patient initial cohort of its phase II trial with nimotuzumab in combination with irinotecan for the treatment of patients with colorectal cancer who have previously failed irinotecan-containing regimens.

Recruitment of the first cohort is expected to be completed within about eight months. The single-arm trial will enroll approximately 100 patients in Canada. The trial will enroll two 50-patient cohorts consecutively, with the first cohort receiving irinotecan on one of the conventional dosing schedules with weekly dosing of nimotuzumab and the second cohort receiving irinotecan on one of the conventional dosing schedules with nimotuzumab every two weeks.

The study principal investigator is Amil Shah at the BC Cancer Agency in Vancouver.

Deals & Collaborations:

Alfacell, US Pharmacia Agree On Onconase Distribution

Alfacell Corp. (NASDAQ:ACEL) has entered into a distribution agreement with USP Pharma Spolka Z.O.O. (USP Pharma), an affiliate of **US Pharmacia**, for the commercialization of Onconase (ranpirnase), Alfacell's lead drug candidate, in Eastern Europe.

Onconase is being evaluated as a treatment for unresectable malignant mesothelioma in a confirmatory phase IIIb registration study.

Under the distribution agreement, Alfacell has granted USP Pharma exclusive rights for the marketing, sales and distribution in Poland, Belarus, Ukraine, Estonia, Latvia, and Lithuania for an initial term that extends for 10 years after the first commercial sale in the territory.

Alfacell and US Pharmacia have entered into a securities purchase agreement pursuant to which US Pharmacia has purchased 533,360 shares of Alfacell's common stock at a price of $2.53 per share. Upon execution of the agreements, Alfacell received total cash payments of $1.5 million, consisting of $100,000 as an up-front signing fee under the distribution agreement and $1.4 million for the purchase of Alfacell common stock under the securities purchase agreement. Alfacell will also be entitled to receive milestone payments based on the achievement of certain regulatory approvals and certain sales goals. Also, Alfacell will receive a transfer price for product sold as well as a significant double-digit royalty rate on net sales.

Alfacell will be responsible for making regulatory filings with and seeking marketing approval from the European Medicines Agency and the manufacturing and supplying of product. USP Pharma will be responsible for all commercial activities and related costs in the territory.

* * *

Coley Pharmaceutical Group Inc. (NASDAQ: COLY) of Wellesley, Mass., and **Dynavax Technologies Corp.** (NASDAQ:DVAX)of Berkeley, Calif., said they have entered into a licensing agreement for TLR Therapeutics patents from Coley.

Under the agreement, Dynavax receives a non-exclusive license under the Coley immunostimulatory oligonucleotide patent estate for the commercialization of Heplisav, a hepatitis B prophylactic vaccine, in phase III trials, the companies said. Coley will receive a $5.0 million up-front payment.

The drug is in a phase III trial in Canada and in Europe, the companies said. The multi-center trial, known as Phase III Heplisav Short-regimen Trial, or PHAST, is comparing a two-dose regimen of Heplisav administered at 0 and 1 month to the conventional three-dose regimen of Engerix-B. The enrollment target is 2,000, ages 11 to 55 years, the companies said.

* * *

CompuCyte Corp. of Cambridge, Mass., and **Cold Spring Harbor Laboratory** of Cold Spring Harbor, N.Y., said they have established the first U.S.-based Regional Quantitative Imaging Cytometry Center of Excellence.

Located at CSHL and run by both organizations, the center will provide educational and training resources for quantitative imaging cytometry based on the CompuCyte laser scanning technology, the collaborators said.

Under the agreement, CSHL and CompuCyte will sponsor an annual symposium and training programs

throughout the year, focusing on new QIC techniques for researchers using LSC systems in cell and tissue-based research, the collaborators said.

* * *

EntreMed Inc. (NASDAQ:ENMD) of Rockville, Md, said it has entered into a collaborative research agreement with the **University of New South Wales** and Children's Cancer Institute Australia for Medical Research to map pathways in the mechanism of action for its lead compound, 2-methoxyestradiol (2ME2 or Panzem) and analogs of 2ME2.

Research will be conducted at CCIA and UNSW under a grant awarded by the Australian Research Council, the company said.

* * *

Labopharm Inc. (TSX: DDS; NASDAQ: DDSS) of Laval, QC, and **Paladin Labs Inc.** (TSX:PLB) of Montreal said they have completed a licensing and distribution agreement under which Labopharm has granted Paladin the exclusive right to market and sell the Labopharm once-daily tramadol product in Canada.

Labopharm will retain co-promotion rights.

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Morphotek Inc., of Exton, Pa., said it has entered into an agreement with **CMC Biopharmaceuticals** of Copenhagen for development, manufacturing and regulatory documentation support of MORAb-028 for advanced melanoma and other cancers.

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Par Pharmaceutical Companies Inc. (NYSE: PRX) has acquired the North American commercial rights to Zensana (ondansetron HCl) Oral Spray from Hana Biosciences Inc.

Ondansetron is used to prevent nausea and vomiting after chemotherapy, radiation and surgery, and following successful development and approval, Zensana could be among the first in its class of 5-HT3 antagonist anti-emetic therapies to be available in an oral spray form.

Under terms of the agreement, Par will make a $5 million equity investment in Hana. Hana would receive milestone payments and royalties on future sales of Zensana.

Par also said it has entered into an agreement with NovaDel Pharma, Inc., to collaborate in the reformulation of Zensana. Following completion of reformulation efforts already under way, Par will reconfirm the product's pharmacokinetic profile and resubmit the New Drug Application to FDA.

* * *

Peregrine Pharmaceuticals Inc. (NASDAQ: PPHM) of Tustin, Calif., said it has licensed worldwide exclusive rights to Beta 2 Glycoprotein 1 protein, an anti-angiogenesis technology, from **M. D. Anderson Cancer Center**.

The agreement would develop and commercialize rights to all forms of clipped or nicked Beta 2 Glycoprotein 1 protein, which was first characterized by Alan Schroit, deputy chairman, Department of Cancer Biology and John Q. Gaines Professor of Cancer Biology at M. D. Anderson Cancer Center.

Peregrine, Schroit and M. D. Anderson will collaborate under a sponsored research agreement to conduct preclinical studies to advance B2GP1 toward clinical trials, the company said.

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Sigma-Aldrich Corp. (NASDAQ:SIAL) of St. Louis and **Sangamo BioSciences Inc.** (NASDAQ: SGMO) of Richmond, Calif., said they have entered into an alliance to develop laboratory research reagents based upon the Sangamo ZFP technology.

Sagamo said it has created ZFP TFs, proteins known as transcription factors, that control gene expression and cell function. Among the applications are cell lines with enhanced protein production performance, panels of knock-out cell lines for drug discovery, as well as stem cell and transgenic animal models.

* * *

Spectrum Pharmaceuticals Inc., (NASDAQ: SPPI) and **Indena** S.p.A. signed a worldwide license agreement for ortataxel, a third-generation taxane classified as a new chemical entity that has demonstrated clinical activity in taxane-refractory tumors.

Oncology Management:

Oncotype DX Breast Cancer Assay Meets Blues' Criteria

Genomic Health Inc. (Nasdaq: GHDX) of Redwood City, Calif., said the Blue Cross and Blue Shield Association Medical Advisory Panel concluded that use of the Genomic Health Oncotype DX breast cancer assay to inform decision making about adjuvant chemotherapy, meets the Blue Cross and Blue Shield Association Technology Evaluation Center criteria for estrogen receptor-positive, node-negative, tamoxifen-treated breast cancer.

Oncotype DX is a diagnostic multi-gene expression test service that predicts breast cancer recurrence, survival within 10 years of diagnosis and chemotherapy benefit. The test has been evaluated in multiple independent studies of 2,600 breast cancer patients.