THE CANCER LETTER

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NCI "Community Cancer Centers" Program In Development, House Report Reveals

By Paul Goldberg

A report by the House Appropriations Committee last week commended NCI for "its foresight in developing the community cancer centers program."

What *is* the community cancer centers program?

Could the House appropriators have meant the NCI-designated Cancer Centers Program or the Community Clinical Oncology Program?

It appears that this is not a typographical error, but an endorsement of a previously unannounced program that Acting NCI Director John Niederhuber

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NCI Programs:

NCI Commits $8 Million More To R01s, Payline To Increase From 11 To 12 Percent

By Kirsten Boyd Goldberg

The NCI Executive Committee decided earlier this week to increase the R01 payline from the 11th percentile to the 12th percentile for the remainder of fiscal year 2006.

Also, the payline for "Star R01s" for first-time investigators would increase from the 17th to the 18th percentile.

The decision adds about $8.3 million to the Research Project Grant budget, Acting NCI Director John Niederhuber said to the NCI Board of Scientific Advisors June 29.

Before voting in favor of the move, the EC debated whether increasing the payline "would send a positive message, [but] it would also maybe increase expectations for 2007 that we wouldn't be able to meet," Niederhuber said.

BSA Chairman Robert Young, president of the Fox Chase Cancer Center, praised the decision. "Let me just say on behalf of the extramural community that the efforts on the part of the staff and yourself to increase the priority payline for the R01 pool, even though it is modest, will not go unnoticed," Young said. "It would be a wonderfully powerful signal of the attitude of your leadership about the preservation of investigator-initiated research, and we appreciate it."

"I wish it could be more," Niederhuber replied. The institute was able to move the resources because "we're more clear on how we're going to end up in September," he said.

As part of the budget planning for next fiscal year, FY2007, NCI

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NCI Developing New Program Of Community Cancer Centers

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apparently views as his priority project.

Reports that accompany House and Senate appropriations bills carry no legislative force, but at least nominally, they represent a congressional mandate. Though bureaucrats often use these documents as cover for controversial initiatives, it is unusual for a science-based agency to announce a program on Capitol Hill before some public vetting or peer review.

No concept describing the program has been published, and few details have been presented to NCI staff or constituents. It is unknown how this program would coexist with the CCOPs, cancer centers, and cooperative groups; how much it would cost, how the funds would be found, and whether it would be funded through grants or contracts.

The appropriations committee report describes the NCI community cancer centers as "a direct mechanism to translate the most promising advances in cancer treatment from major medical research institutions to community hospitals around the country."

The committee appears to be impatient to see the program implemented. "The Committee request a report by Sept. 30, 2007 regarding the feasibility of expanding this pilot program," states the report released June 20.

At a meeting of the NCI Board of Scientific Advisors June 29, Niederhuber described his rationale for a program, without mentioning the community cancer centers or the House report.

"I have a lot of confidence that we will get scientific accomplishments that will allow us to make major impact in this disease. What concerns me is, I think we have absolutely zero infrastructure to translate this to the people where they live in the communities," Niederhuber said in response to a question by board member Hoda Anton-Culver about the need for more resources for population science.

"I will come back to you with an effort and a plan that we are working on to try to address this issue," Niederhuber said. "I've had several get-togethers with other people in the country who also, I think, are beginning to see this as an issue and a problem. We're a research institute, so our investment really has to be in research, and population sciences, and behavioral sciences, in order to help us understand how to direct policymakers."

During a break at the meeting, Niederhuber acknowledged that the community cancer centers program is under development.

"We are working on a program, but it's a little premature to discuss," Niederhuber said to The Cancer Letter. "We are interested in the issue of access, as is the American Cancer Society and other organizations. There have been a lot of internal meetings with a lot of people across the [NCI] divisions. You are well aware of the CCOPs program, and other programs already out there, and this would tie together a lot of things."

Niederhuber said he didn't know whether the program would be administered through grants or contracts.

"I don't know yet," he said. "We might start it as a pilot. It's all in discussions, what the best match is, and how measure it, and will need a lot of planning."

Inserting language into the appropriations committee report isn't a formidable challenge. Lobbyists and advocacy groups accomplish this routinely, and NCI appears to have been making extensive use of this mechanism.

For example, last year, both the House and Senate reports applauded the NCI efforts to "eliminate suffering and death due to cancer" by 2015 and asked the institute to report on progress within a year (The Cancer Letter, July 22, 2005).

Though NCI officials haven't been referring to the 2015 goal in public, the institute's "congressional justifications" which accompany the President's budget proposal for fiscal 2007 report that the battle is going very well indeed.

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The document is posted at http://fmb.cancer.gov/financial/Congjust.htm.

House: Continue to Increase SPORE Funding

The House report directs NCI to continue to increase funding for Specialized Programs for Research Excellence:

"The Committee has long supported [SPOREs], and encourages NCI to provide support for the important work done by SPOREs at a level as close to the amount provided in fiscal year 2004 as possible, and in the current form, until such time as the Translational Research Working Group concludes its evaluation and provides recommendations to support translational research more effectively."

This language gives NCI political cover to increase funding for SPOREs. In March, the NCI advisory boards urged the institute to include outside advisors in the process of making budget cuts in the institute's programs, to make sure that no program is off limits (The Cancer Letter, March 31).

However, at a House appropriations hearing April 6, Niederhuber pledged that he would continue to fund SPOREs at the previously set level. "I am not shifting any money out of the program," Niederhuber testified. "I am going to do my best to put more money into the program" (The Cancer Letter, April 14).

NCI advisors are concerned about the plummeting payline for investigator-initiated grants, which is now at the 11the percentile.

In other highlights, the House report states:

Cancer centers.The committee commends NCI on the success of its cancer centers program. Given that minority populations suffer disproportionately from virtually every form of cancer, the Committee encourages NCI to support the establishment of a comprehensive center at a minority institution focused on research, treatment, and prevention of cancer in African American and other minority communities.

Cancer metastasis to bone. A frequent complication of cancer is its spread to bone (bone metastasis), causing severe bone pain and pathologic fractures. The Committee encourages NCI, in collaboration with NIAMS, NIA, and NIDDK to support research to determine mechanisms and to identify, block and treat cancer metastasis to bone.

Furthermore, the committee encourages NCI to expand research on osteosarcoma to improve survival and quality of life and to prevent metastatic osteosarcoma in children and teenagers who develop this cancer.

Gynecologic cancers. Today, in the United States, one woman will be diagnosed with a gynecologic cancer every seven minutes. That is almost 200 per day and 80,000 in a given year. Furthermore, almost 30,000 women die from a gynecologic cancer each year. Existing NCI funding for SPOREs, program projects, the Early Detection Network, and investigator initiated grants has accelerated basic, molecular-based research discoveries for gynecologic cancers. Recent progress combined with the need for further innovation makes this group of cancers an important focus under NCI's broader "roadmap" initiatives. The Committee encourages NCI to give priority to gynecologic cancers under its Nanotechnology Plan (CNPlan), its Oncology Biomarker Qualifications Initiative (QBQI), and its Cancer Genomics Atlas Project (TCGA), jointly conducted with the National Human Genome Research Institute. This inclusion will allow laboratory discoveries to be translated into clinical applications at the bedside causing a decrease in the mortality rates for women with gynecologic cancer.

Gynecologic oncology clinical trials. Organized in 1970, the Gynecologic Oncology Clinical Trials Cooperative Group (GOG) has conducted over 300 clinical trials involving almost 100,000 patients. With over 550 manuscripts in peer reviewed literature, the GOG is recognized as the leader in the development of new therapies for women with gynecologic cancer. The committee encourages NCI to support translational research involving biologic prognosticators and therapeutic effects of chemotherapy to speed the development and delivery of new cancer treatments to women with gynecologic cancers.

Liver cancer. The committee is pleased that NCI has issued program announcements requesting research projects on hepatocellular carcinoma. The Committee remains concerned, however, with the increasing incidence of primary liver cancer, and the small number of effective treatments, which is in sharp contrast to many other forms of cancer where the incidence is declining and the treatment options are rapidly increasing. The Committee encourages NCI to continue to support the NIDDK sponsored HALT-C clinical trial, which has particular relevance to the NCI mission. NCI is further encouraged to collaborate with the National Institute for Biomedical Imaging and Bioengineering on the development of improved early liver cancer diagnostic techniques.

Lung cancer. The committee remains concerned that the five year survival rate for lung cancer is only 15 percent, thirty-five years after the passage of the National Cancer Act. The Committee recognizes that

lung cancer is the leading cause of cancer deaths for both men and women--accounting for nearly one in every three deaths. The committee encourages the National Cancer Institute to work with CDC, the Centers for Medicare & Medicaid, the Food and Drug Administration, the Agency for Healthcare Quality and Research, the Department of Defense and other federal agencies to coordinate federal efforts on lung cancer in areas including research, early and late state diagnosis, treatment, and disease management, with goal of increasing five-year survival rates and, ultimately, curing lung cancer.

Neurofibromatosis. The committee is pleased that NCI conducted clinical trials of NF patients and encourages it to continue its commitment to NF research. Recognizing NF's connection to many of the most common forms of cancer, the committee encourages NCI to strengthen its NF research portfolio in such areas as further development of animal models, natural history studies, genetic and drug screening, therapeutic experimentation, and pre-clinical and clinical trials. The committee further encourages NCI to apply existing cancer drugs to NF patients in clinical trials both extramurally and intramurally, and to develop new drugs for NF that could then apply to the general population because of NF's connection to many forms of human cancer. The committee encourages NCI to continue to coordinate its efforts with other NIH institutes and government agencies.

The report is posted at http://thomas.loc.gov/home/approp/app07.html.

Kirsten Boyd Goldberg contributed to this report.

House Democrat Seeks Funds For NCI To Pursue 2015 Goal

By Paul Goldberg

Looking at the NCI Website, Rep. Brian Higgins, a freshman Democrat whose district in New York includes Roswell Park Cancer Center, sees bold plans to "eliminate suffering and death due to cancer" nine years from now.

Looking over the President's budget proposal for fiscal 2007, Higgins sees cuts to NCI's budget.

"That's a fundamental disconnect," said Higgins, who is about to introduce an amendment to place $240 million into the NCI budget. "You can't advance an ambitious and inspiring goal without making the commitment of resources that are necessary to get you to that goal."

Observers on Capitol Hill are pessimistic about the amendment's chances of passage, pointing out that offsetting savings would be difficult to find. Moreover, the appropriation bill which Higgins seeks to amend has stalled because of another amendment, which would increase the minimum wage.

"I am joining an effort as a member of Congress to try to achieve the 2015 goal," said Higgins, whose devotion to the goal endures even as the administration is trying to gently back away from the vows taken by former NCI Director Andrew von Eschenbach.

Von Eschenbach, who has left NCI to become acting FDA commissioner, no longer mentions the goal in his speeches. John Niderhuber, his successor at NCI, similarly doesn't mention 2015, and when asked, backs away from the firm deadline. However, the NCI website and publications are still awash in vows and to reach the goal nine years from now.

"I look at their website, I look at their publications, I don't see a pulling back of the 2015 goal, and as far as I am concerned, the goal is important, but it has to be sustained with an adequate commitment for financial resources to achieve the goal," Higgins said.

"In effect, the President's budget for 2007 cut virtually every cancer research and prevention program, and if you look at the budget document, it says that the justification for this is the funding obligations of the Federal government for things like the Iraq and Afghanistan wars and disaster relief," Higgins said. "Budgets are more than just spending plans. They are a representation of what we value, and I just think that cancer research and prevention need to be fully funded."

On June 28, during a brief meeting with Niederhuber, Higgins asked whether NCI is still committed to the 2015 goal.

"My conclusion in talking with Dr. Niederhuber is that they are still committed to the goal, but whether the goal produces an absolute result by 2015 is not as important as the fact that we make progress toward the goal in 2015. If they achieve in with 98 percent success, than that's still a good thing," Higgins said.

"I asked him specifically, 'Look, there seems to be some controversy within the cancer community about this goal,' and he [said], 'That's not important. The goal is not important. But it's good to have goals,' and he explained that as a researcher, when folks submit their applications for grants to NCI and NIH, they always have goals in mind. Some are achievable; some aren't. But the most important thing is that you demonstrate progress in the interim."

NCI Programs:

Niederhuber Plans Review Of NCI Director's Office

(Continued from page 1)

division directors met in a retreat earlier this month and gave presentations on their programs, Niederhuber said. The NCI senior leadership and division directors then used secret ballots to rank each program to decide whether it should receive funding increases, decreases, or a flat budget.

"Phase 2" of these budget deliberations will include review of the institute's "infrastructure-like programs," many of which are housed in the Office of the Director, Niederhuber said.

The director's office includes "quite a large collection of individuals and offices," Niederhuber said. "We will evaluate each of these activities, and where we can consolidate infrastructure."

Cancer Prevention:

Secondhand Smoke Unsafe, Surgeon General Concludes

U.S. Surgeon General Richard Carmona issued a comprehensive scientific report earlier this week that concludes there is no risk-free level of exposure to secondhand smoke.

According to the report, nonsmokers exposed to secondhand smoke at home or work have a 25 to 30 percent increased risk of developing heart disease, and a 20 to 30 percent increased risk for lung cancer.

"The health effects of secondhand smoke exposure are more pervasive than we previously thought," said Carmona, vice admiral of the U.S. Public Health Service. "The scientific evidence is now indisputable: secondhand smoke is not a mere annoyance. It is a serious health hazard that can lead to disease and premature death in children and nonsmoking adults."

Nearly half of all nonsmoking Americans are still regularly exposed to secondhand smoke. Even brief secondhand smoke exposure can cause immediate harm to a person's health, the report said. The only way to fully protect nonsmokers from the dangerous chemicals in secondhand smoke is to eliminate smoking indoors, the report concluded.

"The report is a crucial warning sign to nonsmokers and smokers alike," HHS Secretary Michael Leavitt said. "Smoking can sicken and kill, and even people who do not smoke can be harmed by smoke from those who do."

Secondhand smoke exposure can cause heart disease and lung cancer in nonsmoking adults and is a known cause of sudden infant death syndrome, respiratory problems, ear infections, and asthma attacks in infants and children, the report finds.

"The good news is that, unlike some public health hazards, secondhand smoke exposure is easily prevented," Carmona said. "Smoke-free indoor environments are proven, simple approaches that prevent exposure and harm."

Secondhand smoke contains more than 50 cancer-causing chemicals, and is itself a known human carcinogen. Levels of cotinine, a biological marker for secondhand smoke exposure, measured in nonsmokers have fallen by 70 percent since the late 1980s, and the proportion of nonsmokers with detectable cotinine levels has been halved from 88 percent 1988 to 1991 to 43 percent 2001 to 2002, the report found.

"Our progress over the past 20 years in clearing the air of tobacco smoke is a major public health success story," Carmona said. "We have averted many thousands of cases of disease and early

death and saved millions of dollars in health care costs."

Carmona emphasized, however, that sustained efforts are required to protect the more than 126 million Americans who continue to be regularly exposed to secondhand smoke in the home, at work, and in other enclosed spaces, including automobiles.

The report, "The Health Consequences of Involuntary Exposure to Tobacco Smoke: A Report of the Surgeon General," is available at http://www.surgeongeneral.gov/library/secondhandsmoke/.

ACS Calls For Further Smoke-Free Laws

John Seffrin, CEO of the American Cancer Society, said the report provides "overwhelming evidence" that states and local governments should enact strong and comprehensive smoke-free laws.

"The report confirms that the only way to protect people from secondhand smoke is to eliminate their exposure," Seffrin said. "It also reinforces what many of us in public health community have known for some time—that ventilation systems and separate dining sections in restaurants do not adequately protect people's health, and that smoke-free laws do not harm the financial well-being of businesses."

Also, the report found that there is an unequal burden of exposure, with employees at bars, restaurants, and casinos regularly exposed to tobacco smoke, Seffrin said. These employees are more at risk for developing

health problems.

"We have come a long way since 1964, when the Surgeon General's office released its watershed report on tobacco and cancer," Seffrin said. "That groundbreaking report, which relied upon the data collected and reported by the American Cancer Society in its Hammond-Horn study and Cancer Prevention Study I, was the first widely publicized official recognition that cigarette smoking is a cause of cancer and other serious diseases. In 1986, the Surgeon General's office released the results of the country's first comprehensive scientific analysis of the health effects of secondhand smoke, which included lung cancer, heart disease and life threatening respiratory illnesses. The report confirmed that cigarettes are not merely a personal choice, but a public environmental health hazard."

Currently, 16 states, Washington, D.C., and more than 2,200 communities have passed smoke-free laws, Seffrin said. Other countries, including Ireland, Uruguay, New Zealand, Italy and Sweden, have passed smoke-free laws, and England is scheduled to join these next year. The World Health Organization the Framework Convention on Tobacco Control, calls for all nations to enact smoke-free laws.

In a June 26 speech in Washington, Seffrin urged the U.S. federal government to ratify the WHO treaty, and take a stronger role in worldwide smoking cessation. His remarks are available at www.cancer.org/pressroom.

Laurie Fenton, president of the Lung Cancer Alliance, praised the report for focusing on the dangers of second-hand smoke, and called for more aggressive action supporting early detection and treatment of lung cancer.

"The report issued yesterday by the Surgeon General once again validates how lethal tobacco use is, and reinforces the importance of breaking the addiction and preventing children from picking up that first cigarette," said Fenton.

"Smoking is not cool. It is not sexy. It harms not only smokers but the people around them," she continued.

In praising the significance of the report, Fenton also emphasized, "We cannot lose sight of the fact that we must address the disease of lung cancer in its entirety. Tobacco cessation is the necessary first step but it will not completely eliminate lung cancer."

"Many people now being diagnosed with lung cancer heard the first Surgeon General's report on the connection between smoking and lung cancer forty years ago and quit smoking," Fenton pointed out. "Yet former smokers and people with no connection to smoking or second-hand smoke now account for more than 60 percent of the 174,000 new lung cancer cases that will be diagnosed this year."

Fenton notes, "Lung cancer receives far less federal research funding than the other common cancers, and the public health establishment has been slow to accept new technological advances in CT scanning that can diagnose lung cancer at an earlier, more treatable stage."

"The five year survival rate for lung cancer is still only 15 percent, while other cancers that have received significant federal research funding such as breast, prostate and colon cancers now have 5 year survival rates of 87 percent, 99 percent and 64 percent, respectively."

"We still do not have a coherent, aggressive plan for addressing the disease of lung cancer, and that is simply unacceptable," Fenton concluded. "Whether the patients are smokers, former smokers, or have never had any contact with smoking, no one deserves lung cancer."

Funding Opportunities:

Leukemia & Lymphoma Career Awards Available

The Leukemia & Lymphoma Society provides support for individuals pursuing careers in basic or clinical research in leukemia, lymphoma and myeloma:

—Scholar Awards, $110,000: (stipend $105,000 + $5,000 institutional overhead) per year for five years.

Annual renewals are based on a non-competitive progress report review. Applicants should be highly qualified investigators who have demonstrated their ability to conduct original research bearing on leukemia, lymphoma and myeloma. They are expected to hold independent faculty-level or equivalent positions. The award is not intended for the support of well-established or senior investigators. Applicants should have concomitant support for their research from another source or agency.

—Scholar In Clinical Research, $110,000: (stipend $105,000 + $5,000 institutional overhead) per year for five years. Annual renewals are based on a non-competitive progress report review. Applicants are highly qualified investigators who have demonstrated their ability to design and conduct original clinical research on leukemia, lymphoma and myeloma. They are expected to hold an independent faculty-level or

equivalent position. The award is not intended for the support of well-established or senior investigators. Applicants should have concomitant support for their research from another source or agency. Preference given to applicants whose research involves the clinical trial of new or innovative applications.

—Special Fellow, $60,000: (stipend $56,000 + $4,000 institutional overhead) per year for three years. Annual renewals are based on a non-competitive progress report review. Applicants are qualified investigators who have completed a minimum of two years of postdoctoral research training at the time of review (January 31) and are continuing their research under the direction of a research sponsor.

—Special Fellow In Clinical Research, $60,000: (stipend $56,000 + $4,000 institutional overhead) per year for three years. Annual renewals are based on a non-competitive progress report review. Applicants are qualified investigators who have completed a minimum of two years of clinical hematology, oncology, hematology/oncology or hematopathology training or postdoctoral research training in a clinical discipline, and require research training to conduct future independent clinical research.

—Fellow, $50,000: (stipend $47,000 + $3,000 institutional overhead) per year for three years. Annual renewals are based on a non-competitive progress report review. Applicants are promising investigators with less than two years of postdoctoral research training at the time of review (January 31).

Deadlines: Preliminary Application (submit via Web site); Sept. 15. Full Application: Oct. 1. Guidelines are available from www.LLS.org or Director of Research Administration, The Leukemia & Lymphoma Society, 1311 Mamaroneck Ave., White Plains, NY 10605, (914) 821-8859, email: researchprograms@LLS.org.

LLS Specialized Center Grant Program Seeks Applicants

The Leukemia & Lymphoma Society has initiated a major program to bring together research teams that are focused on the cure or prevention of leukemia, Hodgkin's and non-Hodgkin's lymphoma, and myeloma in order to foster interdisciplinary and synergistic research.

Program Scope: A Specialized Center of Research Grant provides funding for five years. The proposed Center should be interdisciplinary, cohesive and sharply focused. The Center must be composed of at least three relevant scientific projects capable of interacting. The research may be fundamental or applied or an integrated combination of the two approaches. Basic research tied to a related translational research project is encouraged but not mandatory. The most promising ideas and the likelihood that the research will lead to a significant reduction in the morbidity and mortality of these diseases will be viewed favorably regardless of the particular approach. The Center grant will also support scientific core laboratories required by the component research programs.

Eligibility Requirements: An application may be submitted by an individual holding a M.D., Ph.D., or equivalent degree, working in a domestic or foreign non-profit organization, such as a university, college, hospital, institute or laboratory. Applications may be multi-institutional. Applicants need not be U.S. citizens, and there are no restrictions on applicant age, race, gender, or creed.

Funds Available: The Center's annual total cost, direct and indirect, cannot exceed $1.25 million. The aggregate costs over five years cannot exceed $6.25 million. The direct costs, if justified by the aggregate budget may be up to $1.042 million per year. The indirect or institutional costs cannot exceed 20% of the direct costs per year.

Deadlines: Preliminary Application (submitted via website and hard copy): Nov. 1. Full application from selected investigators will be due on March 15. Guidelines are available from: www.LLS.org.

NCI RFAs Available: CCOPs

RFA-CA-07-025: Community Clinical Oncology Program. U10. Letters of Intent Receipt Date: July 28. Application Receipt Date: Aug. 28. Full text: http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-025.html. Inquiries: Lori Minasian, 301-496-8541; minasilo@mail.nih.gov.

RFA-CA-07-026: Minority-Based Community Clinical Oncology Program. U10. Letters of Intent Receipt Date: July 28. Application Receipt Date: Aug. 28. Full text: http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-026.html. Inquiries: Worta McCaskill-Stevens, 301-496-8541; mccaskiw@mail.nih.gov.

In Brief:

Hoppe, Ling To Receive ASTRO Gold Medals

AMERICAN SOCIETY for Therapeutic Radiology and Oncology announced **Richard Hoppe** and **C. Clifton Ling** as its 2006 Gold Medal winners for their accomplishments and contributions in the field of radiation oncology, said **Prabhakar Tripuraneni**, chairman of ASTRO**.** Hoppe is chairman of the Department of Radiation Oncology and the Henry S. Kaplan-Harry Lebeson Professor of Cancer Biology at Stanford University. Under his leadership, Stanford implemented intensity modulated radiation therapy techniques into clinical protocols and clinical use. Hoppe is credited with the development of the Stanford programs for Hodgkin's disease and other lymphomas as well as trials of total lymphoid irradiation to establish transplantation tolerance. He has worked within ASTRO, where he served as both president and chairman of the board of directors. NIH funds Hoppe, an NCI Board of Scientific Counselors member, through his department. Ling, chairman of the Medical Physics Department at Memorial Sloan-Kettering Cancer Center, is known for his work in advanced treatment planning and delivery systems for conformal radiotherapy and intensity modulated radiation therapy for prostate and other cancers. Ling also is recognized for the development of image-based radiotherapy. An active researcher for 30 years, with grant awards from NCI, ACS, DOE, DOD and others, Ling sits on scientific and medical associations including NCI and the Radiation Therapy Oncology Group. The awards will be presented Nov. 7, in Philadelphia during the annual meeting of the society. ASTRO also named 75 individuals who will become Fellows of society. They will receive their designation at a ceremony during the annual meeting. Members of ASTRO are eligible to become fellows if they have been part of the society for at least 20 years, served in a leadership role for the organization and have made a significant contribution to the field of radiation oncology. . . . **M. D. ANDERSON** Cancer Center opened its Proton Therapy Center. It is the first proton therapy facility associated with an NCI-designated comprehensive cancer center, and the fourth in the country to offer advanced beam therapy. The $125 million, 94,000-square-foot center can accommodate 3,500 patients a year, making it the largest in the world. The two-story facility features three gantry treatment rooms, one fixed-beam treatment room, an experimental treatment area, a full range of patient and research support areas, a synchrotron and beam transport system. "We will be able to increase doses of radiation, preserve healthy tissue and treat more patients much more successfully, especially in areas such as cancers of the prostate, eye, lung, brain, and neck, and cancers in children," said **James Cox**, head of the Division of Radiation Oncology at M. D. Anderson. "Conventional radiation therapy, however, remains a proven and vital cancer treatment, and most often will still be the preferred radiation treatment. M. D. Anderson also will explore new ways to best utilize and advance the field, including the interaction of chemotherapy and other molecular agents with proton therapy." The center was funded through a private-public partnership. . . . **ROBERT HOOVER**, director of the Epidemiology and Biostatistics Program in the NCI Division of Cancer Epidemiology and Genetics, received the 2005 Lilienfeld Award from the American College of Epidemiology during its 2006 annual meeting earlier this month. ACE recognized the 2005 awardees at this year's meeting, because last year's was canceled due to Hurricane Katrina. The Lilienfeld Award is presented to an individual for excellence in epidemiology and named in honor of Abraham Lilienfeld. . . . **PATRICIA HARTGE**, a senior scientist at DCEG, also was recognized at ACE's 2006 annual meeting. She received the Distinguished Epidemiologist Award, which is given jointly by the Society for Epidemiologic Research, the American Public Health Association, and ACE. The award is presented every five years to honor major accomplishments and contributions to the field of epidemiology. . . . **CAROLYN STRETE**, chief of the NCI Cancer Training Branch, plans to retire July 1, having worked at NCI from 1982 to 1992 and again from 2001 to the present. Strete received her Ph.D. in clinical psychology from State University of New York at Stony Brook and in 1984 was commissioned to the U.S. Public Health Service Commissioned Corps, where she holds the rank of captain. Prior to her second stint at NCI, Strete held several positions at the National Institute of Mental Health, in peer review administration and scientific program management. During her earlier years at NCI, Strete served as chief of the Prevention, Epidemiology and Cancer Control Peer Review Section and was scientific review administrator of the Cancer Control Grants Review Committee. More recently, in her role as chief of CTB, Strete served as chairman of an NCI Training Inventory Committee to assess the active training programs in the intramural and extramural programs, resulting in a report that can be found at http://www.cancer.gov/aboutnci/training-career-development.

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Business & Regulatory Report

Product Approvals & Applications:

CDC Advisors Recommend Routine HPV Vaccination For Girls 11-12 Years

The Centers for Disease Control and Prevention Advisory Committee on Immunization Practices unanimously recommended that girls and women 11 to 26 years old be vaccinated with Gardasil [Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine] to prevent cervical cancer, precancerous and low-grade lesions, and genital warts caused by human papillomavirus (HPV) types 6, 11, 16 and 18.

The vaccine is sponsored by **Merck & Co. Inc.**

The committee recommended that Gardasil be administered to 11- and 12-year-old females and to females aged 13 to 26 who have not previously been vaccinated, and that nine- and 10-year-old females can be vaccinated with Gardacil at the discretion of their physicians.

The ACIP stated that Pap and HPV screening prior to vaccination

(Continued to page 2)

Clinical Trials:

Genentech Says Phase III Avastin Trial In Pancreatic Cancer Didn't Meet Endpoint

Genentech Inc. (NYSE: DNA) of South San Francisco announced that a phase III trial of Avastin (bevacizumab) in combination with gemcitabine chemotherapy as first-line treatment for advanced pancreatic cancer did not meet its primary endpoint of overall survival.

The trial was stopped at the recommendation of an independent data monitoring board based on an interim analysis indicating that it is very unlikely that significant differences in overall survival will be shown between treatment arms as the data mature.

The study was not stopped due to safety events and no new safety concerns related to Avastin were observed in this trial, the company said. Data from the study will be presented at an upcoming medical meeting.

"We are disappointed in these results and will be evaluating the data to understand potential reasons why Avastin did not add a clinical benefit in this trial," said Hal Barron, M.D., senior vice president, Development and chief medical officer for Genentech. "Chemotherapy has had a limited impact in advancing outcomes for patients with pancreatic cancer, and treatments that may improve survival are desperately needed. We will continue to explore novel biologic and targeted therapy approaches that may lead to improved clinical outcomes for patients with pancreatic cancer."

The randomized, controlled study of 602 patients was sponsored by

(Continued to page 5)

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CDC Advisors Add Gardasil To Vaccines For Children

(Continued from page 1)

are not necessary. The ACIP also recommended that females can receive Gardasil regardless of whether they have or previously had an abnormal Pap test, a positive HPV test or genital warts.

During the meeting June 29, the CDC advisory committee also voted to add Gardasil to the CDC Vaccines for Children program which provides vaccines to children who are Medicaid-eligible, uninsured, underinsured and Native American.

On June 8, FDA approved Gardasil for use in girls and women ages nine to 26 years.

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FDA granted accelerated approval of Sprycel, an oral inhibitor of multiple tyrosine kinases, for adults in all phases of chronic myeloid leukemia with resistance or intolerance to prior therapy, including Gleevec (imatinib mesylate).

The drug is sponsored by **Bristol-Myers Squibb Co.** (NYSE: BMY). The effectiveness of Sprycel is based on hematologic and cytogenetic response rates. There are no controlled trials demonstrating a clinical benefit, such as improvement in disease-related symptoms or increased survival, the company said.

The agency also granted full approval of Sprycel for adults with Philadelphia chromosome-positive acute lymphoblastic leukemia with resistance or intolerance to prior therapy.

Sprycel represents the first approved oral tyrosine kinase inhibitor predicted to bind to multiple conformations of the ABL kinase based on modeling studies, the company said.

At nanomolar concentrations, dasatinib inhibits BCR-ABL, SRC family (SRC, LCK, YES, FYN), c-KIT, EPHA2, and PDGFR-B. By targeting these kinases, dasatinib inhibits the overproduction of leukemia cells in the bone marrow of patients with CML and Ph+ALL and allows normal red cell, white cell, and blood platelet production to resume.

"Sprycel provides a new treatment option for patients with CML or Ph+ALL who are resistant or intolerant to prior therapy," Brian Druker, investigator, Howard Hughes Medical Institute and JELD-WEN chair of Leukemia Research, Oregon Health & Science University Cancer Institute, said in a statement.

Mechanisms of imatinib resistance include mutations in the protein sequence of the BCR-ABL tyrosine kinase, multi-drug resistance gene overexpression, and the activation of alternate signaling pathways involving the SRC family kinases.

The FDA reviewed the efficacy (n=445) and safety (n=911) of SPRYCEL based on the analysis of four phase II multi-center studies in patients with resistance or intolerance to imatinib in all phases of CML (n=409) or Ph+ ALL (n=36). The studies were conducted on five continents (33 countries).

* * *

FDA approved a supplemental New Drug Application for Revlimid (lenalidomide) in combination with dexamethasone as a treatment for patients with multiple myeloma who have received at least one prior therapy.

Sponsored by **Celgene Corp.** (Nasdaq: CELG) of Summit, N.J., Revlimid is also approved for transfusion-dependent anemia due to Low-or- Intermediate-1-risk myelodysplastic syndromes associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities.

In the Revlimid/dexamethasone treatment group, 151 patients (45%) underwent at least one dose interruption with or without a dose reduction of REVLIMID (lenalidomide) compared to 21% in the placebo/dexamethasone treatment group, the company said.

Most adverse events and Grade 3 or 4 adverse events were more frequent in patients who received the combination of Revlimid, compared to placebo/dexamethasone, the company said.

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Bayer Pharmaceuticals Corp. (NYSE: BAY) of West Haven, Conn., and **Onyx Pharmaceuticals Inc**. (Nasdaq: ONXX) of Emeryville, Calif., said Nexavar (sorafenib) tablets have been granted FDA Fast-Track designation for metastatic hepatocellular carcinoma.

FDA approved Nexavar last year for advanced renal cell carcinoma.

A phase III trial of the agent administered as a single agent for advanced liver cancer is underway, the company said. The study, designed to measure differences in overall survival, time-to-symptom progression and time-to-tumor progression of the treatment versus placebo, has finished accrual, the company said. A randomized phase II trial for liver cancer to evaluate the efficacy of Nexavar in combination with doxorubicin is currently accruing.

Nexavar is an oral multi-kinase inhibitor that targets both the tumor cell and tumor vasculature, the company said.

* * *

Bioenvision Ltd (Nasdaq: BIVN) of Edinburgh, Scotland, said the European Commission has granted marketing authorization for Evoltra (clofarabine) for acute lymphoblastic leukaemia in pediatric patients who have relapsed or are refractory to at least two prior regimens.

The licensed indication includes those under 21years at the time of initial diagnosis, the company said.

In the Evoltra clinical study, a median survival of 66.6 weeks was achieved in the 30 percent who responded to treatment with the drug, the company said. In addition to extending life, the agent allows time and opportunity for bone marrow transplantation.

Evoltra has been granted orphan drug designation, providing marketing exclusivity for 10 years in Europe, the company said.

* * *

Cell Therapeutics Inc. (Nasdaq: IC; MTAX) of Seattle said FDA agreed on a new drug application route for Xyotax (paclitaxel poliglumex) for women with lung cancer.

The review of the submission based on interim results of the PIONEER trial with the results of the STELLAR 3 and 4 trials to support the filing, the company said. If the PIONEER trial meets its pre-specified interim endpoint, I said it would submit an NDA in the first half of 2007 and would request a priority review based on the Fast-Track designation, instead of the standard.

The PIONEER trial is targeting 170 sites in the U.S., Eastern Europe, and Latin America with an enrollment of 600 PS2 chemotherapy-naive women with advanced stage NSCLC, the company said. Each study arm of 300 will be randomized to receive either Xyotax (at a dose of 175mg/m(2) paclitaxel equivalents) or paclitaxel (at a dose of 175mg/m(2)) once every three weeks. The primary endpoint is superior overall survival with several secondary endpoints including disease control, response rate in patients with measurable disease, time to disease progression, and disease-related symptoms, the company said.

Xyotax (paclitaxel poliglumex) is a biologically-enhanced chemotherapeutic that links paclitaxel, the active ingredient in Taxol, to a biodegradable polyglutamate polymer, resulting in a new chemical entity. When bound to the polymer, the chemotherapy is rendered inactive, sparing normal tissue exposure to high levels of unbound, active chemotherapy and its associated toxicities.

* * *

Genentech Inc. (NYSE: DNA) of South San Francisco said FDA approved Avastin (bevacizumab) in combination with intravenous 5-fluorouracil-based chemotherapy for second-line metastatic colorectal cancer.

The drug also is approved as a first-line treatment of metastatic colorectal cancer in combination with intravenous 5-FU-based chemotherapy, the company said.

The approval is based on a randomized, controlled, multicenter phase III trial (E3200) of 829 patients with advanced or metastatic CRC who had received previous treatment with irinotecan and 5-FU as initial therapy for metastatic disease or as adjuvent therapy.

The data that treatment with Avastin plus the 5-FU-based chemotherapy regimen known as FOLFOX4 (oxaliplatin/5-FU/leucovorin) had a 25 percent reduction in the risk of death (based on a hazard ratio of 0.75), the primary endpoint, which is equivalent to a 33 percent improvement in overall survival, compared to treatment with FOLFOX4 alone. Median survival for treatment with Avastin plus FOLFOX4 was 13.0 months, compared to 10.8 months for FOLFOX4 alone, the company said.

In the E3200 study, conducted by the Eastern Cooperative Oncology Group, the most common Grade 3-5 (non-hematologic) and Grade 4/5 (hematologic) adverse events which occurred at a higher incidence (>/= 2 percent) in the Avastin plus FOLFOX4 arm, compared to the FOLFOX4 alone arm, were: diarrhea, nausea,

vomiting, dehydration, ileus, sensory neuropathy, other neurologic events, fatigue, abdominal pain, headache, hypertension and hemorrhage, the company said.

* * *

Genitope Corp. (Nasdaq: GTOP) of Redwood City, Calif., said MyVax personalized immunotherapy received FDA Fast Track designation for follicular non-Hodgkin's Lymphoma.

A phase III trial evaluating the immunotherapy was begun for stage III/IV fNHL, the company said. The trial was based upon results from three separate phase II trials, evaluating the long-term efficacy of the treatment. Results from one phase II trial showed nine of the 21 patients remained progression-free as of their last clinical follow-up at 56 to 78 months post-chemotherapy, the company said.

* * *

GlaxoSmithKline (NYSE: GSK) of Philadelphia said FDA has approved Hycamtin (topotecan HCl) in combination with cisplatin, for stage IV-B, recurrent, or persistent carcinoma of the cervix, which is not amenable to curative treatment with surgery and/or radiation therapy.

Following a six-month priority review by FDA, the expanded indication is based on phase III results that demonstrated a survival advantage by using Hycamtin in combination with cisplatin compared to cisplatin alone, the company said.

The randomized, multicenter trial, designed and conducted by the Gynecologic Oncology Group, found that Hycamtin, in combination with cisplatin, was effective in treating cervical cancers which were not amenable to curative treatment with surgery and/or radiation therapy, the company said.

The trial enrolled women with measurable, histologically-proven stage IVB, recurrent or persistent carcinoma of the cervix, who had recovered from the effects of prior surgery, radiation or chemoradiation, the company said. Patients were originally randomized into three arms: single-agent cisplatin (n=146, 50 mg/m2, every 21 days), Hycamtin plus cisplatin (n=147, Hycamtin 0.75 mg/m2, day 1-3 plus cisplatin 50 mg/m2 day 1 every 21 days), or MVAC (methotrexate, vinblastine, doxorubicin, and cisplatin every 28 days). However, the MVAC arm was closed after 64 patients were enrolled, due to excessive toxicity, the company said.

The study showed a statistically significant improvement in overall survival for Hycamtin plus cisplatin arm (log-rank P=0.033), the company said. Median survival for Hycamtin plus cisplatin was 9.4 months when compared to 6.5 months for cisplatin alone. The GOG study was led by Harry Long III, professor of oncology at Mayo Clinic College of Medicine.

* * *

MGI PHARMA Inc. (Nasdaq: MOGN) of Minneapolis said the NDA for Saforis (glutamine in UpTec) Powder for Oral Suspension was accepted for priority review by FDA.

The phase III trial of Saforis was completed in 326 patients with breast cancer who were receiving anthracycline-based chemotherapy regimens, the company said. The primary endpoint, defined as a reduction in incidence and severity of oral mucositis, was met.

Data indicated that treatment with the regimen resulted in a 22 percent relative risk reduction of clinically significant (World Health Organization or WHO Grade 2 or higher) oral mucositis, compared with placebo (p=0.026). In addition, the incidence of severe oral mucositis (WHO Grade 3 or higher) was significantly reduced when compared to placebo (1.2 percent vs. 6.7 percent; p=0.005).

* * *

Millennium Pharmaceuticals Inc. (Nasdaq: MLNM) of Cambridge, Mass., said it has files a supplemental new drug application FDA for Velcade for relapsed or refractory mantle cell lymphoma.

The filing is based on final data from the phase II PINNACLE trial, one of the largest multi-center studies in relapsed MCL to date, which showed a 33 percent overall response rate and an eight percent complete response rate, the company said. The median duration of response was 9.2 months and 13.5 months achieving a complete response. The results are similar to four other phase II trials that recorded overall response rates of 30 to 40 percent with single-agent, the company said.

Velcade has been approved multiple myeloma with at least one prior therapy, the company said. Earlier this year, Millennium and co-development partner, Johnson & Johnson Pharmaceutical Research & Development, L.L.C., initiated a phase III trial with Velcade in combination with rituximab for relapsed or refractory follicular lymphoma.

* * *

Vical Inc. (Nasdaq: VICL) of San Diego and **AnGes MG Inc.** (TSE Mothers: 4563) of Tokyo said they have entered into a collaborative agreement for the Vical Allovectin-7 cancer immunotherapeutic.

Under the agreement, AnGes will provide $100 million in ongoing clinical trial funding and future sales-based milestones for the commercialization of the

immunotherapeutic. Vical retains exclusive marketing rights in the U.S. and elsewhere outside of specified Asian countries, for which AnGes received exclusive rights, the companies said.

Through a series of cash payments and equity investments of $22.6 million, including an initial equity investment of $6.9 million, AnGes said it would fund the phase III trial of the treatment that will be conducted by Vical in the U.S. under a Special Protocol Assessment completed with FDA.

AnGes said it would pay Vical royalties on product sales in the specified Asian countries, plus the above-mentioned milestones as defined sales levels are achieved. Vical also said it would pay tiered royalties based on defined sales levels in the U.S., and fixed royalties on rest-of-world sales. Each company is responsible for obtaining regulatory approvals in any countries where it plans to market Allovectin-7.

The phase III, randomized, multi-center, open-label 375-patient trial for recurrent metastatic melanoma allows for prior treatment with surgery, adjuvant therapy, and/or biotherapy, but not chemotherapy, the companies said. Randomization will be on a 2:1 basis with 250 treated with Allovectin-7 and 125 either of two chemotherapy agents, dacarbazine or temozolomide. The primary endpoint is a comparison of objective response rates at 24 weeks or more after randomization, the companies said.

Allovectin-7 is a plasmid/lipid complex containing the DNA sequences encoding HLA-B7 and beta-2 microglobulin, which together form a Class I Major Histocompatibility Complex, or MHC-I antigen.

Clinical Trials:

Avastin Trial Doesn't Meet Pancreatic Cancer Endpoint

(Continued from page 1)

NCI and led by Cancer and Leukemia Group B. The trial (CALGB 80303) was initiated based on results from a single-arm phase II study combining Avastin with gemcitabine in pancreatic cancer. The phase II study results were first presented in 2003 at the annual meeting of the American Society of Clinical Oncology.

The randomized, placebo-controlled, multi-center trial, was conducted under a Cooperative Research and Development Agreement between the NCI and Genentech. In the study, 602 patients were enrolled at approximately 200 sites and were randomized to receive treatment with gemcitabine plus Avastin or gemcitabine plus placebo as a first-line therapy.

Patients who had received prior chemotherapy for metastatic disease, adjuvant chemotherapy within the previous four weeks or any prior treatment with gemcitabine or Avastin in the adjuvant or metastatic setting were excluded. Patients with a prior history of bleeding events and those who had a surgical procedure, open biopsy, or significant traumatic injury 28 days prior were also excluded from the study.

The statistical plan included pre-specified futility analyses that were conducted and reviewed by an independent data monitoring board.

* * *

ChemGenex Pharmaceuticals (ASX: CXS, Nasdaq: CXSP) of Menlo Park, Calif., and Melbourne, Australia, said it has begun a multinational phase II/III study of Ceflatonin (homoharringtonine, HHT) for chronic, accelerated and blast-phase chronic myeloid leukemia with the T315I bcr-abl point mutation, associated with resistance to Gleevec and two known tyrosine kinase inhibitors under development.

The 81-patient study, which will be conducted in both the U.S. and Europe, has a pimary endpoint of hematologic response rate, and the secondary endpoint of cytogenetic response rate, the company said.

Preclinical studies, conducted by William Plunkett, Department of Experimental Therapeutics at M.D. Anderson Cancer Center, demonstrated that Ceflatonin is active as a single-agent and in-combination with other agents, including imatinib (Gleevec), in CML cell lines with the T315I bcr-abl point mutation, the company said.

In the remission induction phase, administration will be 1.25 mg/m2 HHT by subcutaneous injection two times a day for 14 consecutive days, with cycles repeated every 28 days, the company said. In the remission maintenance phase, patients will receive 1.25 mg/m2 HHT by subcutaneous injection two times a day for 7 consecutive days, with cycles repeated every 28 days. Stratification will depend upon whether they have chronic phase, accelerated phase, or blast phaseCML.

The study will be conducted in two stages, using a Simon two-stage study design for each patient subpopulation. During the first stage, 13 patients from each patient subpopulation (CP, AP, BP CML) will be enrolled. If one or more responses are seen during the first stage of a subpopulation, another 14 patients from that subpopulation will be enrolled in the second stage.

* * *

CuraGen Corp. (Nasdaq: CRGN) of Branford, Conn., and **TopoTarget A/S** (Copenhagen Stock

Exchange: TOPO) of Denmark said they have begun dosing in a phase I trial evaluating the safety and tolerability of PXD101, a small molecule histone deacetylase inhibitor, in combination with cis-retinoic acid for advanced solid tumors.

The trial is being sponsored by NCI under a Clinical Trials Agreement with CuraGen, the companies said.

The phase I trial is an open-label, dose-escalation study led by Thehang Luu at the Department of Medical Oncology at City of Hope. The study would establish the maximum tolerated dose and safety profile of PXD101 in combination with cis-retinoic acid for advanced solid tumors, which are refractory to standard therapies or for which no standard treatment exists.

Up to 24 patients will be enrolled and each will receive PXD101 and cis-retinoic acid in continuous three week cycles until disease progression. Following determination of the MTD, the study will enroll 10 additional patients with tumors available for biopsy in order to carry out planned molecular studies, including evaluation of apoptosis in tumor biopsies, changes in gene expression, and demonstration of upregulation of retinoic acid receptors and retinoid X receptors following treatment with PXD101 and cis-retinoic acid, the companies said.

* * *

Eli Lilly & Co. of Indianapolis said it has begun a phase III trial of Enzastaurin, a multi-targeted, oral, cancer agent.

The treatment will be evaluated as a maintenance therapy for diffuse large B-cell lymphoma non-Hodgkin's lymphoma where remission was achieved following first-line therapy, the company said.

The enzastaurin non-Hodgkin's lymphoma phase III trial (PRELUDE - Preventing Relapse in Lymphoma Using Daily Enzastaurin) is a randomized, placebo controlled study comparing the efficacy, safety and tolerability of the agent, taken orally for up to three years, versus placebo, the company said. The study would enroll 459 patients across 100 sites. The primary endpoint will be overall disease-free survival. Additionally, Lilly said it would assess any biomarkers relevant to enzastaurin as a basis for correlating response to clinical trial outcomes.

Enzastaurin is an oral serine-threonine kinase inhibitor that suppresess tumor growth by reducing the ability of the cell to divide, by increasing apoptosis, and inhibiting angiogenesis, the company said.

* * *

GlobeImmune Inc. of Louisville, Colo., said it has begun a randomized, placebo-controlled, multi-center phase II trial of GI-4000, its therapeutic vaccine for early-stage pancreatic cancer.

The primary goal of the study is to compare the recurrence-free survival at 15 months for treatment with either GI-4000 or placebo, in combination with adjuvant gemcitabine after surgery, the company said.

GI-4000 is a Tarmogen, a GlobeImmune proprietary yeast-based vaccine system, the company said. Tarmogens are whole, heat-killed recombinant Saccharomyces cerevisiae yeast genetically modified to express one or more protein antigens that stimulate the innate immune system, as well as activate disease-specific T cells that identify and destroy cancer or virally-infected cells.

* * *

LAB International Inc. (TSX: LAB, Frankfurt: LD9.F, XETRA: LD9.DE) of Laval said it has begun enrollment in its Fentanyl TAIFUN phase IIb trial.

The agent is a fast-acting Fentanyl formulation delivered using its TAIFUN dry powder inhaler platform, the company said.

The multi-centered, multinational, dose titration, single arm and open-label trial is evaluating the time to significant pain relief with Fentanyl TAIFUN with successful titration of breakthrough cancer pain, the company said. The trial is enrolling 32 cancer patients on maintenance opioid therapy for persistent pain.

The first two patients treated with the agent have achieved successful titration, one with 400 (micro) g dose and the other with 100 (micro) g fentanyl per dose, the company said. For both patients the selected dose was effective in all 5 pain episodes treated under the protocol, with the first observed effects within 5 minutes from administration.

The only product available for the indication is an oral lozenge that requires 15-20 minutes application time, the company said. In contrast, Fentanyl TAIFUN has provided instantaneous availability of fentanyl in the blood, within one minute from inhalation and is providing more rapid pain relief than any existing non-injectable pain medication, the company said.

* * *

Medarex Inc. (Nasdaq: MEDX) of Princeton, N.J., said it has received a Special Protocol Assessment letter from FDA to begin a clinical trial of ipilimumab (MDX-010) in combination with chemotherapy for first-line metastatic melanoma.

The randomized, double-blind, two-arm registrational study of 500 patients with previously untreated stage III or stage IV metastatic melanoma,

would entail administering ipilimumab (10 mg/kg) in combination with dacarbazine, or dacarbazine alone once every three weeks for up to four doses, the company said. Subsequently, where disease progression has not occurred at week 24 there will be a maintenance phase with a single dose of ipilimumab administered once every 12 weeks until disease progression.

The study is designed to assess progression-free survival as the primary endpoint. Secondary endpoints include overall survival, progression-free survival rate at week 12, best overall objective response rate and duration of responses, and disease control rate (complete and partial responses plus stable disease), the company said.

Ipilimumab is a fully human antibody against human LA-4, a molecule on T cells that suppresses the immune response, the company said.

* * *

Novartis of East Hanover, N.J., said it has begun a global expand ed access program for nilotinib (AMN107), a compound in late-stage registration trials for difficult to treat leukemia.

The program is available to all phases of Philadelphia chromosome-positive chronic myeloid leukemia, which are either resistant to or intolerant of treatment with Gleevec (imatinib mesylate) tablets, the company said.

The company said it would submit nilotinib for U.S. and EU regulatory approval in late 2006.

Nilotinib is a targeted, oral therapy that selectively inhibits Bcr-Abl, the definitive cause of Philadelphia chromosome-positive chronic myeloid leukemia and its mutations. FDA has granted both Fast Track designation and orphan drug status to the drug, the company said. The treatment also received orphan drug status from the European Medicines Evaluation Agency.

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Schering AG (FSE: SCH, NYSE: SHR) of Berlin said it has begun two phase II studies in the U.S. and Canada evaluating epothilone, ZK-EPO, for metastatic breast cancer and recurrent ovarian cancer.

The trials would establish proof of concept while assessing objective response rates of the agent in each cancer, the company said.

The single arm, open-label phase II metastatic breast cancer 20-patient trial would administer the drug every three weeks to patients having had up to three previous lines of chemotherapy. Patients will have had previous taxane and anthracycline-based chemotherapy, whether in combination or as separate regimens.

The second phase I/II trial, which will administer ZK-EPO in combination with carboplatin for recurrent ovarian cancer after first-line treatment with platinum-based chemotherapy, will be conducted in 30 centers across the U.S. and Canada.

Additional phase II trials are underway in Europe, evaluating the agent in non-small-cell lung, small-cell lung, breast and ovarian cancers, the company said.

ZK-EPO is an epothilone that overcomes the limitations associated with other microtubule stabilizing agents by combining high potency with a wide therapeutic window, the company said.

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VION Pharmaceuticals Inc. (Nasdaq: VION) of New Haven said it has begun a phase II trial of Cloretazine (VNP40101M) as a single agent in untreated elderly patients with de novo poor-risk acute myelogenous leukemia.

The study would be conducted in 20 North American and European sites with the 85-atient taking one year, the company said.

Deals & Collaborations:

Celera, Medarex Collaborate On Human Antibodies

Celera Genomics (NYSE: CRA) of Rockville, Md., and **Medarex Inc.** (Nasdaq: MEDX) of Princeton said they have formed a strategic collaboration to discover and develop fully human antibodies for multiple cancer indications.

Under the collaboration, the development of therapeutic antibodies against proteins will be identified by the Celera proteomic research discovery efforts as being over-expressed on the surface of tumor cells and subsequently validated through additional research at Celera. The collaboration combines the Celera ability to discover and validate oncology targets with the Medarex expertise in the development of fully human antibody therapeutics.

The companies said they would jointly select targets. Medarex would generate fully human monoclonal antibodies against thee targets using its proprietary UltiMAb Human Antibody Development System, and the two companies would carry out initial validation studies.

The companies said each would have full development and commercialization rights to products arising from its selected research programs, and the other party would be entitled to receive milestone payments. The selecting company may develop antibodies generated under the collaboration internally or through

external partners.

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Chemokine Therapeutics Corp. (OTCBB: CHKT; TSX: CTI) of Vancouver said it has entered into an agreement with **Fred Hutchinson Cancer Research Center** of Seattle to study CTCE-0214, the Chemokine hematological support compound.

CTCE-0214 would be examined in preclinical studies to determine if it could accelerate the repopulation of stem cells to the bone marrow from human umbilical cord blood, the company said. Researchers also will examine the level of engraftment of the cells in the pre-clinical transplant model.

CTCE-0214 is a stable peptide analog of stromal cell-derived factor-1 and an agonist of the SDF-1 receptor called CXCR4, a signaling protein in the proliferation, homing, engraftment and expansion of hematopoietic stem cells and white blood cells, the company said.

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454 Life Sciences Corp. of Branford, Conn., said it is collaborating with **Dana Farber Cancer Center** and **Broad Institute** to detect cancer gene mutations present at extremely low levels.

The sequencing technology was used to analyze mutations in five exons of the Epidermal Growth Factor Receptor gene in tumor samples from 22 patients with lung cancer, the company said. The research proposes that 454 Sequencing would validate the ability of EGFR mutations to predict responsiveness to treatment with an EGFR inhibitor.

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Florida Atlantic University of Boca Raton said it has entered into an exclusive licensing agreement with **CHS Resources LLC** for a cancer therapy, which has emerged from its Center of Excellence in Biomedical and Marine Biotechnology.

CHS Resources would develop and commercialize patent pending technology for skin cancer, the company said. The technology was discovered by Herbert Weissbach, director of the Center for Molecular Biology and Biotechnology and professor at Charles E. Schmidt College of Science, FAU, along with colleagues at the university. Weissbach and his team have formulated a topical skin preparation for CHS Resources, which is being tested for actinic keratoses in a proof-of-concept clinical trial underway at the University of Alabama.

* * *

GlaxoSmithKline (NYSE: GSK) has licensed a portfolio of tumor-specific antigens from and **Ludwig Institute for Cancer Research** of New York.

The licensing agreement follows a long-standing collaboration between both parties on the GSK investigational MAGE-A3 Antigen Specific Cancer Immunotherapeutic for in Non-Small Cell Lung Cancer. The immunotherapy is based on MAGE-A3, a tumor-specific antigen in-licensed by GSK from LICR, the parties said.

Under the agreement, GSK said it has licensed from LICR cancer antigens expressed in cancers, including NSCLC, melanoma, breast cancer, head and neck cancer, bladder cancer and liver cancer.

* * *

Transgene S.A. (Eurolist Paris: FR0005175080) of Strasbourg, France, said it has executed a Cooperative Research and Development Agreement Letter of Intent with NCI to develop melanoma treatments with Steven Rosenberg, chief of the NCI Surgery Branch.

Rosenberg has identified and characterized melanoma tumor-associated antigens, including gp100 and MART-1, and has developed a lymphodepleting non-myeloablative regimen for adoptive cell therapy, the company said.

The collaboration would produce viral-based vectors encoding gp100 or MART-1 for immunization against malignant melanoma, the company said. The immunizations would be given in conjunction with ACT involving tumor antigen-specific T lymphocytes.

The collaboration may also involve new uses of ACT, the company said. The technique, developed by the Rosenberg laboratory at NCI, would consist of an in-vitro conditioning and amplification of a tumor-antigen specific cytotoxic-directed lymphocytes belonging to the patient, then restoring the lymphocytes following a lymphodepleting non-myeloablative chemotherapy. The regimen results in the in-vivo expansion and enhanced activity of the cytotoxic lymphocytes.

To date, of the 35 melanoma patients treated by ACT in a phase II trial, 18 (51 percent) achieved an objective response, with three exhibiting a complete response, the company said.

Transgene and NCI will evaluate candidate cancer vaccines, to assess the boosting effect of the vaccination on the lymphocytes' activity, the company said.

The vaccines would be designed by Transgene using viral vectors to express the Rosenberg melanoma antigens. Such a vaccination has already demonstrated increased in-vivo clonal expansion and maintenance of adoptively transferred tumor-antigen specific cytotoxic lymphocytes in preclinical models, the company said. NCI will conduct pre-clinical evaluation of the vaccines and plans to sponsor a phase I/II trial in 2007.